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INTRODUCTION

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Uncommon Wisdom in Medicine

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“For I have learned to look on nature, not as in the hour of thoughtless youth, but hearing oftentimes the still, sad music of humanity.”
William Wordsworth, 1770-1850

Modern medical science is said to be highly scientific and is believed to be the best panacea for those hapless people who are ill at any given point in time. With all this claptrap, the reality baffles me daily. This morning I had to contend with the death of a dear friend, who saw me, a couple of months ago with what appeared at that time to be an early carcinoma of the pancreas. Although I am not an oncologist, I felt that he had a very bad prognosis with or without conventional treatment. He did go for all the three-pronged attack on his pancreas - surgery, radiation and chemotherapy. His dead body was delivered yesterday after a huge bill from a five star hospital in Mumbai, India! I shall reproduce a letter in toto hereunder from a patient of mine whom I advised against angioplasty ten years ago for a simple stable angina at the age of 76 years! He is doing all that he wants to do even now.

“I met a person who lives in our apartment, who has gone for angioplasty about five or six times! She is on twenty-one tablets! Thanks to your guidance I am in good health!”
Linus Aloysius.

I get enquiries from senior doctors about their problems with statins almost daily. To cap it, I saw the recent documentary by Michael Moore “SICKO” that gives the graphic details of the deplorable state of the medical care system in the US. The medical scenario in the US ranks 37th in the WHO list with Cuba at 39th rank. The US was last but one in the 14 industrialized countries’ study with Japan as the best and Germany the worst! I think it is time we took stock of our foundation lest we should be caught on the wrong foot by society, if we drift along these lines in the years ahead. I have drawn liberally for this editorial from one of my letters to the editor in the British Medical Journal.

When one enters the medical college, the first thing that one is made to learn is to forget one’s common sense[1]. This probably happens much earlier in the present educational system; even as early as one enters the primary school. In the practice of bedside medicine, however, common sense is not just common but it is commoner than what one thinks it is. The statistical science of medicine can, at best, manage to size up cohorts of people but never the individual patient on the bed[1]! It is the past experience of the doctor with his clinical acumen that helps him at that point in time. He has to take a spot decision one way or the other based on his own assessment. None of the entry criteria of the “so called” research studies helps one at that time, as no two individuals are alike in real life. Unfortunately, that is what is presumed in the science of medicine.

The art of medicine is the one that makes the patient’s day. No amount of science and technology will ever be able to replace that humane human being, the doctor that alone could put to rest the universal anxiety that is part of all illnesses since every disease presents through the personality of the patient. Every doctor should become a healer with a heart full of compassion for the ill. The role of the science of medicine is only to sharpen the intellect of the doctor on the bedside. How good is good medical science? While the science of medicine is only a statistical science, and not an absolute science like mathematics, one needs to be
careful in accepting all that is sold these days as scientific medicine[6]. In reality even mathematics becomes shaky. In so far as mathematics is certain it is far removed from reality and when it is closer to reality it is not certain[5]! Medical science has one more drawback.

Science, in reality, is simply making models, mathematical constructs, which with verbal jargon, are supposed to work! So far so good. When such a science is applied to a dynamic human being that is being continuously run with food and oxygen, the linear laws do not seem to work. Human body is not only non-linear, it follows the holistic rules of the universe. Human beings are heavily dependent on their environment, in addition. All these make the present medical science a square plug in a round hole[6]. Change is progress and if we want to progress in medical science, we have to think deeply of changing our mindset and follow the new science of chaos-of non-linearity and holism. Change is not easy, though. Human beings are basically status quoists wanting the comfort of the existing order. We are usually afraid of change and what it might bring in its wake. However, life itself is ceaseless change until death. Hence, there is a need for serious thinking here. Let me think with you, the reader.

Let us examine the science of the very foundation of medicine, sold as the gold standard in medical research, the randomized controlled trials (RCTs). The British claim that it was Archie Cochrane that introduced the term and they claim that the first such study was undertaken by their Medical Research Council in 1940 on the role of streptomycin in tuberculosis and on the role of the whooping cough vaccine. However, there was a very good RCT done in Germany by Roethlisberger and Dixon in 1939 on the role of streptomycin in tuberculosis. There are indications that similar RCTs were conducted by R A Fisher in 1926 in agricultural sciences[5].

Let us examine the definition of RCTs. “A carefully and ethically designed experiment which includes the provision of adequate and appropriate controls by a process of randomization so that precisely framed questions can be answered.” RCTs did a good job in the arena of infectious diseases where the results could be got at the end of the study despite the study’s inbuilt drawbacks. However, in our enthusiasm, we have extrapolated those designs for the study of treatment of risk factors like “raised BP, cholesterol and sugar in the apparently healthy section of the population where the results are not seen at the end of five years study anyway. Then we use the statistical power to predict the future with our results of the RCTs. Here is the problem.

When one has a control population, the same must be identical to the study cohort for the results to be reliable. No two human beings are identical anyway. To cap it, we can only measure a few phenotypic features of both the groups for comparison. These, by any stretch of imagination, could not be taken to match the two groups. Despite this, the RCTs could do a good job in infectious diseases where the results are there to see at the end of the study. Time evolution in the human system being non-linear and solely dependent on all the parameters of the initial state, the mind and the genes included, RCTs could only deliver doubtful answers to the questions posed at the beginning. If we compare this with the definition given above, it becomes clear that all is not well in this field. That would shake the whole edifice of medical science as the foundation is built only with dry sand. How does randomization compensate for our lack of knowledge of the whole of the initial state of the human organism in the study is something that has no answer[5].

Be that as it may, modern medicine could, at best, reach only a minority in this world. Large sections of the population live without the benefit of modern medicine. They also fall sick and they have their own remedies that have not gone through the “rigors” of the RCTs. We must not close our eyes to the possibility that there could be authentic methods in other systems as well that might help us unravel the mystery. Our ostrich like attitude denies the ardent student in the medical school even a remote chance to think about it. One could argue that only modern medicine is scientific and the rest is mumbo-jumbo. Then modern medicine’s audit should show that. The Institute of Medicine audit in the US has shown medical interventions in bad light[7]. The per capita death rate of the grievously injured in the Vietnam War, where hi-tech modern medicine was at hand in Saigon, was slightly worse than the results of Falkland’s War, where the British did not have those facilities close at hand! Cancer audits before and after modern medicine do not show much to write home about, either! Cancer therapy, bypass surgeries, angioplasties, stem cell transplants, genetic engineering, treatment of chronic illnesses, terminal care in the intensive therapy units and, even, assisted delivery in high risk pregnancies do not seem to set the River Ganges on fire[8].

The best of these is the pioneering studies from Prof. David Eddy of Stanford University, a cardiac surgeon turned mathematician, who, with his ten years of painstaking research, has invented a new software tool that has thousands of differential equations to test the efficacy of what we do in medical science arena in a virtual field, named ARCHIMEDES. His studies have belied most, if not all, of our RCT conclusions (david.eddy@archim
This has opened up a new vista for others to follow. Our own studies for the last quarter of a century of the non-linear functioning of the heart using Heart Rate Variability (HRV) have thrown up newer possibilities for diagnosing and prognosticating heart diseases\cite{9}. We have been working on the non-linear wavelet analysis of the conventional ECG using the Continuous Wavelet Transform patterns. The Whole Person Healing Group, a collection of humane scientists lead by Prof. Rustom Roy, the father of nano-technology, a distinguished professor at the Penn State University, based in Washington DC, is doing phenomenal work in authenticating alternate methods in the arena of healing sciences\cite{10}.

The linear thinking in medical sciences with the reductionist attitude does not seem to support the belief that modern medical research is perfect. Far from it, very far. Time has come to think of good alternatives for which there is no dearth. We only have to change our attitude to those methods and we could always use our modern scientific methods to evaluate their efficacy and then accept or reject rather than prejudging their capacity. In my long experience, it is the young student in the medical school, given the freedom to think, that would come up with exciting new possibilities. In my considered opinion, teaching is a more effective way of learning and our students are our best stimulators provided, both of us remain humble and open to correction. Many effective systems of health care have been in existence for “times out of mind” in this world long before the “so called” scientific medicine came on the scene\cite{11}. It is high time that thinkers among the medical leaders, a rare breed indeed, start to look at the alternatives critically for the common good.

We have the power to verify their claims and then choose the wheat from the chaff. Efforts are on to do just that and we hope to let the world know that there are alternatives, which could complement the good things in modern medicine. One good example in modern medicine is emergency care, which cannot be replaced by any of the existing alternatives. That said, I must add that even in that area, much needs to be refined, as many of our interventions seem to be counter productive there. That is for another occasion. This paper does not permit me to go into that area. However, the majority of minor illness syndromes that form the bulk of illnesses on a given day, and the chronic ailments and cancer need some new approach in place of the top-heavy reductionist modern system. We need a holistic system of medical care which also takes into consideration the human mind as the initiator and healer of most illnesses\cite{12}. Let us move from the linear reductionist curative science to the holistic non-linear healing science.

“A fool thinks himself to be wise, but a wise man knows himself to be a fool”

William Shakespeare, 1564-1616

REFERENCES

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Review Article

Knowledge, Attitudes and Practices that Facilitate the Transmission of HIV among Prison Inmates: A Review

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ABSTRACT

The need for an effective response to HIV and behavioural patterns in prisons is a significant national and international concern. In different countries of the world, the rate of HIV infection among prison inmates is high. In some countries, reports showed that the rate of HIV infection in prisons is higher than in the general population. The epidemic is related to risk factors such as drug use, unsafe injection practices, and homosexual relationships, tattooing and sharing of needles. The failure to provide access to adequate prevention, protection, information and care is a violation of prisoners’ right to health as established by international law. As it is known today, the spread of HIV can only be controlled by effective programs designed to educate people about the causes of the infection, its mode of transmission as well as the attitude and behaviour that puts them at risk of becoming infected with HIV and how to avoid exposure to HIV. In this paper we review prisoners’ knowledge about HIV/AIDS, attitudes of the prison inmates and practices that constitute risk of transmitting HIV among prison inmates, the link between the society and prison in the transmission of HIV and offer recommendations to tackle the problems.

KEYWORDS: attitudes, HIV/AIDS, inmates, knowledge, practices, prisons, risk factors, transmission

INTRODUCTION

There are various activities that are known to occur among prisoners¹⁰. These activities have been identified as constituting risk for HIV infection²,³. Several studies have identified transmission of HIV in prison, based on testing for HIV antibody, identifying sero-conversion in inmates after more than five years of continuous incarceration³,⁴. Sexual activity between male inmates is not uncommon²,³. A USA Federal Bureau of Prisons study in 1982 reported that 30% of federal prison inmates engaged in homosexual activity while incarcerated⁵,⁶. In a 1984 study of Tennessee inmates, 17% reported homosexual activity in prison². Former prisoners surveyed in New York reported use of makeshift devices for safer sex, such as fingers of latex gloves, when condoms were not available⁷. The frequency of homosexual rape in prisons is extremely difficult to estimate and the activity difficult to control. The victim who reports rape in prison faces a probability of further suffering and worse injury. The Federal Bureau of Prisons study reported that 9-20% of federal inmates, especially new or homosexual inmates were victims of rape⁸. The text of the Prison Rape Reduction Act of 2002 states that the best expert estimate of the number of individuals sexually attacked at least one time during their incarceration is a national median of 13.6%. Other incidents of interpersonal violence (including fights involving lacerations, bites, and bleeding in two or more participants) present some risks for HIV transmission. These risk activities in prisons do not involve consenting participants, and educational programs are not likely to prevent HIV transmission in these situations. Housing more than one inmate per cell, common now in crowded institutions especially in developing countries, is a major contributing factor to incidents of violence and sexual assault.

British investigators interviewed 452 released prisoners about activities before, during, and after prison stays and found that persons engaged in fewer incidents of HIV risk behaviour in prison, were associated with increased risk. Those who reported engaging in homosexual activity while in prison also reported doing so with greater frequency outside, although they used condoms only outside. Reported sharing of syringes increased during imprisonment, as did less effective methods of syringe cleaning⁹. In another report

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from the United Kingdom, intravenous drug users (IDUs) who were former prisoners reported a high prevalence of injection and sexual risk behaviour while in prison; 33 out of 50 had injected drugs, and five out of 50 had had sex with two to 16 men[4]. Although imprisoned IDUs do not use drugs with the frequency that they can outside, they do share injection equipment more and sterilize it less because of scarce resources. A handmade syringe may be fashioned from parts of pens and light bulbs. Prisoners may also share toothbrushes, another potential source of HIV infection, in facilities where they are not issued, where inmates are unable to purchase their own, or where infection control precautions are not understood[5].

Tattooing is widely practiced in prisons and is usually performed without fresh or sterile instrument. It involves multiple skin punctures with recycled, sharpened, and altered implements such as staples, paper clips, and the plastic ink tubes from ballpoint pens. Prison wisdom holds that tattooing that causes blood to flow results in the best quality image and is least likely to become infected. Homemade pigment is delivered intradermally (at a sharp angle) rather than through direct puncture. Metal points connected to a battery or other electrical source are capable of producing vibration, increasing the number of skin punctures exponentially, thereby creating a better tattoo, but also increasing the probability of HIV transmission. Body piercing is becoming more popular in prison as in the outside community, and clean instruments for this practice are similarly unavailable.

Problem Statement
Globally, the incidence of HIV infection continues to be on the increase. HIV has been recognized as an important problem in prisons because of the common practice of unsafe sharing of needle and unsafe sexual practices. The population mainly affected in the spread of HIV infection is the age group of 20-39 years and the age group constitutes the majority of the inmates of prisons. These youths will be discharged eventually from prisons and return to the society and this may further increase the cases of HIV/AIDS in the general population. A rise in the incidence of HIV/AIDS among the prisoners will be an additional cost in government’s spending on health. For the majority of people in detention or custody there is no provision of clean needles. Also, there is paucity of counselling and support for prisoners living with HIV/AIDS. The problem of HIV/AIDS cuts across every society, the prison inclusive. The lack of retrievable data notwithstanding, anecdotal reports from clinical practice have shown that there is a high prevalence of HIV and STDs in prisons.

Aim of the study
The objective of this study was to review the level of knowledge, attitudes and practices of prison inmates that constitute risk for the transmission of HIV.

REVIEW
Despite the remarkable progress that has been achieved in gaining a scientific understanding of the HIV infection as well as the nature and progression of AIDS, the search for an effective treatment has proven to be elusive. As of today world wide, the main response to the HIV/AIDS epidemic has been preventive interventions[8,9]. Attitudes and practice studies are generally used to acquire information that would be required in designing health promotion and health education intervention programs that would be used to impact knowledge, alter attitudes and behaviour or practices that are risky to health.

ATTITUDES AND BEHAVIOUR INCREASING RISK FOR TRANSMISSION OF HIV IN PRISON
In Lesotho as well as many African countries, preventing HIV in prisons is a neglected area. A review of the literature showed very scanty published reports about HIV/AIDS in prisons. According to few commissioned reports, there are no medical facilities or medicines in most prisons and no trained nurses or paramedics specifically assigned to the prisons. Reports further remarked that overcrowding and poor food exacerbated the spread of diseases like HIV/AIDS and Tuberculosis in the prison. The prisoners were not provided with food of nutritional value, adequate for health and strength. Unfortunately, the mortality rate among the prisoners had increased, partly due to malnutrition and malnutrition is shown to be a contributor to HIV disease progression[10].

In South Africa, the prison environment creates many situations of high-risk behaviour for HIV transmission and the most common examples of such behaviour are homosexual activities, tattooing and scarring, gang-related violence and intravenous drug use[11]. HIV/AIDS in the prison has been a subject of court debate in South Africa. However, it is generally seen as the responsibility of prison authority to protect prisoners against rape and assault from fellow prisoners[12,13]. A study was carried out in Joyceville Penitentiary, a medium-security federal prison for men in Kingston, Ontario, Canada, by the Queen’s University HIV/AIDS Study Group in 1998[14]. The authors assessed the HIV and Hepatitis C sero-prevalence and the associated risk factors among inmates in the Canadian prison. The results showed that, out of 520 prisoners, 355
(68%) volunteered a blood sample and 350 of 355 filled out a questionnaire. It was found that 1.7% were HIV positive compared with 1.0% in the same prison and 33% were hepatitis C-positive as against 27.9%. 27.1% reported no risk behaviour and out of these, 6.3% were hepatitis C-positive as of 1995. Fifty-seven percent (57%) had been tattooed both inside and outside the prison and only 10.9% reported being tattooed outside the prison while 11.1% had been tattooed inside the prison. Injection drug use in the prison was found to have doubled from 12% in 1995 to over 24.5% in 1998. Out of the six prisoners (1.7%) who were HIV positive, five had used injection drugs at some time; 11.4% reported sharing injection equipment inside and outside prison; 7.7% reported sharing inside but not outside the prison and of these 66.7% were hepatitis C-positive and 6.6% reported sharing outside but not inside; of these 73.3% were hepatitis C-positive. It was concluded in the study that behaviour related risks that transmits hepatitis C can also transmit HIV and that the introduction of HIV-positive individuals with established high-risk behaviour patterns into the prison environment is going to lead to a rapid increase in HIV sero-prevalence. The authors also remarked that the prison is a public health disaster in process. Based on the study results, the authors recommended that needle exchange and effective drug rehabilitation programs should be introduced. It was also recommended that methadone maintenance should be made accessible for all heroin users entering prison and that efforts should be made to undertake intensive education programs with peer involvement to prevent prisoners starting injection drug use. If these recommendations are accepted and implemented, they could provide means for reducing the transmission of HIV infection in prisons. Unfortunately, most of these recommendations are just on paper in many countries, particularly the developing countries.

The sero-prevalence of HIV was assessed between January 1994 and December 1999 among adult males incarcerated in Rhode Island, USA. According to the authors, the aim of the study was to know the sero-prevalence of HIV in this group because it could help to estimate the sero-conversion risk after sexual assault in a given community and to determine the need for HIV post exposure prophylaxis and the best choice of medications. Records of all inmates who entered Rhode Island’s state prison for the reason of being charged with or convicted of a sexual offence between January 1994 and December 1999 were examined. Charged inmates routinely undergo HIV antibody testing voluntarily while convicted inmates must submit to testing at the time of incarceration. The results showed that out of 1524 men in Rhode Island with a sexual offence, 524 (34%) were convicted for the period under study. Out of 1524 charged men, 65% were classified as white, 19% as black and 15% as Hispanic. Out of 524 convicted men, 71% were classified as white, 18% as black and 10% as Hispanic. Sixty percent of the charged men and 54% of the convicted men were younger than 40 years. HIV test results were available for 1422 (93.3%) inmates and it showed a relatively low prevalence of approximately 1% among the inmates charged or convicted. This HIV prevalence appeared to be lower than the overall prevalence for the Rhode Island prison system (3.2%) at the midpoint of the collection period but higher than HIV prevalence in the general population of males (0.34%) in the state. The authors thought that it may be reasonable to extrapolate their findings to predict HIV transmission risk following sexual assault in that particular state and therefore to guide when to offer or recommend HIV post exposure prophylaxis.

Substance use is a behaviour known to carry a high risk for transmission of HIV both in the general population and in the prison. A consecutive case study was done on substance use in remand prisoners in Durham prison, a male remand prison in the UK, between October 1995 and April 1996. This was to determine the prevalence of drug and alcohol use among newly remanded prisoners and to assess the effectiveness of prison reception screening. All new prisoners, about 548 men aged 21 and over, were screened at reception by a health care officer, for physical and mental health problems as well as substance use. A standard prison questionnaire was used. It was found that before remand, 57% of the men were using illicit drugs, 33% met DSM-IV drug misuse or dependence criteria and 32% men met misuse or dependence criteria for alcohol. Seventy-one percent (71%) of the men were judged to require help due to their drug or alcohol use. It was concluded that prevalence of substance misuse in the newly remanded prisoners was high and this fact had been overlooked before the study and as a result only few received entry into a detoxification program.

KNOWLEDGE, ATTITUDE AND PRACTICE
ISSUES IN THE MANAGEMENT OF HIV/AIDS IN PRISONS

The quality of health care provided to prisoners has always been a concern in most countries, and the task of managing prisoners infected with HIV is daunting. A group of specialist HIV care providers from the King’s College Hospital reviewed their experience in caring for prisoners at Wandsworth and Brixton prisons in south London between 1994...
and 1999. It was a retrospective cohort study. Six inmates were newly diagnosed as positive to HIV antibodies and, 75 out of the 121 who claimed that they had previously been tested positive were confirmed as positive for the antibodies to HIV-1 and 25 were negative. The other 21 refused to be tested and out of these, 14 gave information to support their claims including their HIV treatment centers. The information proved to be false in all cases. Reasons for these false claims included the desired intention to get a letter pleading mitigating circumstances in court or a request for food supplements, sedatives or opioids.

Out of the 81 patients confirmed positive for the antibodies to HIV-1, 77% were white and 16% were black-African. The median age was 33 with a range of 23-65 years. The HIV risk factor was injection drug use (59%). The inmates were reviewed regularly to assess clinical status and adherence to anti-retroviral treatment. It was found that they were more likely to keep appointments in prison as compared with the hospital outpatient cohort (88% versus 67%). Reasons advanced for non-attendance, included attendance at court or hospital or legal or social visit (35%), transfer to another prison (25%), failure to locate prisoner (13%) and lack of clinic time (6%). Out of the 34 HIV-1 positive inmates that met the requirement for anti-retroviral treatment, 47% were taking it. Self-reported adherence to anti-retroviral treatment exceeded 90%, and this compared very well with the rate reported from a London outpatient cohort[26]. Sixty-three percent (63%) of the inmates receiving anti-retroviral treatment reported occasions of not receiving their medications as prescribed due to various reasons such as confinement to cell and travel to court, hospital or another prison. Other reasons like prescription error and drug unavailability were cited infrequently. Nineteen percent (19%) of the inmates receiving the treatment required at least one admission to the hospital for median of seven days (range 3 - 84) for clinical conditions that included respiratory tract infections, investigation for possible Mycobacterium tuberculosis, and treatment for lymphoma or Kaposi's sarcoma, meningitis and neuropsychiatry problems. The authors concluded that almost a quarter of prisoners who claimed to be HIV positive were not, and several logistic problems that had an impact on patient monitoring and adherence to anti-retroviral treatment were identified. It was then recommended that HIV status must be confirmed in all prisoners, and that there should be regular review of the services provided for prisoners who are HIV-1 positive.

A study was conducted in Lowmoss prison, Glasgow, and Aberdeen prison, UK, in 1996. Objectives of this study were to determine the frequency of injecting drugs, inside prison, and use of sterilizing tablets to clean needles in the previous four weeks, to assess the efficiency of random mandatory drug testing in detecting prisoners who inject heroin inside the prison, and to determine the percentage of prisoners who had been vaccinated against hepatitis B. Results revealed that 41% of Lowmoss and 37% of Aberdeen prison inmates had a history of injecting drug use, but only 4% of inmates had ever been offered hepatitis B vaccine. Two Lowmoss prisoners (both drug injectors) tested positive for HIV antibody; HIV prevalence was 0.7% overall and 1.7% for injector inmates. At Aberdeen, two prisoners (both non-injectors and heterosexual) were HIV positive and the HIV prevalence was 1.4% but nil for injector inmates. Forty-two Lowmoss prisoners and 31 Aberdeen prisoners had injected inside prison in the previous four weeks. The use of sterilizing tablets to clean injection equipment in the past four weeks was found to be broadly concordant as local arrangements in both prisons satisfactorily allowed prisoners to access sterilizing tablets for the purpose of harm reduction. It was then concluded that sterilizing tablets and hepatitis B vaccine should be offered to all prisoners, and that random mandatory drug testing underestimates injector inmates’ harm reduction needs.

**KNOWLEDGE, ATTITUDES AND PRACTICES REGARDING HIV/AIDS OUTSIDE PRISONS**

Many studies have been conducted outside prisons on the knowledge, attitudes and practices (KAP) regarding HIV/AIDS. A study titled “Knowledge, attitudes and risk behaviour for contracting HIV/AIDS among adolescents in schools” was undertaken in Lesotho[22]. This is a KAP study that assessed the knowledge, attitudes and practices among adolescents in the secondary and high schools in Lesotho. It was a quantitative study. A self-administered questionnaire was used in order to maintain complete anonymity and privacy, and to increase the response rate. The study was done in registered secondary and high schools in Lesotho. The target population was students aged 15-19 years. Sampling was by cluster random sampling method. Fifteen schools were chosen from out of three districts and students were randomly selected from these schools. Before its administration, all aspects of questionnaires were explained thoroughly to the participants. The research showed that the students had inadequate knowledge of HIV/AIDS. About 99% of the students had knowledge deficit on the early signs and symptoms of AIDS, its mode of transmission and preventive measures. Eighty percent (80%) of the students did not consider themselves to be at risk of contracting HIV infections. Sixty percent of
the students were sexually active with low condom use. Also, the study showed that over 50% of the students had negative attitude towards people with AIDS and many believed that traditional medicines were effective against HIV/AIDS. Majority of the students felt that it was necessary for HIV/AIDS education to be taught in schools. These findings revealed that there is a need to train educators, for example, teachers and nurses, regarding HIV/AIDS. There is also a need to develop an agreed-upon curriculum for the training of educators and for classroom students teaching purposes.

In 2002, a HIV/AIDS behavioural surveillance survey was conducted in Lesotho by the concerted efforts of Family Health International, Sechaba Research Consultants, Lesotho Ministry of Health and Social Welfare, U.S. Agency for International Development (USAID) and Lesotho AIDS Programme Co-ordinating Authority. Some of the objectives of this survey were: (1) to obtain data in standardized format that will enable comparison with other behavioural surveillance studies carried out in other countries, (2) to assess the relative success of the HIV prevention efforts taking place in selected sites, and (3) to provide information on the behavioural trends of some target groups in the same areas where intervention from projects are being offered. It was a quantitative study on the population that was prone or vulnerable to contract HIV infection and influence the dynamics of the overall epidemic. Seven population groups that met these criteria were identified. These are the youth at school between 15-19 years old (male and female), the youth out of school between 15-24 years old (male and female), male miners, taxi drivers/assistants, soldiers, low-income migrant women and female sex workers. The report showed that 90% of the in-school youths had heard of HIV/AIDS and that knowledge of HIV prevention methods was fairly high at 61%. The median age at first sex was 15 years for males and 16 years for females. Condom use at first sexual encounter was low among the male in-school youths ranging between 33-37%, but higher among females which was about 70%. It was also reported generally in the study that the male youths both in- and out-of-school tended to have sexual partners of the same age while the female youths reported having older partners. The study reported that the use of alcohol was common among female sex workers (57%), and 16% reported having used drugs. Only 26% of the female sex workers reported the consistent use of condoms with their clients, and 26% of them reported having had STD symptoms in the past 12 months. The knowledge related to HIV was also low among the female sex workers and only 41% of them responded correctly to all the three prevention methods. The study also showed that the low-income migrant women were a fairly mobile group with about 1/3 of them reported having been away from home for more than one month. A significant proportion of them reported never using condoms with non-regular partners although awareness of condoms was as high as 72%. For the adult male target populations (military, miners and taxi drivers/assistants), both the military and taxi driver reported significant mobility with 42% from the military and 40% of the taxi drivers reporting being recently away from home for more than a month. Only about one fourth of the adult male population reported having ever used drugs while more than half of them reported regular use of alcohol for the past four weeks. It is reported that between 75% and 80% of the adult male respondents had sex with non-regular partners in the last twelve months. Awareness of condom use was high (99%) among the male adult populations with the soldiers reporting highest level of awareness, but the consistent use of condoms was generally low among the adult male populations. The soldiers reported the highest level of knowledge about HIV/AIDS among the male adult populations. HIV testing was found to be low in all the groups put together. The authors came to the following conclusions: (1) condom usage is low among all groups, (2) youths started engaging in sexual activities at a very young age, (3) knowledge about HIV/AIDS did not necessarily translate to safer sexual behaviour, (4) multiple partnership is a common practice among the youth and the adult groups, and (5) that female sex workers tended to have their first sexual encounter at a young age and also to have received money for sex at a young age. It was recommended that the prevention programs that focus on partner reduction and delay of sexual debut should be developed and promoted in the country, and that HIV/AIDS prevention activities for all target groups including the schools should be intensified. It was also recommended that youth centers for activities against HIV/AIDS should be established, and that a strong volunteer counselling and testing (VCT) program including the training of more HIV/AIDS counsellors should be developed and implemented. However, this survey did not take into consideration certain behaviour that could add to the risk of contracting HIV infection such as male circumcision in the circumcision schools, sharing of sharp instruments such as shaving blades amongst household members and friends, as well as homosexual activities. In a society where significant percentage of the youth use drugs/alcohol and engage in high-risk sexual behaviour, it is not impossible that certain of their activities may result into criminal offences and lead them
to the prisons if found guilty. There is therefore, a relationship between youth behavioural patterns, number of youth in prisons and HIV transmission.

A USA-based non-governmental organization (NGO) called Save the Children (SC), with technical assistance from the Johns Hopkins University, conducted a rapid knowledge, attitudes, beliefs and practices (KABP) study related to AIDS among rural Zimbabweans\[24\]. The objectives were to test a rapid KABP survey methodology and to assist SC to provide data that would contribute to their final project evaluation. A total of 660 respondents, aged 18-45 years, selected by a modified 30-cluster sampling method were interviewed, in two SC project areas. The authors noted that although knowledge about HIV/AIDS was high, a number of misconceptions about HIV transmission and unfavourable attitudes to people with AIDS were recorded. Out of the five knowledge and attitudes variable that could be compared with the baseline survey results, four showed favourable changes while one showed an unfavourable trend. Comparing responses from those who were educated by SC with those who had other sources of information about HIV/AIDS, higher level of knowledge and greater willingness to care for family members with AIDS was seen in the SC educated group. However, there were no differences seen in other attitudes, beliefs, or in practices regarding condom use. The authors concluded that rapid KABP survey approach was successful in providing quantitative data, useful for project evaluation and for developing HIV/AIDS intervention strategies.

A survey was conducted anonymously in Vietnamese community in their homes in California, USA\[25\]. Knowledge about modes of HIV transmission was usually accurate, but few still believed that HIV could be transmitted through casual contact, and from needles used in hospitals (63%). Isolation of the HIV infected people was agreed to by 45%. In respect of sexual practices, 31% reported never having sex, while 8% had two or more sexual partners in the past 12 months. Six percent of men had visited prostitutes and of these, 24% had visited two or more times in the past 12 months and half of those encountered were outside USA. It was reported that most of the sexually active unmarried respondents never used or only sometimes used condoms and less than 1% had injected drugs.

A written survey to study and characterize the behaviour, attitudes, experiences and knowledge of 405 university students about HIV/AIDS was done\[26\]. Data was analysed by microcomputer. It was found that 55% of them considered themselves 'sexually active' while 8.1% had sexually transmitted disease. A significant percentage of them reported participating in high risk behaviour although they were concerned about HIV/AIDS. The authors then concluded that knowledge and concern do not appear to be sufficient for preventing risk prone behaviour and indicated a need to reconsider some of the HIV/AIDS education and prevention efforts.

A project was undertaken in 1991, in Grahamstown, South Africa. After a questionnaire was administered to assess attitudes to AIDS, a lecture on AIDS was given\[27\]. A second questionnaire administered six weeks later showed a marked improvement in the attitudes to AIDS. Most of the participants agreed that AIDS education for children should begin with those aged 8-12 years. However, further follow up study was not carried out in this group to find out how many more of the respondents continued to improve on their attitudes to HIV/AIDS. The use of drugs is closely associated with actions that would be risky for the transmission of HIV. For example, men or women who abuse alcohol are more likely to be sexually irresponsible. Demographic and Health Surveys from some African countries had confirmed this relationship\[28,29\]. In western countries, intravenous drugs form an important mode of transmission of HIV as the addicts shared used needles and syringes which are contaminated with blood infected with HIV among them\[30\].

**RECOMMENDATIONS AND POLICY IMPLICATIONS**

This review work gave an insight into the beliefs, knowledge and practices of the inmates in prisons regarding HIV/AIDS. From observation, any campaign program intervention against HIV/AIDS in the prison must not be targeted at the prisoners alone but the prison officials and the entire community must be involved. Support of the government, non-governmental organizations (NGOs) and all other stakeholders would be needed in the campaign against HIV/AIDS in prisons. It is recommended that the interventions and strategies enumerated below should be put in place.

**HIV/AIDS Education and Counselling in Prisons**

There may be prisoners who have never heard of HIV/AIDS and this is of great concern. Education and training programs about HIV/AIDS is recommended. Multi-sectoral approach should be adopted. Partners in this effort should include the correctional service authority, ministry of health and social welfare, private sector, non-governmental organizations (NGOs), national AIDS committee, community based AIDS and health organizations as well as concerned individuals. HIV/AIDS campaign team that would involve the Ministry of health, and Ministry of education.
Continuing Education and Skills Development

Regular lecture sessions should be provided in prisons. Areas to be covered should include sexuality, HIV/AIDS, STI, family planning and contraceptive methods. Topics on the preventive methods for infectious diseases, the hazards of unprotected sex or high-risk sexual behaviour, alcohol and drug abuse should also be taught. This should be provided in both male and female prisons. Other themes of discussion should include change in risky behaviour pattern and methods to limit harmful effects that would result from drug and alcohol abuse as well as unprotected sexual intercourse including rape.

Information, Education and Communication Materials

This is an important aspect of the education program. The information, education and communication (IEC) materials such as brochures and pamphlets should be freely available in prisons. They should also be provided to the inmates on their admission to the prison. These materials should be written and illustrated in a local language for easy understanding. Particular attention should be paid to sexually transmitted diseases and HIV/AIDS, defining the disease profile, which would include symptomatic and asymptomatic patients, drug therapy and other method of treatment in each case. Radio sets should be provided in the prisons since electronic media including radio form a major source of information about HIV/AIDS.

Peer Counselling

The inmates should be involved as peer educators. This could be organised in the form of plays and group information meetings, group workshops to educate fellow inmates. Peer facilitators network should be established. This strategy may be highly effective as a result of brotherhood and increased trust among the inmates. It would be a cost saving strategy in some African countries where there are shortages of staff.

Staff Training

There should be preventive educational program for the prison staff as well as the management. The aim should be to create and promote awareness on safe working methods. This program should be available as an induction course immediately upon entering the prison service. The syllabus of such a program should include topics like identification and prevention of communicable diseases, response to the needs of prisoners, HIV/AIDS and other STDs.

Medical Personnel for the Prisons

Medical officer should be appointed to coordinate all the health programs in the prison including that of HIV/AIDS. The medical officer should also have knowledge of psychiatry. Each prison should have at least one nursing staff with adequate knowledge and training in the area of HIV/AIDS education and counselling. He/She should work with the prison medical officer, other health workers, prison authorities and the various HIV/AIDS program managers. He/She will be expected to train the inmates on universal precaution practices, and arranging information and education sessions relating to health for the inmates and staff.

Update the Reception/Pre-Release Medical Examination

This is to detect any abnormal clinical condition including infectious diseases such as sexually transmitted diseases, tuberculosis and HIV/AIDS upon admission to, and prior to release from the prison. The current medical examination done for potential prisoners in some countries does not take into consideration the issue of HIV/AIDS. The screening may be in the form of symptom questionnaire and inquiry into past and current medical condition, which can be done by specially trained staff on admission and prior to release from the prison. The physicians can do physical examination along with chest X-ray and STD screening test. In keeping with the WHO guidelines, HIV/AIDS testing should be offered voluntarily with informed consent of the inmates after the person had received adequate information and counselling about HIV/AIDS prior to admission and release from the prison.

Accommodation for the Prisoners and Staff

Overcrowding in prisons will mitigate the outcome of the HIV/AIDS prevention campaign in prisons, as it would increase high-risk sexual behaviour and worsen the clinical condition of those who are already ill. Overcrowding is linked to the spread of tuberculosis in prisons. According to United Nation’s (UN) committee on crime prevention and control recommendations on the standard minimum rules for the treatment of prisoners in 1984, when sleeping accommodation is in individual cells or rooms, each prisoner shall occupy by night a cell or room by himself[31]. It is not desirable to have two prisoners in a cell[31,32]. Efforts should be made to provide adequate and healthy accommodation for the prisoners.
Personal Hygiene

Prison authorities should try as much as possible to provide the prisoners with facilities for proper care of their hair and beard. Men should be able to shave regularly and should not be allowed to share sharp shaving instruments like razor blades. An instrument that is contaminated with blood infected with HIV will facilitate the spread of HIV among inmates, if used by an uninfected inmate.

Standard Universal Precautions

Prison staff and inmates should be taught universal precaution against blood-borne pathogens including HIV and Hepatitis. All used inmate care equipment that have been exposed or soiled with blood or body fluids, secretions and excretions should be disposed off carefully so as to prevent contamination of the environment and transfer of micro-organisms to other inmates or employees. Instruments that must be reused must be adequately sterilized. Protective instruments like masks, gloves, eye goggles and clothing that protect against potential contacts with various infectious materials must be provided for use when need arises.

Protection for Prison Inmates

Prison authorities should try as much as possible to ensure that all necessary measures such as adequate staffing, surveillance and disciplinary measures are taken care of to protect prison inmates from rape, sexual violence and coercion. Prison gang network should be fought against by the prison authorities.

REFERENCES

Original Article

Early Improvement of Infarct-Associated Mitral Valve Regurgitation and Likelihood of Successful Thrombolysis: Color Doppler Echocardiographic Study

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ABSTRACT

Objective: To determine whether early successful thrombolysis can improve infarct-associated mitral valve dysfunction

Design: Cohort study conducted between February 1997 and January 2004

Setting: Coronary care unit and non-invasive cardiac laboratory, Department of Medicine, Farwania hospital, Kuwait

Subjects: One hundred and twenty five patients with ST segment elevation and acute myocardial infarction associated mitral valve regurgitation/mitral regurgitation (MR) were included in the study.

Interventions: Cardiac enzymes and 12-lead electrocardiogram were done for all patients. Transthoracic echocardiography, pulsed Doppler and color Doppler echocardiogram were done on admission and within 24 hours after thrombolytic therapy.

Main Outcome Measures: Infarct-associated MR in hospital outcome.

Results: Predictive indices revealed that the early improvement of infarct-associated MR after thrombolytic therapy is an indicator to predict successful thrombolysis status. The sensitivity was 86%, specificity = 79%, accuracy = 83%, positive predictive value = 62% and negative predictive value = 38%. Stepwise logistic multivariate analysis revealed a significant correlation between the age of the patients, chest pain to thrombolytic therapy interval and the early improvement of MR after thrombolytic therapy of acute myocardial infarction (p < 0.05). Patients with post-thrombolysis improvement in MR had a significantly lower incidence of in-hospital post-infarction angina, reinfarction, sustained ventricular tachycardia and congestive heart failure than patients without improvement (p < 0.05).

Conclusion: Early improvement of infarct-associated MR in patients with acute myocardial infarction treated with thrombolytic therapy suggests successful thrombolysis.

KEY WORDS: acute myocardial infarction, mitral valve function, thrombolytic therapy

INTRODUCTION

Mitral valve regurgitation/mitral regurgitation (MR) is a frequent complication of acute myocardial infarction and has several etiologies[1]. In the setting of acute myocardial infarction, MR is most commonly due to valvular dysfunction without structural disease and may result from altered ventricular geometry, incomplete mitral leaflet coaptation, papillary muscle dysfunction and regional wall motion abnormalities[2]. The functional MR after acute myocardial infarction is not related to left ventricle chamber size, ejection fraction, or regional wall motion abnormalities. Left ventricle sphericity is a primary determinant of the etiology of functional MR[3]. The past decade has witnessed tremendous growth in the understanding of the mechanisms underlying acute infarction, accompanied by the development of chemical and mechanical techniques designed to abort the process and lessen the extent of necrosis. It is possible that the same processes that lead to myocardial salvage during reperfusion may limit or reverse mitral valve incompetence[4]. The coronary revascularization with percutaneous transluminal coronary angioplasty or coronary bypass grafting may be useful in restoring mitral valve competence, improving hemodynamics and increasing survival in patients with ischemic MR[5].

We hypothesized that early improvement of MR after thrombolytic therapy for acute myocardial infarction predicts successful thrombolysis and better in-hospital outcome.

The aim of the study was to:

1. Investigate the relation between the early improvement of infarct-associated mitral valve regurgitation after thrombolytic therapy and the likelihood of successful reperfusion.

2. Study the association between the early
improvement of infarct-associated mitral valve regurgitation after thrombolysis and the in-hospital course of the patient sample.

**PATIENTS AND METHODS**

**Study patients:**

One hundred and twenty-five patients with acute myocardial infarction associated MR were included in the study. All patients were admitted by their physicians to the coronary care unit in Farwania hospital. All patients were evaluated clinically by looking at history and doing a physical examination, 12-leads ECG, plain chest X-ray and routine laboratory investigations.

Exclusion criteria included patients with rheumatic heart disease, mitral valve prolapse, previous myocardial infarction, intraventricular conduction disturbances, atrial fibrillation, acute pulmonary edema, severe MR, patients with one of the following contraindications to thrombolytic therapy; history of bleeding diathesis, recent (< 6 months) cerebrovascular accident (CVA), active peptic disease, recent (< 6 weeks) surgery or trauma or severe hypertension (> 180 mmHg systolic or > 120 mmHg diastolic blood pressure). None of the patients had a revascularization procedure before the qualifying myocardial infarction.

Exclusion was based on: medical history, physical examination and 12-lead electrocardiogram.

**Thrombolytic therapy:**

Seventy-eight patients received i.v. streptokinase infusion (1.5 million U over 60 minutes) followed by i.v. heparin infusion. Patients with history of previous use of streptokinase were excluded. Forty-seven patients were treated with 100 mg of rt-PA administered i.v. over 90 minutes. Immediately before the initiation of rt-PA therapy, an i.v. bolus of 5000 IU of heparin was administered and followed by continuous infusion of 1000 IU/h for at least five days. Aspirin was given on admission to CCU and continued at a daily dose of 100 mg.

**Cardiac enzymes:**

Blood samples were obtained every eight hours during the 1st day and once daily from the second day for determination of total serum creatine kinase (CK), MB isoenzyme (CK-MB) fraction and troponin I.

**Electrocardiogram:**

Standard 12-lead ECG was recorded on admission to CCU and every three hours thereafter during the 1st 24 h after admission. Beyond the 1st 24 h, a 12-lead ECG was recorded daily throughout the hospital stay. All ECGs were recorded with identical (marked) positions of the chest leads.

Voltage criteria for diagnosis of AMI was the presence of new > 0.2 mV (> 2 mm) ST segment elevation in two or more ECG leads.

**Transthoracic echocardiography:**

Two-dimensional and M-mode echocardiography was performed for all patients of the study with the use of Toshiba Power Vision or GE vivid 7 and a 3.5 MHZ phased array transducer. The leading edge to leading edge convention was used. Left ventricular dimensions were measured at or immediately below the tips of mitral leaflets and averaged over five heart cycles. Left ventricular end-diastolic volume, end-systolic volume and ejection fraction were determined from apical two and four chamber views using Simpson’s formula. Tracing of endocardial borders in end diastole and end-systole was performed in the technically best cardiac cycle. Left ventricular segmental wall motion score index was calculated by using a 16 segment model. Wall motion for each segment was graded as normokinesia = 1, hypokinesia = 2, akinesia = 3 and dyskinesia = 4. Wall motion score index was calculated by summing the scores for each segment and dividing by the number of analysed segments.

Pulsed and color-coded Doppler was obtained from the standard apical four chamber view. The transducer was then manipulated to obtain the maximal flow velocity as assessed by the auditory and spectral outputs. The Doppler measurements were made during at least three cardiac cycles using the darkest part of the spectral recording and were then averaged. MR was considered present, if blue, green or mosaic signals were seen originating from the mitral valve and spreading into the left atrium during systole. For each patient the maximal area of the regurgitant jet and regurgitant jet area/left atrial area in all three planes (left parasternal long axis, apical four chamber and apical two chamber views) were measured.

Severity of MR was graded on the basis of the method described by Helmcke et al, which correlates Doppler color flow findings with angiographic scoring. No regurgitation was classified as grade 0; a MR jet occupying 5 - 19%, 20 to 39% and ≥ 40% of the left atrial area represented, respectively, mild (grade 1), moderate (grade 2) and severe (grade 3) MR.

The study subjects were divided into two groups:

Group I: included 75 patients with early improvement of infarct-associated MR (within 24 hours after thrombolysis).

Group II: included 50 patients without early improvement of infarct-associated MR.
Coronary angiography:
Coronary cine angiography was performed for all study patients either in Egypt, India, Syria or Kuwait. Coronary stenoses were quantified visually to detect the extent and severity of the coronary lesions and to detect the culprit lesion with residual coronary stenosis. The luminal narrowing of > 50% was considered a hemodynamically significant coronary artery lesion.

Infarct related artery flow was quantitated using the Thrombolysis in Myocardial Infarction (TIMI) flow grades: TIMI 0 (no perfusion) = no flow beyond the occlusion; TIMI 1 (penetration without perfusion) = slow and incomplete opacification of the vascular bed by contrast material; TIMI 2 (partial perfusion) = slow but complete opacification of the vascular bed by contrast material with slower clearance and TIMI 3 (complete perfusion) = prompt and complete opacification of the vascular bed by contrast material with rapid clearance as in an uninvolved artery.

Statistical analysis:
Continuous variables are summarized as a mean ± standard deviation (SD). Comparison between two groups was performed with t-test for continuous variables and chi-square test for categorical variables. A p-value < 0.05 was considered statistically significant and a p-value < 0.01 was considered statistically highly significant. A stepwise multivariate regression model was used to identify possible independent variables associated with early improvement of MR after thrombolysis of acute myocardial infarction. The strength of the association with early reversion of MR after thrombolysis was presented as 95% confidence intervals. Potential confounding of clinical variables was entered as independent variables.

The validity of early improvement of MR after acute myocardial infarction to detect successful thrombolysis was assessed by estimating the predictive indices and Kappa coefficient to determine the overall agreement with the data obtained from the coronary angiography.

Kappa coefficient value (k) = (Observed frequency of agreement - Expected frequency of agreement) / (Total observed - Expected frequency of agreement). Predictive indices such as true positive (TP), true negative (TN), false positive (FP), false negative (FN), sensitivity, specificity, accuracy, positive predictive value and negative predictive value were calculated.

Receiver operating characteristic (ROC) curve (grade of sensitivity versus false positive) was used to identify the sensitivity and false positive of certain value of the variable with area under curve and probability of error with sensitivity 100% to detect usefulness of early MR improvement after acute myocardial infarction for prediction of successful thrombolysis in patients with TIMI flow 2 & 3.

The agreement between the two observers was verified by using the method of Bland and Altman. Mean of the difference between two observers and SD were calculated to obtain limits of agreements. Upper limit of agreement = mean of difference + 2SD. Lower limit of agreement = mean - 2SD. For good agreement at least 95% of values must lie within the limits of agreement.

RESULTS
Clinical characteristics:
With regards to the age of the patients, there was no significant difference between both groups of the study (48.34 ± 6.29 versus 49.2 ± 4.13 years, respectively, p < 0.13). There was no significant difference between both groups as regards their gender [65 (86%) versus 41 (82%) males, (p < 0.07) and 10 (7%) versus 9 (5%) females, (p < 0.11) respectively]. There was no significant difference between both groups regarding the percentage of patients with history of smoking, hypertension, diabetes mellitus and hypercholesterolemia [48 (64%) versus 36 (72%) patients, (p < 0.1), 26 (34%) versus 21 (42%) patients, (p < 0.08), 24 (32%) versus 20 (40%) patients, (p < 0.1) and 16 (21%) versus 14 (28%) patients, (p < 0.11)] respectively. There was a significant increase in the heart rate on admission in patients from group II than those from group I (108.15 ± 6.63 versus 89.5 ± 7.92 beats/minute, p < 0.05) but there was no significant difference in the systolic and diastolic blood pressure between patients from both groups (134.8 ± 13.63 versus 125.22 ± 9.31 mmHg, p < 0.09 and 92.8 ± 6.30 versus 87.94 ± 8.14 mmHg, respectively, p < 0.07).

There was no significant difference between the patients of both groups with regards to the time between chest pain and the initiation of thrombolytic therapy in CCU (72.5 ± 125.22 ± 9.31 mmHg, p < 0.07) and 12.3 versus 83.9 ± 14.3 minutes, p < 0.07). There was no significant difference between the patients from both groups (134.8 ± 13.63 versus 125.22 ± 9.31 mmHg, p < 0.09 and 92.8 ± 6.30 versus 87.94 ± 8.14 mmHg, respectively, p < 0.07).

There was no significant difference between the patients of both groups with regards to the time between chest pain and the initiation of thrombolytic therapy (72.5 ± 12.3 versus 83.9 ± 14.3 minutes, p < 0.07).

Presenting ECG:
The ECG of all patients from both groups showed sinus rhythm without ectopics and intraventricular conduction defects. There was no significant difference between both groups as regards the electrical axis deviation, PR interval and heart rate corrected QT interval (+36° ± 8.2° versus +46° ±
Early Improvement of Infarct-Associated Mitral Valve Regurgitation and Likelihood of...

9.4°, \( p = NS \), 144.1 ± 13.9 versus 139.4 ± 8.5 msec, \( p = NS \), and 345.3 ± 13.8 versus 367.6 ± 11.4 msec, \( p = NS \), respectively).

All patients presented with ST segment elevation > 2 mm in the chest leads from V3 to V6 or inferior leads. Five patients in group I versus seven patients in group II had ST segment elevation in V3 to V5. There were 27 patients in group I versus 20 patients in group II who had ST segment elevation in lead I, aVL, V5 and V6. There were 43 patients in group I versus 23 patients in group II who had ST segment elevation in inferior leads. There was a non-significant difference between both groups as regards ST segment elevation on admission (3.4 ± 1.1 versus 2.9 ± 1.4 mm, \( p < 0.11 \)).

ECG after thrombolysis:

There was a non-significant difference between both groups as regards ST segment elevation after thrombolysis (1.3 ± 0.5 versus 1.6 ± 0.7 mm, \( p < 0.10 \)). No significant change was noted as regards electrical axis deviation, QT interval, QT dispersion ECG before and ECG after thrombolysis between both groups. No patients had new left or right bundle branch block after thrombolysis in both groups. Only six patients in group I versus 11 patients in group II had persistent ST segment elevation > 2 mm at time of transfer to chest hospital for coronary angiography (\( p < 0.13 \)).

Coronary angiography:

There was no significant difference in the number of the patients who had single vessel disease in the group I versus those of the group II [49 (61%) versus 30 (60%), \( p < 0.07 \)]. As regards two and three vessel disease, there was no significant difference in the number of the patients in both groups (\( p < 0.11 \)). There was significantly more residual coronary stenosis in the patients with early reversion of infarct-associated MR than those without early reversion of MR after thrombolysis (60.9 ± 13.7 % versus 75.4 ± 11.2 %, \( p < 0.05 \)), but there was a non-significant difference between both groups as regards the site of culprit lesion in LAD (\( p < 0.06 \)). There were significantly more coronary collaterals in patients from group I compared with those of group II (45 (60%) versus 17 (33%), respectively, \( p < 0.01 \)), Table 1. As regards the infarct related artery, there was no significant difference between both groups with reference to LAD (56% versus 49%, \( p < 0.06 \)). There were significantly more patients in group II who had left circumflex coronary artery culprit lesion than the patients from group I (60% versus 27%, \( p < 0.05 \)), but there were significantly more patients in group I who had right coronary artery culprit lesion than the patients in group II (73% versus 40%, \( p < 0.05 \)), Fig. 1).

Table 1: Coronary angiography in both groups of the study

<table>
<thead>
<tr>
<th>Variables</th>
<th>Group I n (%)</th>
<th>Group II n (%)</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Culprit lesion of IRA:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proximal LAD</td>
<td>55 (73)</td>
<td>33 (67)</td>
<td>NS</td>
</tr>
<tr>
<td>Mid LAD</td>
<td>20 (27)</td>
<td>17 (33)</td>
<td>NS</td>
</tr>
<tr>
<td>Single vessel disease</td>
<td>46 (61)</td>
<td>30 (60)</td>
<td>NS</td>
</tr>
<tr>
<td>Two vessel disease</td>
<td>20 (27)</td>
<td>14 (28)</td>
<td>NS</td>
</tr>
<tr>
<td>Three vessel disease</td>
<td>9 (12)</td>
<td>6 (12)</td>
<td>NS</td>
</tr>
<tr>
<td>Residual coronary stenosis</td>
<td>60.9 ± 15.1</td>
<td>75.4 ± 12.2</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Coronary collaterals</td>
<td>45 (60)</td>
<td>17 (33)</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

IRA = infarct related artery, n = number of patients, NS = not significant

Fig. 1: Percentage of the patients with early improvement of MR after thrombolysis of acute myocardial infarction versus those without, as regards the infarct-related artery

In group I, 65 (86%) patients achieved TIMI 2-3 flow and 10 (14%) patients achieved TIMI 0-1 flow. In group II, 11 (22%) patients achieved TIMI 2-3 flow and 39 (78%) patients achieved TIMI 0-1 flow.

Echocardiography and Doppler study:

There was a non-significant difference with regards to the left ventricular end-systolic dimension and left ventricular ejection fraction in the patients of both groups (43.8 ± 5.2 versus 48.8 ± 4.6 mm, \( p < 0.10 \) and 54.3 ± 4.6 versus 50.7 ± 6.9 %, \( p < 0.12 \) respectively). There was a significant decrease in MR jet area / left atrial area ratio and left ventricle segmental wall motion score index in the patients of group I than those of group II (15.81 ± 5.92 versus 25.61 ± 4.73 and 1.32 ± 0.41 versus 1.91 ± 0.53, respectively, \( p < 0.05 \), Table 2).

Grading of MR:

Out of 75 patients from group I, 58 patients presented with MR grade I which reverted to MR grade zero within 24 hours (reduction in MR jet area / left atrial area ratio by < 15%), and out of 17 patients presented with MR grade II, 14 patients had reversion of MR to grade I and only three
patients had a reversion of MR to grade zero within 24 hours (reduction in MR jet area / left atrial area ratio by > 15%).

On discharge, there were only 14 patients with MR grade I and three patients with MR grade II in group I, but in group II, there were 22 patients with MR grade II and 28 patients with MR grade I.

There were no patients in both groups who developed mechanical complications such as pericardial effusion, cardiac tamponade, ventricular septal defect, or intracardiac thrombus.

**In-hospital outcome:**

There was a significant decrease in the percentage of patients in group I who had post-MI angina, re-infarction, sustained ventricular tachycardia and congestive heart failure as compared with those from group II [6 (8%) versus 12 (28%), 2 (3%) versus 8 (6%), 8 (11%) versus 12 (24%) and 3 (4%) versus 16 (32%) respectively, p < 0.05, Fig. 2]. There was no patient in both groups who had hemorrhagic complications after thrombolytic therapy.

**Forward stepwise logistic analysis:**

Multivariate analysis revealed a significant relation between age of the patients (R = 0.2134 & 95% CI = 1.025 - 3.191, p < 0.05), residual coronary stenosis (R = 0.3753 & 95% CI = 1.511 - 3.091, p < 0.05), chest pain to thrombolytic therapy interval (R = 0.4212 and 95% CI = 1.390 - 2.118, p < 0.05) and

**Receiver operating characteristic (ROC) curve:**

ROC curve data of early MR improvement after acute myocardial infarction for prediction of successful thrombolysis in the patients with TIMI flow grade 2-3. 100% sensitivity has a 37% error.
The sensitivity was 90%, false positive = 32% (specificity = 68%), in cases with 10% reduction in MR jet area / left atrium area ratio. The sensitivity was 80%, false positive = 20% (specificity=80%), in cases with 40% reduction in MR jet area / left atrium area ratio (Fig. 3).

Reproducibility:
There was no significant difference in inter-observer variability and intra-observer variability with regards to measurement of MR jet area / left atrium area ratio (p < 0.08, Table 5) and there was a good agreement between MR jet area / left atrium area ratio measurements by both observers as > 95% of the measurements were between the upper and lower limits of agreement (mean + 2SD & mean - 2SD, Fig. 4).

DISCUSSION
It is widely recognized that MR can develop during the course of acute myocardial infarction. The previously published frequency of this complication varies with the techniques used for detection but ranges from 10 to 55%\cite{10}. Lehmann et al reported a 13% prevalence of MR within the first seven hours of symptom onset\cite{11}. This valvular lesion was more common in patients with anterior infarction, but it did not correlate with peak creatine kinase levels or early ventricular dilation. Moreover, the early presence of MR was the strongest predictor of cardiovascular mortality, with relative risks of 7.3 at 10 days (95% confidence interval (CI) 1.4 to 38.4) and 12.2 at one year (95% CI 3.5 to 42.0). It is logical to hope that timely restoration of valvular competence may improve this otherwise poor prognosis.

Optimal restoration of valvular function requires an understanding of the underlying pathogenesis. Unfortunately, the mechanisms involved in this complication appear to be multifactorial. At one extreme is frank papillary muscle rupture, leading to immediate hemodynamic compromise and often to a quick demise\cite{12}. At the other is a more subtle disruption of the complex architecture that comprises the valve and its supporting sub-valvular apparatus\cite{13}. Further, controversy exists as to whether mitral valve incompetence is largely a problem of restricted papillary muscle and leaflet motion, leading to incomplete valve closure, or to exaggerated leaflet movement beyond the line of closure, producing valve prolapse\cite{14}.

The classic interventional approach to mitral valve dysfunction in this setting has been surgical replacement or repair, usually in conjunction with coronary artery bypass procedures. Uncontrolled series have suggested a survival benefit over that of medical treatment alone, although perioperative mortality can range up to 41%\cite{15}. Because of this high surgical risk, an effective alternative approach to restoring valve competency would clearly be preferable\cite{16}.

In theory, re-establishing perfusion in the infarct related artery early in the course of an evolving myocardial infarction might restore the functional integrity of the mitral valve without surgery. Several investigators have reported anecdotal evidence that supports this concept. Shawl et al were apparently able to reverse moderate and severe acute MR in five patients undergoing emergency coronary angioplasty during infarction, as evidenced by a significant improvement in pulmonary capillary wedge pressure after reperfusion. Follow-up contrast ventriculography at a mean of 35 months revealed no MR in three out of four patients tested\cite{17}. This same technique was successfully applied by Heuser et al to three patients with severe regurgitation, two of whom were in cardiogenic shock at the time of the procedure\cite{18}.
The mean pulmonary wedge pressure decreased from 34 to 10 mmHg after successful coronary dilation in these three patients, with no clinical heart failure or auscultatory evidence of MR observed at one-year follow up. Hickey et al retrospectively reported on nine patients undergoing angioplasty within 24 h of the onset of infarction. Six of the nine patients experienced complete reversion of MR after successful reperfusion[19].

Previous studies after reperfusion with thrombolytic therapy demonstrated a positive correlation between the severity of the residual lesion[20] or the TIMI perfusion grade[21] of the culprit vessel and the likelihood of recurrent angina or reinfarction, or both.

Our results showed a significant statistical difference in vessel patency after thrombolysis in patients with early reversion of infarct-associated MR than those without. Out of 125 patients with mild / moderate MR in our study, only 75 patients (60%) had an early reversion after successful thrombolytic therapy, and this is in agreement with the study of Tenenbaum et al[22]. The effect of thrombolysis on the incidence and severity of MR is controversial. Although it was shown to improve contraction of the posterobasal segment and reduce the incidence of significant MR in patients with inferior myocardial infarction, it had no effect on restoring valvular competence in another study[22].

The results of this study confirm those of the angiographic study by Lamas et al, which focused on the outcome of mild MR in a large group of patients[23]. The presence of moderate and severe MR was shown to identify a high risk group of patients who often progress early to congestive heart failure and have more extensive coronary atherosclerosis.

Although early improvement of MR after acute myocardial infarction was associated in the present study with a significantly higher patency rate of the infarct related artery, absence of early reversion of infarct-associated MR did not exclude patency of the infarct related artery. However, even if reperfusion occurred among patients without early reversion, a more severe residual stenosis and lower TIMI perfusion grade might be anticipated with less myocardial salvage and with a higher incidence of in-hospital complications, especially reinfarction and congestive heart failure. Thus, early reversion of infarct-associated MR is not accounted for by any degree of reperfusion but requires for its occurrence adequate reperfusion, which results in significant myocardial perfusion and salvage. Therefore, patients without early reversion of infarct-associated MR must be monitored very carefully and designed for catheterization at any sign of recurrent ischemia[22].

CONFOUNDERS
1. With regards to coronary collaterals, there was a significantly more increase in the number and percentage of the patients in group I compared with those of group II, and this may confound the results.
2. The reperfusion injury after the thrombolytic therapy in successful revascularization may also confound our results.

LIMITATIONS OF THE STUDY
1. Relatively small number of patients.
2. Patients with severe MR were not included in the study.
3. Coronary angiography was not performed early (within 90 minutes) after thrombolysis.
4. Myocardial contrast echocardiogram was not done as it detects myocardial blood flow and perfusion.
5. The study was not completely blind to observers.

CONCLUSION
We conclude that despite limitations and confounders of our study, early improvement of infarct-associated MR in patients with acute myocardial infarction treated with thrombolytic therapy suggests successful thrombolysis, better epicardial coronary artery perfusion grade and left ventricular function and a better in-hospital course.

ACKNOWLEDGMENT
We thank Dr. Mousa AJ Akbar, Consultant Cardiologist for his great help in revising the echo reports.

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infarction is associated with short and long term left ventricular remodeling. Heart 2001; 85:527-532.


Original Article

Adverse Events Following Measles and Rubella Immunization Campaign in Shahrekord, Iran; 2003-2004

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ABSTRACT

Objective: To report on the adverse events following the administration of Measles and Rubella (MR) vaccine during an immunization campaign in Shahrekord, Iran.

Design: Prospective study conducted between December 2003 and January 2004.

Setting: Nurseries, primary schools, high schools and universities in Shahrekord, Southwest of Iran.

Subjects and Methods: Four thousand children and students from the above institutions were randomly selected and recruited. They were followed up for one month after vaccination for any adverse events. Data collected using a questionnaire and physical examination were analyzed using SPSS 11 software.

Main outcome measure: Adverse events following MR vaccine administration

Results: The overall incidence rate of adverse events was 25.4%. Lymphadenopathy (8.7%), fever (8.3%) and sore throat (7.3%) were the most prevalent complications. Incidence of lymphadenopathy and arthralgia was higher in males (p < 0.01, p < 0.02 respectively), whereas myalgia was more common in females (p < 0.002). Lymphadenopathy was less common in the older age groups. Fever frequency was higher in the 5-10 and 21-25 age groups (p < 0.001). Myalgia and arthralgia was seen with higher frequency in the 11-15 and 16-20 age groups (p < 0.001). Skin rash was more common in the 5-10 and 11-15 age groups (p < 0.001).

Conclusion: Large scale interventions such as this vaccination campaign in a population revealed adverse events, but the frequency of serious adverse events with MR vaccine was low. Therefore, the benefit to risk ratio of such a campaign is favorable and such programs can be undertaken safely.

KEY WORDS: adverse events, measles, rubella, vaccination

INTRODUCTION

Measles and Rubella (MR) are viral diseases with worldwide distribution. Measles is a contagious disease with a mortality rate of about 1-5 percent in developing countries and this disease remain the leading cause of vaccine preventable death. In each country, the aim has been to reduce mortality rate and other complication of measles by large scale vaccination programs. In Iran, immunization program for this disease started in 1967 and is usually offered as two doses for all children at nine and fifteen months of age. World Health Organization (WHO) recommended that to prevent future outbreaks and to achieve high population immunity with the aim of interrupting measles transmission, mass immunization campaign should be conducted. Although Rubella is a mild disease, the ability of the virus to affect the fetus and create Congenital Rubella Syndrome (CRS) is a real health problem. Despite 95% coverage of vaccination in Iran, there have been measles outbreaks that occurred in persons 10-25 years old. The WHO advises vaccination of all children and adult females for elimination of rubella. This advice resulted in the National Center for Control of Disease, Iran to offer a national measles immunization campaign which was conducted from December 2003 to January 2004. This immunization campaign was also a unique opportunity for rubella control. Measles and rubella vaccines are attenuated vaccines. Thus vaccine administration may cause fever, adenopathy, arthritis, arthralgia and other adverse events. This research reports the adverse events of combined MR vaccine during a national vaccination program in 4000 vaccinated individuals in Shahrekord, Iran.

SUBJECTS AND METHODS

This is a prospective investigation in which the study population consisted of 174,757 persons...
Adverse Events Following Measles and Rubella Immunization Campaign in Shahrekord city located in southwest of Iran. These persons were vaccinated in a national MR vaccination campaign\textsuperscript{[5]}. The vaccination campaign was carried out during 32 days from December 2003 to January 2004.

A sample size of 4000 individuals was randomly selected from among vaccinated children in nurseries and also vaccinated students in primary schools, high schools and universities. In this campaign a combined attenuated MR vaccine manufactured by Merio India Co. was used. These 4000 cases were followed up for one month on days 3, 7, 10 and 30 after vaccination to evaluate the adverse events of immunization. Each individual was subjected to physical examination by trained general practitioners to observe adenopathy, local reactions and arthritis. A questionnaire form about adverse events of MR vaccine such as diarrhea, fever, cough, sore throat, headache and adenopathy was also used for every individual. The collected data was entered into the SPSS (11\textsuperscript{th} version) software and were analyzed using descriptive and analytic tests (such as, t-test and chi-square test).

RESULTS

Out of 4000 study cases 1837 (45.9 \%) were female and 2163 (54.1 \%) were male (Table 1).

Table 1: Age distribution of vaccinated individuals

<table>
<thead>
<tr>
<th>Age group</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-11</td>
<td>904</td>
<td>22.6</td>
</tr>
<tr>
<td>11-15</td>
<td>1925</td>
<td>48.12</td>
</tr>
<tr>
<td>16-20</td>
<td>926</td>
<td>23.15</td>
</tr>
<tr>
<td>21-25</td>
<td>245</td>
<td>6.12</td>
</tr>
<tr>
<td>Total</td>
<td>4000</td>
<td>100</td>
</tr>
</tbody>
</table>

Adverse events related to MR vaccine occurred in 1805 (25.4\%) vaccinated individuals, (Tables 2 and 3). There was no death resulting from the administration of MR vaccine during the period of the campaign.

There was a significant difference in the rate of agreements between lymphadenopathy, arthralgia, myalgia and gender. Incidence rate of lymphadenopathy and arthralgia was higher in males (p < 0.01 and p < 0.022 respectively). Myalgia was more frequent in females (p = 0.002). There was no significant relationship between skin rash and fever with gender (p = 0.27). There was a significant difference in the rate of agreements between adenopathy, fever, myalgia, arthralgia, rash and age. Adenopathy was more frequent among individuals aged 16-20 years (p < 0.001).

Fever was more frequent in children aged 5-10 years and adults aged 21-25 years (p < 0.001). Myalgia and arthralgia was more frequent in individuals aged 11-15 years and 16-20 years. (df = 3, p < 0.001). Skin rash was more common among children aged 5-10 and 11-15 years (df = 3, p < 0.001).

DISCUSSION

The MR Immunization campaign in Iran was performed on the age group 5-25 years. The majority of the vaccine recipients were aged 11-15 years\textsuperscript{[5]}. Adverse events were detected in 25.4\% of 4000 vaccinated individuals and the most frequent complications were lymphadenopathy and fever. Considering the number of signs as adverse events, presence of two signs together was more frequent (Table 2).

In an investigation performed in London city on adverse events of MR vaccination, the frequency of lymphadenopathy, fever and skin rash was 23.8, 16.8 and 26.9\% respectively\textsuperscript{[8]}. However, in our study the frequency of these adverse events was 8.7, 8.3 and 2.1 respectively. The very sharp difference between results of the two studies may be due to precision of examination, age groups of the population studied or vaccine components.

In another study performed in Japan, 66 children received MR vaccine and were followed up for the adverse events. Fever and skin rash were observed...
in 17 and 3 children respectively\textsuperscript{[9]}. The result of this study regarding fever is not in agreement with our results. This difference may be due to the fact that in our study the age distribution had a wider range.

In another study performed in Saudi Arabia, fever was the most frequent adverse event of MR vaccine\textsuperscript{[10]}. In our study, fever after adenopathy is the most frequent adverse event. In another study in Australia, three mild local reactions and another two severe local reactions were reported. The incidence rate reported was 0.3 per 100,000 administered\textsuperscript{[11]}. In our study, three cases out of 4000 (incidence rate = 0.1\%) developed mild local reactions following MR vaccination.

In Costa Rica, a system of surveillance for vaccine safety detected 60 cases of adverse events per 100,000 individuals attributed to MR vaccines. Of these events 70\% were reported by health professionals\textsuperscript{[12]}. In our study the incidence rate of adverse events is 25.4\%.

In the majority of investigations, adverse events of MR vaccine have been evaluated voluntarily based on physician or other health care worker reports, whereas in our study all 4000 vaccine recipients were prospectively and actively followed to detect any adverse events, using a questionnaire and physical examinations.

CONCLUSION

Large scale interventions such as this vaccination campaign in a population revealed adverse events but the frequency of serious adverse events with this MR vaccine was low. The benefit to risk ratio is favorable and such campaigns can be undertaken safely.

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REFERENCES

Factors associated with Smoking Habits among Kuwaiti Students in the Age Group 9-18 years

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ABSTRACT

Background: Smoking is now recognized as a major public health problem. It is noticed that the majority of regular smokers begin their smoking at an early age
Objectives: To study the risk factors associated with smoking behavior of Kuwaiti students in the age group 9-18 years
Design: Cross-sectional survey during the year 2001
Setting: Kuwait Government Schools
Subjects: A sample of 3338 Kuwaiti students using a questionnaire
Main Outcome Measures: The association between smoking status of the students and smoking family members and friends, family structure, parental education level, poor school performance and potentially aggressive personality of the student. In addition, we compared their knowledge about the health hazards of smoking.
Results: The prevalence of smoking among the students was 4.6%. The prevalence of smoking among students in the age group 15 to 18 was 18% in males and 0.68% in females. The results showed that peers and family members had significant influence on smoking behavior of the students (p < 0.001). Fathers at the extreme level of education and mothers of intermediate and above educational level exhibited an inverse relationship with the smoking status of the students (p = 0.055, p = 0.02) respectively. Smoking status was significantly related to poor school performance and tendency to aggression (p < 0.001). Lastly, smoking students were less knowledgeable about the health hazards of smoking than non smoking students (p < 0.001).
Conclusion: Peers, family members, family structure, parents’ educational level, students’ school performance and tendency to aggression were all influencing students’ smoking behavior. Attention should be given to improve health education at school and family level and improving social skills of the students to decrease peer group pressure.

INTRODUCTION

Smoking is the single and most important preventable cause of morbidity and mortality worldwide. Literature in this area of research has grown substantially over the last few decades. Researchers attempt to raise the degree of awareness among teenagers all over the globe. World Health Organization (WHO) believes that smoking is the largest preventable cause of death worldwide. It is estimated that more than 2.5 million premature deaths each year throughout the world can be attributed to tobacco smoking. Moreover, epidemiological studies documented the consequences of tobacco smoking as one of the important causes of premature mortality in most of the developed countries. It is noticed that the majority of regular smokers begin smoking at an early age. Risk factors have been under investigation in many countries and within different cultures in an attempt to control and/or prevent adolescent smoking. Research in smoking habits revealed that the most consistent and powerful predictor of whether an adolescent smokes is whether his friends smoke. There is also evidence of a family circle of smokers, whereby parents who smoke for a variety of reasons, will in time produce children who are more likely to become smokers.

Recently, in USA, a study conducted on school students showed that current smoking was significantly associated with peer networks. In Brazil, smoking among adolescent in the age group 10-19 years was studied. It showed that smoking is associated with older age, older smoking sibling, three or more smoking friends and low school performance. In New Zealand smoking habit was studied among students in the age group of 14 - 15
years and it showed that socio-economic status was increasingly associated with smoking prevalence in girls only.

Among Arab nations however, a study in Syria\cite{9}, for example, showed that peer influence was evident in all stages of smoking process especially in males. Parental smoking was an important association factor among smokers. The combination of parent and sibling smoking was the strongest predictor of smoking status of the survey.

In the Arabian Gulf area, a study conducted in Abha, Saudi Arabia\cite{10} among university students showed that friends were the main source of the first cigarette. Jarallah et al\cite{11} studied the predictors of smoking among male junior secondary school students in Riyadh. By multivariate analysis, he showed that factors such as knowledge of harmful effects of smoking, age, whether smoking was allowed in the presence of friends or brothers and previous smoking, were statistically significant determinants of current smoking.

In Bahrain, smoking habits among medical students was studied\cite{12}. The study showed that the proportion of smokers among male living alone or with friends was higher than those living with their families. In Kuwait, similar studies showed that the most important risk factor positively associated with smoking initiation is the history of smoking among sibling\cite{13}. It is also found that the highest risk of initiation of smoking among adult males is for those with history of smoking in the family and friends circle.

In this study however, we focussed attention to investigate factors associated with smoking behavior among Kuwaiti students in the age group 9-18 years.

A cross-sectional survey was conducted during the year 2001 on school students in Kuwait government schools. Kuwait is made up of six Governorates. During the planning stage, the sample size was calculated to be proportional to all governorates (Capital, Hawalli, Ahmadi, Farwania, Jahra, and Mubarak Al-Kabeer) based on the statistics obtained from the Ministry of Education. A written permission was obtained from the Ministry of Education for each governorate to conduct the study. A female school and a male school were randomly chosen using random tables for each of the three education levels (elementary, intermediate and high school) at random starting from 4th grade of primary school (age 9 years) to 4th grade in secondary school (age 18 years). A total of 36 schools were selected. The questionnaire was pilot tested on a sample of 100 students, and some of the questions were modified to make them clear before it was formally administered. To minimize non-response and under-reporting, respondents were told that the information obtained would be confidential and used only for scientific purposes.

Ten percent students of these selected schools were randomly chosen with a calculated sample size of 3600 students (type 1 error $a = 5\%$, type 2 error $b = 5\%$, allowable error $= 5\%$, and test power $= 95\%$). At the time of the questionnaire however, only 3338 students were present in the classes with a non-respondent rate of 7.3%. Although the respondents were 3338 the frequency in each table may appear less than 3338 due to the missing values which may vary from question to question. Questions were given in several formats including binary (yes, no), normal and 4-point likert scale. The questions covered several areas. Students were asked if their fathers, mothers, sisters, brother or friends were smokers. Then they were asked if they lived with one parent, both parents or others; the education level of their parents (illiterate, elementary, intermediate, secondary, university and above) and if their parents were frequently absent from home at night. Thirdly, questions were directed to assess certain personality characteristics of the student. These included: school performance (excellent, very good, good, failure and failure was considered as poor school performance); if the student liked quarreling with others using force; liked dangerous actions; liked to be in a car with a driver driving dangerously; if he used a seatbelt and if he likes to carry a knife with him. Lastly, a student was questioned about whether he considered smoking as a health hazard or not. Data were coded and entered into SPSS version 12. Thus, the data were checked and audited for entering mistakes or wrong code. Several statistical analysis procedures were implemented which statistically summarize measures in the form of frequency and percentages and Chi-square test for association.

RESULTS AND FINDINGS

The overall prevalence of smoking among the students was 4.6%. However, considering different age groups the prevalence was 0.5% in the age group 9 - 11, 1.9% in the age group 12 - 14 and 15.4% in the age group 15 - 18 years. According to gender the overall prevalence in males was 9.3% and 0.2% in females and within the age group 15-18, it was 18% for males and 0.68% for females.

Table 1 shows the association between the students’ smoking status and smoking among family members and friends. From the table, smoking status of family members and friends was significantly associated with smoking status of the students ($p < 0.001$). Compared to smoking family members, smoking friends had the highest association with smoking students (67.9%, $p < 0.001$). Within family members however, brothers
Factors associated with Smoking Habits among Kuwait Students in the Age Group 9-18 years

December 2007

had the highest association (51.1%, \( p < 0.001 \)), followed by smoking fathers (44.4%, \( p < 0.001 \)), smoking mothers (12.1%, \( p < 0.001 \)) and lastly smoking sisters (4.71%, \( p < 0.001 \)).

This study also considered the effect of social and family characteristics on smoking behavior of the students. These included family structure, parents’ educational level and absence of parents from home at night. It was shown that 17% of smoking students came from families with separated parents, \( p = 0.055 \). Moreover, 29.3% of smoking students had their fathers absent from home at night; 5.5% with absent mothers, \( p = 0.15, p = 0.293 \) respectively. Smoking among the students was inversely related to fathers’ educational level in the two extremes, \( p = 0.055 \). Mothers with intermediate and higher educational level also had an inverse relation to the smoking status of their children, \( p = 0.002, Table 2 \).

Our study also showed that certain behavior patterns such as poor school performance (15.8%), quarrelling with friends (35.1%), liking dangerous maneuvers (56.7%), liking reckless driving (45.7%), not using seat belts (62.5%) and liking to carry a knife (55.9%) were all significantly associated with smoking students, \( p < 0.001, Table 3 \).

Lastly, there was a significant difference between knowledge of the hazards of smoking among smokers (70.4%) and non-smokers (88.5%, \( p < 0.001, Table 4 \).

DISCUSSION

Despite the fact that the questionnaires were anonymous, there is reason to believe that the prevalence of smoking was underestimated as a result of underreporting. Wagner et al\(^\text{[14]}\) and Coltas\(^\text{[15]}\) discussed that self-reporting may underestimate the smoking prevalence in the populations studied. In our study the prevalence of smoking among students was 4.6%. The GYTS (Global Youth Tobacco Survey) survey in Kuwait - 2001\(^\text{[16]}\) estimated the prevalence of current smoking among students of the age 13 to 15 to be 14.9%. Comparing this result with our study, it is evident that a lower result was obtained in our study. This seems logical since we focused our attention on a wider age range (9 - 18). On the other hand, the prevalence of smoking among the age group 15

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**Table 1:** The association between smoking status of family members and friends on smoking behavior of the students

<table>
<thead>
<tr>
<th></th>
<th>Nonsmoker</th>
<th>Smoker</th>
<th>All Responders</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoker Father</td>
<td>992 (31.7)</td>
<td>55 (44.4)</td>
<td>1047</td>
<td></td>
</tr>
<tr>
<td>Non-smoker Father</td>
<td>2142 (68.3)</td>
<td>69 (55.6)</td>
<td>2211</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Total</td>
<td>3134</td>
<td>129</td>
<td>3258</td>
<td></td>
</tr>
<tr>
<td>Smoker Mother</td>
<td>57 (1.8)</td>
<td>15 (12.1)</td>
<td>72</td>
<td></td>
</tr>
<tr>
<td>Non-smoker Mother</td>
<td>3051 (98.2)</td>
<td>109 (87.9)</td>
<td>3160</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Total</td>
<td>3108</td>
<td>124</td>
<td>3232</td>
<td></td>
</tr>
<tr>
<td>Smoker Brother</td>
<td>744 (23.7)</td>
<td>69 (51.1)</td>
<td>813</td>
<td></td>
</tr>
<tr>
<td>Non-smoker Brother</td>
<td>2400 (76.3)</td>
<td>66 (48.9)</td>
<td>2466</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Total</td>
<td>3144</td>
<td>135</td>
<td>3279</td>
<td></td>
</tr>
<tr>
<td>Smoker Sister</td>
<td>34 (1.1)</td>
<td>6 (4.71)</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>Non-smoker Sister</td>
<td>3093 (98.9)</td>
<td>123 (93.3)</td>
<td>321</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Total</td>
<td>3127</td>
<td>135</td>
<td>3262</td>
<td></td>
</tr>
<tr>
<td>Smoker Friend</td>
<td>389 (12.4)</td>
<td>91 (67.9)</td>
<td>480</td>
<td></td>
</tr>
<tr>
<td>Non-smoker Friend</td>
<td>2738 (87.7)</td>
<td>43 (32.1)</td>
<td>2781</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Total</td>
<td>3127</td>
<td>134</td>
<td>3261</td>
<td></td>
</tr>
</tbody>
</table>

\( f = \) frequency

**Table 2:** The association of family structure and social factors with smoking behavior of the students

<table>
<thead>
<tr>
<th>Social and Family Factors</th>
<th>Non-smoker students</th>
<th>Smoker students</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not living with Parents</td>
<td>310 (9.8)</td>
<td>23 (17)</td>
<td>0.055</td>
</tr>
<tr>
<td>Father Education:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Illiterate</td>
<td>89 (2.9)</td>
<td>3 (2.3)</td>
<td></td>
</tr>
<tr>
<td>Elementary</td>
<td>117 (3.9)</td>
<td>7 (5.3)</td>
<td></td>
</tr>
<tr>
<td>Intermediate</td>
<td>625 (20.0)</td>
<td>39 (29.3)</td>
<td>0.055</td>
</tr>
<tr>
<td>Secondary</td>
<td>938 (30.9)</td>
<td>41 (31.3)</td>
<td></td>
</tr>
<tr>
<td>University &amp; above</td>
<td>1267 (41.7)</td>
<td>41 (31.3)</td>
<td></td>
</tr>
<tr>
<td>Mother Education:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Illiterate</td>
<td>286 (9.4)</td>
<td>18 (14.1)</td>
<td></td>
</tr>
<tr>
<td>Elementary</td>
<td>244 (8.1)</td>
<td>11 (8.6)</td>
<td></td>
</tr>
<tr>
<td>Intermediate</td>
<td>560 (80.5)</td>
<td>33 (28.8)</td>
<td>0.002</td>
</tr>
<tr>
<td>Secondary</td>
<td>922 (30.4)</td>
<td>38 (29.7)</td>
<td></td>
</tr>
<tr>
<td>University &amp; above</td>
<td>1019 (33.6)</td>
<td>28 (21.9)</td>
<td></td>
</tr>
<tr>
<td>Father absent at night</td>
<td>607 (20.5)</td>
<td>39 (29.3)</td>
<td>0.015</td>
</tr>
<tr>
<td>Mother absent at night</td>
<td>109 (3.7)</td>
<td>7 (5.5)</td>
<td>0.293</td>
</tr>
</tbody>
</table>

\( f = \) frequency
to 18 was 18% among males and 0.68% among females which is higher than that of the younger age group (13-15) students in GYTS survey. There was a noticeable difference in the prevalence of smoking among males and females in our study. This difference was also evident in other surveys conducted on Kuwait population. For example, in a survey in 1987 the prevalence of smoking among Kuwaiti males and females of the age 12 years and above was 27.4% and 2.1% respectively[17]. Another survey in 1996 reported the smoking prevalence above the age of 15 to be 32.1% in males and 1.5% in females[18]. In general, patterns of smoking in males and females are different in developing countries. Females in developing countries tend to have lower rates of smoking and start smoking later than males[21]. This is mainly the result of social cultural, religious or economic factors. For example, it maybe considered improper and indecent for females to be smoking in public; in addition, there may be religious and economic arguments against it. It is noteworthy that in a study in Kuwait by Menon et al in 2000[3] 85% of female smokers preferred to smoke in the privacy of their home. Because of negative social cultural connotations, females, particularly girls may underreport their smoking habits.

The data of this study also revealed that peers and family members have major influence in smoking behavior of students. This finding is consistent with previous studies of Moody et al[14], Jarallah et al[11] and Hassan et al[19]. According to the social learning theory[20] children are more likely to model themselves on people they regard as worthy, people they regard as similar to themselves, and models of their own sex. Smokers begin their smoking habits by mimicking their friends, co-workers, family members in general and their parents in particular.

Our finding that smoking behavior of friends had the highest association with smoking behavior of students, especially among males, is also consistent with findings reported by Radovanoric et al[9], Alexander et al[8] and Jarallah et al[11]. Throughout adolescence, youngsters experience feeling of uncertainty about their self-image and consider themselves more or less dependent on the opinion and judgment of peers. Meeting these expectations of one’s group is essential for preventing loss of friends, becoming a loner and eventually loosing one’s social identity[21].

It was also evident that family structure had influence on smoking behavior of the students. Smoking was more prevalent in students of families with separated parents and those with frequently absent parents from home. Separated or absent parents may cause children to spend time with other people, peers as a source of social and physiological support. Also those who come from broken families are more likely to be involved in activities such as smoking[22].

An inverse relationship between the prevalence of smoking and education has been repeatedly observed in different parts of the world, both among males and females. We observed an inverse relationship between the smoking status of students and fathers being at the two extremes of the educational scale. This is consistent with the results of the study of Jarallah et al[11]. On one hand, the highly educated are presumably more knowledgeable about the health consequences of smoking, while on the other hand, illiterates may be more conservative. Both groups may have in common the wisdom that could prevent their children from taking up smoking. Mothers with intermediate and higher educational levels were found to be inversely related to smoking status of their children. One may conclude that by their knowledge about the harmful effect of smoking these mothers may have protected children from starting to smoke.

In addition, our study revealed that poor school performance was significantly more common among smoking students as compared to non smoking students. This finding goes with that of Miller and Blant[23]. We also found that smoking was significantly associated with risk taking and aggressive behaviour such as quarreling with friends, liking dangerous maneuvers, not using seat belts and liking to carry a knife. This finding was consistent with that of Lynskey et al[24], Choquet et al[25], Byrd et al[26] and Jackson et al[27].

Finally, our observation that smoking students were less knowledgeable than nonsmoking students about the hazards of smoking is logical. This follows the findings in studies of Abolfatouh et al[28] and Giser et al[29] which clearly demonstrated the importance of health education at this age group.

CONCLUSION

This study highlighted several facts regarding our investigation of the factors associated with smoking behavior in Kuwait. Results showed that peers, parents, family structure, parent educational level were among factors that are associated with adolescence smoking. Moreover, poor school performance and tendency to aggression were also associated with smoking students. Therefore, preventive measures should be taken and seriously implemented. This includes school campaigns where awareness among parents, teachers and students is raised by organizing seminars. We concentrate particularly on teaching social skills and strengthening self efficacy in order to reduce
peer pressure. Attention should be given to those who suffer social instability. Meanwhile, we do not claim that we have identified all factors that contribute to the problem of smoking. We rather say that further investigations are needed and in depth studies should be conducted to thoroughly outline the causes of this longstanding problem.

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Original Article

A Five Year Study of the Mode of Delivery and Immediate Outcome of Term Singleton Breech Delivery

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ABSTRACT

Objective: To evaluate the mode of delivery and the immediate maternal and neonatal outcome of 690 consecutive term singleton breech deliveries in a single center

Study Design: Retrospective observational study

Setting: Farwania Hospital, Ministry of Health, Kuwait

Subjects: A review of the maternal and neonatal charts of all women who delivered singleton breech fetuses between 1999 and 2003 was undertaken. They are classified into: Group A - Women who fulfilled the criteria for trial of vaginal delivery which was further divided into two sub-groups:

A1 - Women who ultimately delivered vaginally and,
A2 - Women who had emergency cesarean section during trial of vaginal delivery.

Group B - Women who did not meet these criteria and underwent scheduled cesarean section.

Main Outcome measures: Maternal and neonatal outcome

Results: Group A consisted of 408 (59.1%) women who fulfilled the criteria for vaginal delivery. In this group 304 (74.5%) delivered vaginally (A1 subgroup). One hundred and four women (25.5%) had emergency cesarean section during trial of vaginal delivery (A2 subgroup). Group B consisted of 282 (40.9%) women who did not fulfill the criteria for vaginal delivery and underwent scheduled cesarean section. The overall cesarean section rate was 55.94%. There were no maternal deaths. Maternal morbidity occurred in both groups but did not assume statistical significance.

Conclusion: There was no significant difference in the outcome of babies born following a trial of vaginal delivery and scheduled cesarean section in selected cases of term singleton breech presentation. Careful selection of cases resulted in 75% of cases being offered a trial of vaginal delivery and to achieve it successfully.

INTRODUCTION

Breech deliveries occur in approximately 3% of all term singleton deliveries. Risk of poor perinatal outcome is associated with vaginal birth in most reports[1]. For the same reason their management remains one of the most controversial topics in obstetrics. Over the recent past, it has been widely held that a policy of routine cesarean section (CS) improves the perinatal outcome in these pregnancies without increasing the rate of maternal mortality or morbidity.

The Term Breech Trial (TBT)[1] was a multicenter, randomized, controlled clinical trial that compared planned CS and planned vaginal birth for 2088 women who had a singleton fetus in a frank or complete breech presentation at term and who were without contraindications to labor and/or vaginal birth. It concluded that planned CS reduces risk of adverse perinatal outcome.

The impact of this report in Kuwait was a rising CS rate. Women in this part of the world have a high parity and concern that CS delivery may have an impact on the future reproductive potential of women made the results of this study unacceptable in most centers.

We adopted a policy of careful selection of candidates with a singleton breech presentation at term and offered them a trial of vaginal delivery. The purpose of this study was to compare immediate neonatal and major maternal mortality and morbidity after term vaginal and abdominal delivery of a singleton breech fetus in a single center where uniform criteria had been applied in selecting the mode of delivery.

SUBJECTS AND METHODS

Between January 1, 1999 and December 31, 2003, 690 women had term singleton breech deliveries

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at our center. This represented 2.4% of all term deliveries during this five year period.

Gestational age was determined on the basis of the last menstrual period when menstrual cycles were regular. If menstrual cycles were irregular or not available, an ultrasound performed between the eighteenth and twenty second week of gestation was used to calculate the gestational age.

When breech presentation was suspected on clinical examination in a patient during late third trimester, ultrasound was done to confirm the presentation, type of breech, placental localization and expected fetal weight. Ultrasound was also done in patients with previously undiagnosed breech who came to the hospital in labor to confirm above parameters.

During the study period, following criteria were applied to select candidates for trial of vaginal delivery:

- Frank or complete breech presentation
- No evidence of feto-pelvic disproportion
- Expected fetal weight of 1500 - 3800 gm
- Absence of previous scar on the uterus, previous perinatal mortality or severe morbidity
- Nulliparity was considered a contraindication to vaginal delivery
- No evidence of hyperextension of head

Every attempt was made to estimate expected fetal weight by ultrasonography when possible. Expected fetal weight was estimated by clinical assessment when unbooked patients presented in advanced labor. Only in four cases we had to resort to clinical estimation of fetal weight as these patients were in advanced labor with the cervix more than 7 cm dilated at the time of admission to labor ward.

The final decision regarding the route of delivery was made by the most senior obstetrician present on the basis of these preset criteria. The protocol for management of labor was based on the following broad guidelines. Induction of labor by PGE2 vaginal pessaries was used for standard obstetrical indications. Induction of labor with amniotomy or syntocinon was not used. All fetuses were monitored by continuous electronic fetal monitoring throughout labor. Cervical dilatation and descent of the breech during labor was plotted on the partogram for early identification of abnormal progress. Augmentation of labor by amniotomy and/or syntocinon was used to treat ineffective uterine contractions in labor. After full dilatation of the cervix descent of the breech to the pelvic floor was expected within one hour and delivery being anticipated within one hour of beginning active pushing. An experienced midwife, two obstetricians and a neonatologist were present at delivery in most cases.

The choice of anesthesia and analgesia during labor was decided by the woman and her caregivers. Delivery was by means of assisted breech delivery. The key principles of vaginal breech delivery were:

- Never be in haste
- Always keep fetus with back anterior
- To allow the delivery of the fetus up to the umbilicus spontaneously and minimum intervention thereafter with no traction of the body

Difficulty in delivery of the shoulders was dealt with by Lovset’s maneuver. Controlled delivery of the aftercoming head using either the Mauriceau-Smellie-Veit technique or forceps was employed. Episiotomy was not used routinely for all cases.

On the basis of intention to treat the study population was divided into two groups. Group A comprised of 408 women who met the criteria for vaginal delivery. Group B comprised of 282 women who were judged unsuitable for vaginal delivery according to these preset criteria and who therefore underwent scheduled CS before labor.

The data from group A were further analyzed by subdividing the group into two sub-groups. Group A1 were those who actually delivered vaginally and group A2 were those who eventually underwent CS in labor.

The primary maternal outcome measures were intrapartum and neonatal mortality, incidence of five minute Apgar scores of less than six, incidence of endotracheal intubation before twenty four hours of age, admission to neonatal special care unit, incidence of other traumatic intrapartum or postpartum complications and incidence of neonatal sepsis (proven by culture).

The primary maternal outcome measures were mortality and major non-febrile morbidity like hysterectomy, cervical laceration, thrombosis, hemorrhage (> 1500 ml blood loss or the need for blood transfusion), collapse, coagulation abnormalities, readmission to hospital or wound dehiscence.

Statistical package (Epicalc 2000) was used for data analysis. The difference between the proportions of the groups was tested by the Z test. A value of p less than 0.05 was considered significant.

RESULTS

Out of a total number of 690 cases who had breech presentation at term, Group A consisted of 408 (59.1%) women. These women were offered a trial of vaginal delivery. Of the women who were offered a trial of vaginal delivery 304 (74.5%) ultimately had an assisted breech delivery and 104 women (25.5%) had an emergency CS in labor.

Group B consisted of 282 women (40.9%) who had scheduled CS. The overall CS rate in breech
presentation was 55.94% and the vaginal delivery rate was 44.06%.

The common indications for non-elective CS in labor were: failure to progress - 35 (33.6%), presumed fetal distress - 28 (26.9%), diagnosis during labor of exclusion criteria - 14 (13.4%), cord prolapse - 2 (1.9%) and eclampsia - 2 (1.9%).

The indications for elective CS were: primigravid breech -134 (47.5%), previous CS with breech - 93 (32.9%), estimated fetal weight (EFW) greater than 3800 gms - 34 (12%), maternal request - 12 (4.2%), intra-uterine growth retardation (IUGR) - 3 (1%), previous myomectomy - 1 (0.3%), footling - 2 (0.7%), hydrocephalus - 1 (0.3%), previous intra-uterine fetal death (IUFD) - 1 (0.3%) and previous neonatal death (NND) - 1 (0.3%).

No maternal deaths occurred during the period. Maternal morbidity occurred in both groups. Table 1 presents selected maternal outcome variables in patients with trial of vaginal breech delivery and scheduled CS.

One patient in group A had incomplete rupture of uterus following delivery of an anencephalic fetus which required laparotomy and repair. Another patient had traumatic postpartum hemorrhage following cervical tear which was repaired and the patient received two units of blood postoperatively. Two patients in Group B developed deep venous thrombosis.

Using the Epicalc 2000 test, there was no significant difference in maternal outcome between the two groups (p > 0.05).

There were two stillbirths and three neonatal deaths in the study period. One of the still births was an anencephalic fetus. The second patient presented with IUFD following premature rupture of membranes and cord prolapse at home. Three babies died in the immediate neonatal period because of multiple congenital anomalies.

Table 2 presents selected neonatal outcome variables in patients who had a trial of vaginal delivery (Group A) versus scheduled CS (Group B).

The immediate neonatal condition was assessed by Apgar scores only because cord blood gases are not routinely done in our center. There was a trend towards more infants who had a trial of vaginal delivery to have an Apgar score less than six. However they did not reach statistical significance. The neonates admitted to the NICU in the immediate neonatal period in both groups were all discharged well from the hospital within ten days. Of course long term follow up is required to see the ultimate outcome of these babies to identify whether there were any long-term sequelae. Using the Epicalc 2000 test, there was no statistical significance in the immediate neonatal outcome in any of the selected outcome variables between Groups A and B.

The data were also further analysed between three groups. Group A1 consisted of patients who had assisted vaginal delivery, Group A2 consisted of patients who had emergency CS during trial of vaginal delivery and Group B consisted of patients who had scheduled CS.

Table 3 represents the statistical analyses of selected maternal outcome variables between the three groups and Table 4 represents the statistical
analyses between selected neonatal outcomes between the three groups.

DISCUSSION

The policy of routine CS has been adopted in most centers following the results of the TBT. This would dramatically increase the overall CS rate with its impact on future reproductive potential. Most centers are now reporting an increase from 50 to 80% in CS rates for breech presentation. A recent study demonstrated that this may decrease perinatal mortality from 0.35 to 0.18%. It means that approximately 175 extra CSs will have to be performed to prevent one perinatal death. Thus in the future, we will have to counsel and treat more pregnant women who have undergone CS. There is always the risk of scar rupture during labor, albeit small in future pregnancies. The rate of repeat CS for the next baby after elective CS for breech presentation is 43.8%. In the long term, it would lead to increasing number of obstetricians lacking clinical experience in conducting breech vaginal deliveries.

Given the interests of the population to maintain high parity and avoid CS, a long and hard thought has to be given to whether the results of the TBT can be applied here as well. In many clinics we have managed vaginal breech deliveries following a protocol for selecting cases for trial with a tradition of years without notable adverse effects. It was in this context that this retrospective study was conducted. Our study confirmed that vaginal breech delivery can be accomplished with good perinatal outcome.

We did not find a statistically different risk of neonatal complications between infants born after a trial of vaginal delivery (whether born vaginally or after CS in labor) and those born by elective CS. After exclusion of the major malformations, all neonatal complications were resolved by the time of discharge. One limitation was the absence of information on long-term maternal and infant outcome.

Regarding maternal outcomes, the case that had incomplete rupture uterus during the delivery of an anencephalic fetus deserves special mention. This patient was a grand multipara who had no antenatal checkups. Consequently anencephaly was diagnosed when an ultrasound was performed when she reported near term. Labor was induced with prostaglandin vaginal pessary, 3 mg, which was applied once and she had amniotomy and syntocinon augmentation eight hours later. She was in labor for seven hours and had an easy vaginal delivery. Rupture uterus was diagnosed with the delivery of the placenta and she had a laparotomy and repair immediately thereafter. We believe that the cause of the rupture uterus was not the vaginal breech delivery per se, but multifactorial, taking into account the fact that she was a grand multipara and received prostaglandin induction followed by labor augmentation with amniotomy and syntocinon.

The fact that two patients developed deep venous thrombosis following CS despite thromboprophylaxis emphasizes the need for careful evaluation of risk factors and stricter postoperative care and awareness.

The TBT used, data collected from 121 centers in 26 different countries. This will certainly collect a large number of cases for analysis and consequently have greater statistical power. We recognize that observational studies may be biased and that a comparison of policies for breech deliveries will be more valid in randomized trials. But it is also worth noting that ensuring consistent quality of care and data collection over such a wide population is difficult. Also changes in demographic and population set ups in different countries are likely to influence practice and decisions. Our data results are from a single institution in which uniform criteria were applied prospectively for the selection of patients for trial of vaginal delivery.

There was a trend towards more babies being born with Apgar scores less than six. This finding is in agreement with earlier reports. It is possible that variables such as assignment of Apgar scores, decision to intubate etc. were influenced by the neonatologists awareness of the route of delivery. It also suggests a greater tendency for acute fetal distress during delivery causing transient perinatal hypoxia. Therefore, when managing breech deliveries, special attention has to be paid to possible signs of fetal distress. In the TBT continuous electronic fetal monitoring was not a prerequisite for trial of vaginal delivery. It is likely that at least a few cases of perinatal mortality and morbidity may have not been diagnosed in the absence of continuous monitoring which could have been avoided by timely CS.

The finding of a low Apgar score may have limited prognostic value for long term morbidity and thus is of questionable clinical importance. Probably the most effective means of reducing the risk of low five minute Apgar scores is for a CS to be undertaken more liberally during labor if fetal heart rate monitoring is not reassuring. In such a situation the need for long term follow up of infants delivered by breech presentation has to be emphasized. Good perinatal outcome following vaginal delivery in breech presentation at term has been reported in two studies following the TBT.

Our study permitted approximately 60% of women with breech presentation at term to attempt vaginal delivery out of which 75% delivered
vaginally. These results are comparable with other published studies. In one large single center study[13] a trial of labor was offered in 72% cases with a success rate of 53%. In another such study, trial was offered to 55% of women with a success rate of 70%[14].

It is also noteworthy to understand that delivering a fetus by CS is not risk free. The fetus has to be brought through both abdominal and uterine incisions and is best accomplished by an obstetrician who is an expert in vaginal breech delivery. In the United States, majority of maternal-fetal medicine units network faculty concluded that residency training for vaginal breech delivery was inadequate. Maintenance of skills in vaginal breech delivery is important in large obstetric units[15]. Furthermore, women would be denied the option of vaginal delivery even when they request it. We suggest that careful selection of women to whom we propose a vaginal delivery, and the presence in the labor ward of an experienced team of obstetricians, anesthetists and neonatologists may be more important in the ultimate outcome than the planned mode of delivery.

CONCLUSION

Difference in short term outcome variables in term breech presentations delivered following a trial of vaginal delivery and scheduled CS did not assume statistical significance. Serious maternal morbidity occurred in both groups but the difference was not statistically significant. Seventy five percent women offered a trial of vaginal delivery after careful selection of cases were successful in completing it. In this context there is no sufficient data to warrant routine CS for all term, singleton, breech presentation in units having practiced vaginal breech delivery for years with minimal adverse outcome.

REFERENCES


Original Article

Prevalence of Asymptomatic Bacteriuria and Associated Host Factors in Women with Type 2 Diabetes in Shahrekord, Iran; 2005

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ABSTRACT

Objective(s): Asymptomatic bacteriuria (ASB) is common among diabetic women. The aim of this study was to determine the prevalence and risk factors for ASB in women with diabetes.

Design: Prospective cross-sectional study

Setting: Chahar-Mahal province, Iran

Subjects and Methods: One hundred women with type 2 diabetes and 100 normal women (control) who had no abnormalities of the urinary tract were recruited. Demographic data and information regarding previous history of urinary tract infections (UTIs), duration of diabetes and presence of pyuria was collected. Baseline serum creatinine and fasting blood sugar levels (FBSL) were measured.

Main outcome measure(s): Prevalence and risk factors for ASB in normal and type 2 diabetic women.

Intervention: The prevalence of ASB and related risk factors in the two groups and the rate of ASB progressing to symptomatic UTI in a six-month period were evaluated.

Results: The prevalence of ASB was 20% in diabetics and 4% in control group (p < 0.05). Pyuria was present in 80% of diabetics with ASB. Symptomatic UTI in previous year was the only risk factor for ASB (p < 0.05). During a follow-up of six months, 40% diabetics with ASB developed to symptomatic UTI.

Conclusions: The prevalence of ASB is increased in women with diabetes. We recommend screening for detection and treatment of ASB in diabetic women.

KEY WORDS: asymptomatic bacteriuria, diabetes type 2, pyuria

INTRODUCTION

Asymptomatic bacteriuria (ASB) is defined as the presence of at least $10^5$ colony-forming units (CFU) / ml of one or two bacterial species in clean-voided midstream urine sample from an individual without symptoms of a urinary tract infection (UTI) [1]. Patients with diabetes have an increased risk of infections, with the urinary tract being the most prevalent infection site [2,3]. Besides, the rates of complications of UTI and upper tract involvement are much higher than in the general population. ASB in diabetic patients carries an increased risk of symptomatic UTI [4]. The prevalence of ASB is about three times higher in diabetic women (ranging from 15 to 30%) than in non-diabetic women (less than 10%) [1,6-8]. Local secretion of cytokines and increased adherence of uropathogens to uroepithelial cells have been proposed to account for the greater prevalence of bacteriuria in diabetic persons [5,6]. The prevalence of pyuria in young nondiabetic women with ASB is about 32%. The same rate in diabetic women is estimated to be about 70-80% [6,8].

Various risk factors for ASB in women with diabetes have been suggested, including sexual intercourse, age, duration, metabolic control, and complications of diabetes [1,5,6,8-10]. Some studies showed that, the number of symptomatic UTI in the previous year increased the risk of developing ASB in diabetic women [11]. Mendusa and coworkers [7] postulated that there is no association between fasting glucose concentration and ASB in diabetic women.

Escherichia coli, in diabetic patients, as in others is the most common uropathogen [7,10]. Other Enterobacteriaceae including Proteus, Klebsiella, Enterobacter and Citrobacter spp., Pseudomonas aeruginosa, Enterococcus spp., Gardnerella vaginalis, Streptococcus and Staphylococcus spp., Candida albicans and other fungi have been reported [7,10,15]. The probability of a more severe course of the infection and the proportion of resistant pathogens is also higher in diabetic patients than in nondiabetics [8,16].

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There is a trend in clinical practice to treat patients with diabetes who have ASB[4]. Some studies have not recommended antibacterial treatment in ASB for prevention of UTI complications in diabetic patients[6,17]. In contrast, other reports have suggested at least one course of appropriate antibiotic therapy in an effort to eradicate the pathogen or the postulated pathogen from the urinary tract[11,13,18], although in some reports, this is based solely on empiric evidence[48].

Some studies[11] have reported that decreasing renal functional tests is a consequence of ASB in diabetic patients. Geerlings[22] showed that 23% of patients with diabetes type 2 and ASB progressed to symptomatic UTI within two months and postulated that ASB is the most important risk factor for developing UTI in diabetic women. It is known that more UTI related complications (e.g. bacteremia, renal abscesses, renal papillary necrosis) are seen in patients with diabetes versus individuals without diabetes[22]. There are no published studies about ASB, the relationship between ASB and UTI and the need to initiate empiric therapy, especially in diabetic patients in Iran. The present study was undertaken to resolve these issue with reference to the women diabetic population in Shahre-kord city of Iran.

MATERIALS AND METHODS

In an analytical cross-sectional study, 100 nonpregnant women between the ages of 31-81 years with diabetes (type 2) but without any abnormalities of the urinary tract and 100 women without diabetes (as control group) were recruited. The groups were well-matched demographically. ASB was defined as the presence of at least 10⁵ CFU/ml of one or two bacterial species in a culture of clean-voided midstream urine from an individual without symptoms of UTI. Urine samples were kept at 4 ºC for up to two hours before culture. The urine was plated onto 5% sheep blood agar (Difco, USA) and MacConkey agar (Difco, USA) plates. A calibrated loop designed to deliver 0.01 milliliter of urine was used for urine inoculation. The plates were streaked by touching the loop to the center of the plate, from which the inoculum spread in a line across the diameter of the plate. Then, loop was drawn across the entire plate, crossing the first inoculum streak numerous times to produce isolated colonies. Once plated, urine cultures were incubated at 35 ºC aerobically. The results were read after 24 hours. Colonies were counted on each plate. The number of CFUs was multiplied by 100 to determine the number of microorganisms per milliliter in the original specimen[22]. The presence of WBCs ≥ 10/mm³ of urine was considered as significant pyuria[22]. Microorganisms were identified according to standard bacteriologic procedures[22].

Exclusion criteria were pregnancy, recent hospitalization or surgery within the past four months, known urinary tract abnormalities or recent urinary tract instrumentation, symptoms of a UTI such as dysuria, frequency or urgency, abdominal discomfort or fever, or the use of antimicrobial drugs during the previous 14 days. A consent form was filled in by the patient at the beginning of the study. The patients who developed symptomatic UTI were referred to an urologist for further evaluation and initiation of therapy. All patients were interviewed during the first visit of the study and their medical history was obtained using a standardized questionnaire. The questionnaire included age, duration of diabetes, and urinary tract surgery during the previous years and UTI during the past year. Laboratory values for serum creatinine, pyuria and fasting glucose concentration were also obtained. During follow-up for six months, any progression of ASB into symptomatic upper or lower urinary tract infections were determined. Risk factors were analyzed according to the differences between patients with and without ASB. Differences between patients with and without ASB were tested with the Mann-Whitney test for continuous variables (age and duration of diabetes). Chi-square test was used for variables like pyuria and number of UTIs during the past year. P-value < 0.05 was considered to be statistically significant. SPSS statistical software for windows (version 11) was used.

RESULTS

Out of the total study group with type 2 diabetes (n = 100), 20% had ASB. Only 4% of nondiabetic patients (control group) had ASB (p < 0.05). Pyuria was present in 80% of diabetic and 25% of non-diabetic patients with ASB (p < 0.05). Escherichia coli was isolated in 55% patients with ASB. Other isolated microorganisms included coagulase-negative Staphylococci (20%), Enterococcus spp. (15%), Klebsiella pneumoniae (10%).

Eighty percent of diabetic women with ASB and 17.5% of those without ASB had pyuria (p < 0.05). Besides, 40% percent of diabetic women with ASB had history of symptomatic UTI in the past year. There was no correlation between age, fasting glucose concentration, duration of diabetes and the presence of ASB in diabetic women. In contrast, significant association was evident between symptomatic UTI during the past year and the presence of ASB in patients (p < 0.05, Table 1). Chi-square test showed that no association was evident between past history of UTI and presence of pyuria. During a follow-up of six months, 40% (eight patients) of diabetic women with ASB had at least one episode of symptomatic UTI; five (62.5%) developed symptomatic lower UTI (cystitis) and
three (37.5%), symptomatic upper UTI (pyelonephritis). In diabetic patients without ASB, symptomatic lower UTI was detected in only five (6.3%) patients (p < 0.05). Upper UTI was not found in these patients. There was an association between age and progression from ASB to symptomatic UTI in our patients (p = 0.048). No association was found between duration of diabetes, fasting glucose concentration and development of UTI in diabetic patients with ASB (Table 2). Besides, in our study, no association was found between serum creatinine and presence of ASB in diabetic women.

DISCUSSION

In this study, we found that the prevalence of ASB was higher in diabetic than in nondiabetic women. Also, _Escherichia coli_ was the predominant microorganism isolated from diabetic patients. These findings were confirmed by other reports\[1,4,6,8,10,15\]. Makuyana and coworkers\[11\] isolated groups B and D _Streptococci_, _Staphylococcus aureus_, and _Pseudomonas_ spp. from diabetic women with ASB. In our study, such isolates were not prevalent.

Although, age has also been postulated as the most important risk factor for ASB in type 2 diabetic patients in some reports\[14,23\], in the current study we could not find an association between age and the presence of ASB in diabetic women. In contrast, as shown in Table 2, age of patients was an important risk factor for developing UTI in diabetic women with ASB. It was shown in this study that, the average age in diabetic women with UTI was lower than patients without UTI. Therefore, it can be concluded that, other factors such as sexual activity and menstrual period in young diabetic women may be included as predisposing factors for progression of ASB to symptomatic UTI. This is worth further future study and investigation.

Another risk factor for ASB in type 2 diabetic patients in this study was at least one episode of UTI during the previous year. Previous UTI as a risk factor for ASB indicates that bacteriuria can be present with or without symptoms in the same patient. In some reports\[14,23,24,25\], the presence of UTI during past year, has also been postulated as an important risk factor for ASB in diabetics. It can be concluded that, the colonization of uropathogens in urinary tract of diabetics after episodes of UTI, local secretion of cytokines and increased adherence of bacteria to uroepithelial cells in these patients, can accelerate the prolonged release of bacteria from urinary tract resulting in bacteriuria.

Some studies\[26\] found that diabetic women with ASB have lower urinary cytokine concentrations and therefore, decreased urinary leukocyte numbers compared with nondiabetic women with ASB. But, in our study, 80% of women with type 2 diabetes and ASB had pyuria compared to 25% in nondiabetic women. The correlation between pyuria and ASB has also been reported by other studies\[7,10,11,15\]. Meiland and associates\[19\] have reported that decreasing renal functional tests is a consequence of ASB in diabetic patients and therefore, they recommended regular screening of diabetic patients for ASB. Geerlings\[20\] showed that 34% of diabetic women with ASB had impaired renal functional tests. In our study, we did not find any association between patients’ serum creatinine and presence of ASB.

Some reports\[4,7,8,10,27\] have shown that the duration of diabetes is associated with ASB in diabetic patients. In the present study, we could not find...
any association between duration of diabetes and presence of ASB in diabetes type 2 women. Meiland et al[20] have also reported that this relationship was not present in patients with diabetes type 2 and only was found between ASB and diabetes type 1.

Geerlings[21] showed that 23% of patients with diabetes type 2 and ASB developed to symptomatic UTI within two months and postulated that ASB is the most important risk factor for developing UTI in diabetic women. These findings have been confirmed by Ooi and coworkers[24]. In this study, after a six months follow-up of diabetic women with ASB, a considerable percentage of patients progressed to symptomatic UTI. Therefore, we can conclude that ASB could be considered an essential risk factor for developing UTI in diabetic patients.

No consensus exists regarding the treatment of ASB in diabetic patients. Many experts recommend treating ASB in diabetic patients because of the frequency and severity of upper UTIs[22,23]. On the other hand, some studies believe that the benefit of treatment is doubtful[24,29]. This contrast is believed to be due to a lack of follow-up studies of diabetic women with untreated ASB. In this study, as mentioned above, after a six months follow-up of diabetic women with ASB, 40% developed symptomatic UTI. Therefore, although a further investigation about approach in diabetic patients with ASB is suggested, based on our findings, we recommend screening and treatment of ASB in diabetic women.

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We are grateful to Pajooheshi center of Shahrekord University of Medical Sciences for financial support. We also wish to thank Dr. Momeni and Dr. Maleki who participated in this study.

REFERENCES
ABSTRACT

Objective: To study the relationship between glycemic control (as assessed by measurement of plasma glucose and glycated hemoglobin - HbA1c) and insulin levels with oxidative stress, tumor necrosis factor-alpha and antioxidant status in type 2 diabetes mellitus.

Design: Single measurement of the biochemical parameters in serum of diabetic patients and controls.

Settings: The outpatient clinic of the Amala Cancer Hospital, Kerala, India.

Subjects: Forty patients with type 2 diabetes mellitus (30 male, 10 female). Thirty patients had diabetes-induced complications, whereas 10 did not. Ten normal patients (8 male, 2 female) acted as controls.

Main outcome measures: Serum parameters of oxidative stress, antioxidant enzymes and tumor necrosis factor.

Result: The blood glucose and HbA1c levels of normal group were found to be heterogeneously significant (p < 0.001) in diabetic groups. There were no significant changes in the insulin levels between the two diabetic groups, while it was significantly low (p < 0.001) in normal group. Significant elevation of malondialdehyde (MDA), hydroperoxide, and conjugated diene were found in both groups. The superoxidedismutase (SOD) and catalase levels were lower in complicated diabetic group. There were no significant alterations in the glutathione levels. Levels of glutathione peroxidase (GPx) and glutathione reductase (GR) were significantly low (p < 0.001) in complicated diabetic group. Tumor necrosis factor-α was higher in both groups and the increase was significant (p < 0.001) in the complicated diabetic group.

Conclusion: These results indicate that poor diabetic control is associated with increased oxidative stress and reduced antioxidant activity in type 2 diabetic patients.

KEY WORDS: antioxidant enzymes, glutathione, oxidative stress, tumor necrosis factor

INTRODUCTION

It is now known that oxygen at high concentrations can damage the liver, kidney, brain and other organs. The concept of biological free radicals is partially responsible for turning oxygen into a menace. Free radicals are unstable and extremely reactive chemical species, which have an unpaired electron in their structure[1]. The most important free radicals are the radical derivatives of oxygen. Increased oxidative stress may result from over production of precursors to reactive oxygen radicals and/or decreased efficiency of inhibitory and scavenger systems. The stress, then may be amplified and propagated by an autocatalytic cycle producing tissue damage and cell death[2,3]. Cell damage will in turn, result in elevated production of reactive oxygen species (ROS). High levels of ROS have been found to play a role in the pathogenesis of type 2 diabetes mellitus. Altered antioxidant defenses in diabetes might lead to the development of diabetic induced complications.

Increased plasma level glucose is also responsible for the damage to cell membranes through non-enzymatic glycosylation of proteins, auto-oxidation of glucose and increased metabolism of glucose by the sorbitol-polyol pathway[4].

The expression of tumor necrosis factor-alpha (TNF-α), a cytokine secreted by macrophages and T cells was found to be increased in adipose tissue of obese animals and obese humans[5,6]. TNF-α blocks insulin receptor tyrosine kinase activity[7] and GLUT-4 expression[8]. TNF-α has been shown to play a major role in the patho-biology of insulin resistance and development of type 2 diabetes mellitus.

The present study was undertaken to find out the role of oxidants and antioxidants in the pathogenesis of diabetes mellitus, especially in the case of diabetes related complications. We evaluated the enzymatic and non-enzymatic antioxidant activity in serum and erythrocytes of type 2 diabetes patients and compared it with normal persons. We have also
tried to relate the oxidative status in diabetes with serum TNF-α levels.

PATIENTS AND METHODS

Both newly detected and known diabetic subjects diagnosed for type 2 diabetes were enrolled, including those who were on anti-diabetic therapy. The diagnosis of diabetes was based on the guidelines recommended by the American Diabetes Association[9].

Patients with type 2 diabetes mellitus (n = 40; 30 male and 10 female) were recruited from the Amala Hospital, Thrissur. All diabetic patients had undergone treatment with sulphonylureas (either glibenclamide or glipizide). Normal controls (n = 10; 8 male and 2 female) were recruited from Amala Cancer Research Centre. None of the study subjects was taking antioxidant vitamins at the time of blood sampling. Ten out of 30 in the complications groups had microvascular involvement (nephropathy). The other 20 complicated diabetic patients had microvascular complication (coronary artery disease). For experimental purpose they were grouped as follows. Group I - diabetic patients with complication (n = 30); Group II - diabetic patients without complications (n = 10); Group III - normal controls (n = 10).

Blood was taken from a forearm vein from the individuals according to protocol approved by the Institution Human Experiments Review Committee. One part was aliquot into ethylenediamine tetra acetic acid (EDTA)-containing tubes for the measurement of glycated hemoglobin (HbA1c) as well as enzymatic assays. Another part of the blood was collected separately, centrifuged at 1500 rpm x 20 minutes, serum aspirated and immediately stored at -20º C. The serum was used for glucose, insulin, lipid peroxidation (LPO), hydroperoxides and conjugated dienes estimations.

Insulin assay was done using the method of Morgan and Lazarow[10] with a radioimmunoassay kit provided by Board of Radiation and Isotope Technology, BARC, Mumbai, India. Blood glucose was determined by the glucose oxidase method[11]. TNF-α was determined by the ELISA method (Titerzyme-EIA).

Erythrocytes were prepared by the method of Minami and Yoshikawa[12] and superoxide dismutase (SOD) was estimated in erythrocytes by the modified method of McCord and Fridovich[13]. The assay is based on the ability of the enzyme to inhibit the reduction of nitroblue tetrazolium (NBT) by superoxide, which is generated by the photo reduction of riboflavin. One unit of enzyme activity is defined as amount of enzyme giving 50% inhibition of the reduction of NBT and expressed as units/g Hb.

Catalase activity in blood was determined by the method of Aebi[14], by measuring the rate of decomposition of hydrogen peroxide at 240 nm. A decrease in absorbance was observed after the addition of H₂O₂ to the reaction mixture containing the erythrocytes, which is used as the source of catalase. Units of activity were determined from the E₅₅₀ of H₂O₂. Reduced glutathione (GSH) activity in the blood was measured by the method of Moron[15], based on the reaction with 5-5' dithiobis (2-nitrobenzoic acid). Values were calculated from a standard graph of GSH treated with the same reagent. Glutathione peroxidase (GPx) activity in blood was determined by the method of Paglia and Valentine[16] based on the degradation of hydrogen peroxide in the presence of reduced glutathione. Reduction of GSH concentration was determined by reacting with 5-5' dithiobis (2-nitrobenzoic acid) and values were calculated from a standard plot of GSH. The activity of glutathione reductase in blood was determined by Racker's method[17], based on the amount of NADPH consumed during the conversion of oxidized glutathione to reduced glutathione. The decrease in absorbance/min was followed using 1 min intervals for 5 min at 340 nm and the concentrations were calculated from the E₅₅₀ of NADP. Lipid peroxidation in serum was done by the TBA method as modified by Ohkawa[18], using thiobarbituric acid method. Hydroperoxides and conjugated dienes in erythrocytes were determined by the modified method of John and Steven[19]. In both tests, samples were first extracted in chloroform and methanol and the lower layer was taken to dryness. The remaining lipid residue was dissolved in 1.5 ml cyclohexane and the absorbance was taken at 233 nm. For the estimation of hydroperoxides, the lipid residues were treated with potassium iodide and cadmium acetate and the absorbance was then measured at 353 nm. Hemoglobin was estimated by the cyanmethemoglobin method using Drabkin's solutions[20] and protein was estimated by Lowry's method[21].

Statistical calculations were performed using Star View soft ware package. All values are expressed as mean ± SD. Comparisons of values between groups were made using one way ANOVA followed by Bartlett’s test and p-value < 0.001 and < 0.05 were considered significant[22].

RESULTS

A total of 40 diabetic patients were studied, of which 30 were male and 10 were female. Their mean age was 53.35 ± 4.98 years. The mean duration of diabetes was 9.16 ± 5.64 years. The mean post prandial blood glucose level of diabetic patients was 233 ± 102.29 mg%.
Table 1: Levels of post prandial serum glucose, HbA1c, TNF-α and insulin in normal and diabetic patients

<table>
<thead>
<tr>
<th>Groups</th>
<th>Serum glucose (mg/dl)</th>
<th>HbA1c (%)</th>
<th>TNF-α (pg/ml)</th>
<th>Insulin (IU/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>254.30±</td>
<td>15.47a</td>
<td>127.27a</td>
<td>21.80a</td>
</tr>
<tr>
<td></td>
<td>± 107.61</td>
<td>± 5.30</td>
<td>± 58.79</td>
<td>± 16.15</td>
</tr>
<tr>
<td>II</td>
<td>170.20±**</td>
<td>12.89a</td>
<td>73.70 b**</td>
<td>27.00a</td>
</tr>
<tr>
<td></td>
<td>± 46.29</td>
<td>± 3.27</td>
<td>± 21.99</td>
<td>± 13.72</td>
</tr>
<tr>
<td>III</td>
<td>112.21**</td>
<td>6.30**</td>
<td>30.70**</td>
<td>12.28**</td>
</tr>
<tr>
<td></td>
<td>± 11.62</td>
<td>± 1.06</td>
<td>± 3.74</td>
<td>± 2.83</td>
</tr>
</tbody>
</table>

Means having different superscripts are significant at **p < 0.001, *p < 0.05.
Superscripts indicate the significance between diabetic and normal groups.

Table 3: Effect of diabetes on lipid peroxidation, hydroperoxide and conjugated diene in erythrocytes

<table>
<thead>
<tr>
<th>Groups</th>
<th>LPO (n moles/ml)</th>
<th>HP (U/g Hb)</th>
<th>CD (U/g Hb)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complicated diabetic</td>
<td>5.78a 2.47a 2.65a</td>
<td>± 1.13 ± 0.79 ± 0.80</td>
<td></td>
</tr>
<tr>
<td>Uncomplicated diabetic</td>
<td>5.11a 1.98b 2.17b</td>
<td>± 0.70 ± 0.63 ± 0.48</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>4.04** 1.37** 1.45**</td>
<td>± 0.52 ± 0.36 ± 0.36</td>
<td></td>
</tr>
</tbody>
</table>

Means having different superscripts are significant at *p < 0.01, **p < 0.05.
LPO: Lipid peroxidation; HP: Hydroperoxide; CD: Conjugated diene.

Table 2: Levels of antioxidant enzymes in normal and diabetic patients

<table>
<thead>
<tr>
<th>Groups</th>
<th>SOD1 (U/g Hb)</th>
<th>CATALASE2 (k/g Hb)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complicated diabetic</td>
<td>953.30* 86.96*</td>
<td>± 127.53 ± 18.91</td>
</tr>
<tr>
<td>Uncomplicated diabetic</td>
<td>1050.53* 93.69*</td>
<td>± 193.84 ± 16.21</td>
</tr>
<tr>
<td>Normal</td>
<td>1336.72** 109.07**</td>
<td>± 231.06 ± 11.31</td>
</tr>
</tbody>
</table>

Means having different superscripts are significant at *p < 0.001, **p < 0.05.

SOD - Superoxide dismutase
Superscripts indicate the significance between diabetic and normal groups.

Table 4: Levels of glutathione, glutathione peroxidase and glutathione reductase in erythrocytes of normal and diabetic patients

<table>
<thead>
<tr>
<th>Groups</th>
<th>GSH (n moles/ml)</th>
<th>GPx (U/l)</th>
<th>GR (U/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complicated diabetic</td>
<td>185.78 15.15 7.82</td>
<td>± 25.12 ± 2.98 ± 1.17</td>
<td></td>
</tr>
<tr>
<td>Uncomplicated diabetic</td>
<td>197.74** 17.60** 8.87**</td>
<td>± 14.39 ± 2.69 ± 0.78</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>197.40*** 19.82*** 9.44***</td>
<td>± 28.63 ± 1.66 ± 0.65</td>
<td></td>
</tr>
</tbody>
</table>

Means having different superscripts are significant at *p < 0.001, **p < 0.05.

GSH: Glutathione; GPx: Glutathione peroxidase; GR: Glutathione reductase
Superscripts indicate the significance between diabetic and normal groups.

Thirty out of forty diabetics (75%) were suffering from one or more diabetic-induced vascular complications (nephropathy or coronary artery disease). The mean age of complicated diabetics (Group I) was 55.46 ± 3.47 years compared to a mean of 47 ± 2.98 years for the uncomplicated diabetics (Group II). The mean duration of diabetes in Group I was 11.58 ± 4.19 years compared to a mean of 1.80 ± 1.79 years in Group II. The mean postprandial blood glucose levels in Groups I and II were 254.32 ± 107.59 mg/dl and 170.20 ± 46.29 mg/dl respectively (Table 1).

The blood glucose levels of the normal control group (Group III) were heterogeneously significant (p < 0.001) with diabetic patients. Group I showed highest glucose level (254.30 ± 107.61) when compared Group II (70.20 ± 46.29) and Group III (112.21 ± 11.62) patients. The elevations of glycated hemoglobin levels were comparable with that of plasma glucose levels of the same group. Among the diabetic groups (I and II) HbA1c did not differ significantly but the difference was significant when compared to Group III (p < 0.001, Table 1).

TNF-α level in Group II patients significantly low (p < 0.001, 73.7 ± 21.99) when compared with Group I (127.27 ± 58.79). TNF-α level showed no significant difference between Group II and III. Group I showed a highly significant increase in TNF-α levels when compared with Group III (p < 0.001, Table 1).

There were no significant changes in the insulin levels between Group I and II. However, Group II showed significant increase in the insulin levels as compared to Group III (p < 0.05). Even though the insulin levels were increased in Group I, the increase was not significant (Table 1).

The changes of in vivo antioxidant levels like superoxide dismutase and catalase are shown in Table 2. The SOD level was found to be significantly low in Groups I and II compared to Group III. The catalase levels did not show significant changes among the diabetic groups but were significantly higher in Group III (p < 0.05).

Lipid peroxidation, which is measured as the malondialdehyde formed (MDA), was not heterogeneously significant between the diabetic groups. However, the lipid peroxidation levels were significantly low in Group III as compared to Groups I and II (p < 0.001). Hydroperoxides and conjugated dienes were not significantly different in diabetic groups. Hydroperoxide levels in Group III were significantly low when compared to Group I (p < 0.001). The conjugated diene levels in diabetic patients were significantly higher than the control group (p < 0.001, Table 3).
Glutathione levels of diabetic patients as well as controls were not found to be significant. Glutathione peroxidase levels in Group I were significantly low when compared with Group II and III (p < 0.001). Glutathione reductase levels in Group II and III were significantly higher when compared with Group I (p-value <0.001, Table 4).

DISCUSSION

In this study, we found that poor glycemic control in diabetic patients was associated with decreased free radical scavenging activity. In hyperglycemia, glucose undergoes auto-oxidation and produces free radicals that in turn lead to peroxidation of lipids in lipoproteins. Elevated levels of lipid peroxidation, hydroperoxide and conjugated diene seen in diabetic patients are clear manifestations of excessive formation of free radicals resulting in tissue damage. The activity of superoxide dismutase was found to be lower in diabetic patients when compared to normal. This decrease in SOD activity could result from inactivation and/or glycation of the enzyme, which are known to occur in diabetes. GSH is a major nonprotein thiol in living organisms and plays a central role in coordinating the body’s antioxidant defense processes. Perturbation of GSH status of a biological system can lead to serious consequences. In our study we could not find any difference in the blood GSH levels of normal and diabetic patients. However, many of the enzymes related to the GSH protein have been found to be lowered in diabetes. GPx catalyses the reaction of hydroperoxides and reduce glutathione to form glutathione disulphide (GSSG). GPx levels were found to be lowered in diabetic patients. Glutathione reductase, which reduces oxidized glutathione, was also lower in diabetics. Similarly catalase which reduces H2O2 has been found to be significantly lowered in diabetic patients when compared with normal and it was comparable with earlier results.

Long-term vascular complications still represent the main cause of morbidity and mortality in diabetic patients. Although prospective randomized long-term clinical studies comparing the effects of conventional and intensive therapy have demonstrated a clear link between diabetic hyperglycemia and the development of secondary complications of diabetes, they have not defined the mechanism through which excess glucose results in tissue damage. Evidence has accumulated indicating that oxidative stress may play an important role in the etiology of diabetic complications. This hypothesis is supported by the evidence that many biochemical pathways associated with hyperglycemia such as glucose autooxidation, polyol pathway, prostanoid synthesis and protein glycation are the result of the increased production of free radicals.

In our study we have observed that TNF-α levels increased significantly in many diabetic patients who had complications. TNF-α has been shown to have a critical role in insulin resistance. In septic shock the TNF-α level is increased and resistance to insulin has been reported. Exposure to TNF-α has been shown to decrease GLUT-4 protein in cultured cells producing a decrease in the glucose transport. It has been shown that TNF-α blocks the insulin receptor tyrosine kinase activity.

CONCLUSION

Herbal extracts are reported to be useful in diabetic conditions and the exact roles of these extracts have not been identified. We have reported earlier that many of the plants extracts also have significant antioxidant activity, which has been shown to reduce glucose level during diabetic conditions. Increased TNF-α levels in alloxan diabetic animals were found to be decreased by the plant extracts (Sabu & Kuttan, unpublished) indicating that herbal extracts could inhibit TNF-α levels. This may be another mechanism of their action. Antioxidants and TNF-α inhibitors may thus be important in the control of diabetes and its long-term complications. In the present study diabetic patients with increased TNF-α were found to have increased insulin levels when compared to normal controls, which in turn can produce insulin resistance.

REFERENCES

Mothers' Knowledge, Fears and Self-Management of Fever: A Cross-Sectional Study from the Capital Governorate in Kuwait

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Primary Health Care, Shamiya Clinic, Capital Health Region, Kuwait

OBJECTIVE: To survey mothers about their knowledge concerning fever in children, how they manage it at home, what their fears of fever are and to study the relationship between mothers knowledge and fear with the educational level and number of children.

Setting: Primary health care clinics in the capital health region in Kuwait

Subjects: Five hundred and twenty accompanying mothers of feverish children.

Method: A cross-sectional questionnaire survey.

RESULTS: 34.8% of mothers would recognize fever by the general appearance of the child, 32.6% by touching the child; one third (32.6%) would measure the temperature. More than 60% use digital thermometers, 15.7% would use mercury thermometers. The association between the educational level of mothers and method used to measure the temperature was statistically significant (p < 0.05). The most common site mothers use for measuring temperature of a child less than 3 years was the armpit (57.3%). The majority of mothers (81.6%) believed that teething can cause fever in children. Approximately 60% of all mothers believed that an untreated fever could lead to convulsions. The association between perceived consequences of fever and level of education was statistically highly significant (p < 0.005). A significant association was also found between perceived consequences of fever and number of children (p < 0.05).

Conclusion: Doctors should spend enough time with mothers attending a feverish child, explaining and answering their queries about fever, and providing adequate information that might allay their fear and promote an appropriate fever management at home.

KEY WORDS: children, fever management, Primary health care, temperature

INTRODUCTION

Fever is defined as a body temperature above the normal range; a rectal temperature above 38.0 °C, an oral temperature above 37.8 °C, and an axillary temperature above 37.2 °C are all considered as fever. Children in the age group of 3 to 36 months have approximately six febrile episodes per year, representing the highest incidence of fever during childhood[1], and it is estimated that fever is the primary complaint for as many as one third of all pediatric consultations in general practice[2,3]. Although fever was considered a protective response for thousands of years, and was even induced by physicians to combat certain infections, the advent of antipyretic drugs has led to the common belief that fever is maladaptive and harmful[4-6]. Parents have shown a lot of anxiety and unrealistic fears of fever, and they generally see it as the main component of an illness in their children which often prompts them to seek immediate medical care[3-6]. In Britain, Kai interviewed socially disadvantaged parents and identified a fear that causes panic when children are feverish[11]. Therefore, mothers’ knowledge and perception of fever may determine the degree of their anxiety and fear, and reflect on the way the fever is managed at home[12].

We conducted this study to explore mothers’ ideas, knowledge and concerns about fever in their children and their home management strategy and to study the relationship between mother’s knowledge about fever and their fears with the educational level and number of children. The conclusions of this survey will help doctors in their management of a feverish child.

SUBJECTS AND METHOD

A cross-sectional survey was conducted over a six-month period in the capital governorate. The capital health area, one of the five health areas in Kuwait, was chosen as our study area because of the convenience of the investigators who are working in this area. During the period from March – August 2004, a survey was carried out in the four primary health care polyclinics which were the only clinics open during weekends. Choosing these polyclinics and weekends would enable the investigators to...
include subjects from all residential areas (as their regular clinics would be closed) to ensure enrolment of a truly representative capital population which is a mixture of different socioeconomic and educational strata. The study population consisted of 520 mothers who accompanied their feverish children and were willing to participate in the study; we expected mothers to be the main caregivers at home. The number of subjects taken from each polyclinic was proportional to the total number of children registered there. Investigators (doctors) explained the purpose of the study to the mothers and each female parent, with her permission, was given a suitably structured standard questionnaire in Arabic to complete while sitting in the waiting rooms. It contained different questions, most of which were selected from a published and validated questionnaire on knowledge, concerns and management of fever in children. Some additional questions were also added, when considered important, to achieve the aim of the research. Socio-demographic data obtained included age of the mother, level of education attained, and monthly family income and the number of children. Appropriateness of responses to questions was determined on the basis of current medical literature. No assistance was given during the completion of the questionnaire. Mothers who couldn’t read Arabic were excluded from the study.

The questionnaires collected were hand-checked for completeness before data entry and analyzed using appropriate statistical tests. The analysis was done on SPSS (Statistical Package for Social Sciences, version 13.0). The descriptive statistics, frequencies and percentages, were used to describe socio-demographic characteristics. Pearson Chi-square test of independence was used to test the association between educational status and the number of children registered there. Investigators (doctors) explained the purpose of the study to the mothers and each female parent, with her permission, was given a suitably structured standard questionnaire in Arabic to complete while sitting in the waiting rooms. It contained different questions, most of which were selected from a published and validated questionnaire on knowledge, concerns and management of fever in children. Some additional questions were also added, when considered important, to achieve the aim of the research. Socio-demographic data obtained included age of the mother, level of education attained, and monthly family income and the number of children. Appropriateness of responses to questions was determined on the basis of current medical literature. No assistance was given during the completion of the questionnaire. Mothers who couldn’t read Arabic were excluded from the study.

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The majority of mothers (81.6%) believed that teething can cause fever in children. Only 8.9% did not believe so, and 9.5% of mothers were not sure. There was no statistically significant association between the educational level of mothers and method used to measure temperature was statistically significant (p < 0.05).

The most common site that mothers used for measuring temperature of a child less than three years of age was the armpit (57.3%), followed by the ears (19.2%) and then the anus (17.5%). The least common site was the mouth (6.1%). In order to monitor fever, 37.5% mothers would check their child temperature less than four hourly, 37.3% four hourly, 10.8% six hourly and 14.4% more than six hourly. 62.7% thought it was not necessary for every febrile child to be prescribed antibiotics. On the other hand, 21.7% of mothers’ thought that every febrile child should be prescribed an antibiotic. The remaining 15.6% of mothers’ were not sure. The association between perceived need of antibiotics and educational status was statistically very highly significant (p < 0.001).

The majority of mothers (81.6%) believed that teething can cause fever in children. Only 8.9% did not believe so, and 9.5% of mothers were not sure. There was no statistically significant association between the educational level of mothers and the preferred site of temperature measurement, frequency of temperature recording, and teething as a cause of fever.

Description of the mothers’ self management of fever is shown in Table 3. The child was considered febrile at body temperatures of 37 °C or less by

<table>
<thead>
<tr>
<th>Variables</th>
<th>n</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean ± SD)</td>
<td>33.68 ± 6.91</td>
<td></td>
</tr>
<tr>
<td>Number of children (mean ± SD)</td>
<td>3.45 ± 1.78</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Level of education</th>
<th>n</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than high school</td>
<td>79</td>
<td>15.2</td>
</tr>
<tr>
<td>High school</td>
<td>110</td>
<td>21.2</td>
</tr>
<tr>
<td>Diploma</td>
<td>133</td>
<td>25.6</td>
</tr>
<tr>
<td>University or higher</td>
<td>198</td>
<td>38.1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Family income</th>
<th>n</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 500 KD</td>
<td>65</td>
<td>25.0</td>
</tr>
<tr>
<td>500 – &lt;1000 KD</td>
<td>193</td>
<td>37.2</td>
</tr>
<tr>
<td>1000 – &lt;1500 KD</td>
<td>160</td>
<td>30.8</td>
</tr>
<tr>
<td>1500 KD and above</td>
<td>101</td>
<td>19.5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Number of children</th>
<th>n</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 – 2</td>
<td>182</td>
<td>35.0</td>
</tr>
<tr>
<td>3 – 4</td>
<td>192</td>
<td>36.9</td>
</tr>
<tr>
<td>5 – 6</td>
<td>125</td>
<td>24.0</td>
</tr>
<tr>
<td>≥ 7</td>
<td>21</td>
<td>4.0</td>
</tr>
</tbody>
</table>

KD = Kuwait Dinar
40.7% of the mothers, at 38 ºC and above by 57.2% and 2.1% did not know when to consider their child feverish. The table also reveals that 52.4% of all mothers would give antipyretic medication when the body temperature is 38 ºC. About 39% of mothers initiated antipyretic treatment for a body temperature of 37 ºC, and 7.4% of mothers would wait till the temperature reached 39 ºC or more. When a child is feverish, 13.8% of mothers gave antipyretic, 3.0% of mothers applied sponge bathing, 8.1% stated they would take the child to a doctor immediately while three fourth of the mothers’ (75.0%) gave antipyretics, applied sponge bathing and consulted a physician as well. Oral medications were preferred by 45.2% of mothers, rectal medications by 17.1% and both by 37.7%. The mothers’ main sources of knowledge about fever in children were the doctors and nurses (37.1%), relatives and friends (29.6%), reading (24.9%), pharmacists (0.8%), and others (7.5%).

Table 2: The relationship between educational status of the mothers and the perception of fever

<table>
<thead>
<tr>
<th>Variables</th>
<th>All Subjects</th>
<th>Less than high school</th>
<th>High school</th>
<th>Diploma</th>
<th>Graduate</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
<td></td>
</tr>
<tr>
<td>Fever recognition</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>General looks</td>
<td>174 (34.8)</td>
<td>26 (33.3)</td>
<td>43 (40.6)</td>
<td>44 (34.6)</td>
<td>61 (32.3)</td>
<td>0.582</td>
</tr>
<tr>
<td>Touching child</td>
<td>163 (32.6)</td>
<td>30 (38.5)</td>
<td>32 (30.2)</td>
<td>43 (33.9)</td>
<td>58 (30.7)</td>
<td></td>
</tr>
<tr>
<td>Measuring temperature</td>
<td>163 (32.6)</td>
<td>22 (28.2)</td>
<td>31 (29.2)</td>
<td>40 (31.5)</td>
<td>70 (37.0)</td>
<td></td>
</tr>
<tr>
<td>Kind of Thermometer used</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mercury thermometer</td>
<td>67 (15.7)</td>
<td>9 (17.6)</td>
<td>21 (23.9)</td>
<td>19 (16.8)</td>
<td>18 (10.3)</td>
<td>0.019</td>
</tr>
<tr>
<td>Digital thermometer</td>
<td>26 (62.7)</td>
<td>26 (51.0)</td>
<td>48 (54.5)</td>
<td>68 (60.2)</td>
<td>125 (71.8)</td>
<td></td>
</tr>
<tr>
<td>Fore-head strip</td>
<td>92 (21.6)</td>
<td>16 (31.4)</td>
<td>19 (21.6)</td>
<td>26 (23.0)</td>
<td>31 (17.8)</td>
<td></td>
</tr>
<tr>
<td>Site</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anus</td>
<td>89 (17.5)</td>
<td>14 (17.9)</td>
<td>22 (20.4)</td>
<td>25 (19.1)</td>
<td>28 (14.5)</td>
<td>0.097</td>
</tr>
<tr>
<td>Mouth</td>
<td>31 (6.1)</td>
<td>10 (12.8)</td>
<td>6 (5.6)</td>
<td>6 (4.6)</td>
<td>9 (4.7)</td>
<td></td>
</tr>
<tr>
<td>Arm pit</td>
<td>292 (57.3)</td>
<td>45 (57.7)</td>
<td>59 (54.6)</td>
<td>79 (60.3)</td>
<td>109 (56.5)</td>
<td></td>
</tr>
<tr>
<td>Ears</td>
<td>98 (19.2)</td>
<td>9 (11.5)</td>
<td>21 (19.4)</td>
<td>21 (16.0)</td>
<td>47 (24.4)</td>
<td></td>
</tr>
<tr>
<td>Temperature checking frequency</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than four hours</td>
<td>190 (37.5)</td>
<td>35 (46.7)</td>
<td>37 (34.6)</td>
<td>52 (39.7)</td>
<td>66 (34.0)</td>
<td>0.227</td>
</tr>
<tr>
<td>Every four hours</td>
<td>189 (37.3)</td>
<td>20 (26.7)</td>
<td>37 (34.6)</td>
<td>53 (40.5)</td>
<td>79 (40.7)</td>
<td></td>
</tr>
<tr>
<td>Every six hours</td>
<td>55 (10.8)</td>
<td>8 (10.7)</td>
<td>12 (11.2)</td>
<td>15 (11.5)</td>
<td>20 (10.3)</td>
<td></td>
</tr>
<tr>
<td>More than six hours</td>
<td>73 (14.4)</td>
<td>12 (16.0)</td>
<td>21 (19.6)</td>
<td>11 (8.4)</td>
<td>29 (14.9)</td>
<td></td>
</tr>
<tr>
<td>Need of antibiotics</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>113 (21.7)</td>
<td>30 (38.0)</td>
<td>26 (23.6)</td>
<td>24 (18.0)</td>
<td>33 (16.7)</td>
<td>0.001</td>
</tr>
<tr>
<td>No</td>
<td>326 (62.7)</td>
<td>38 (48.1)</td>
<td>61 (55.5)</td>
<td>88 (66.2)</td>
<td>139 (70.2)</td>
<td></td>
</tr>
<tr>
<td>Not sure</td>
<td>81 (15.6)</td>
<td>11 (13.9)</td>
<td>23 (20.9)</td>
<td>21 (15.8)</td>
<td>26 (13.1)</td>
<td></td>
</tr>
<tr>
<td>Teething</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>422 (81.6)</td>
<td>70 (88.6)</td>
<td>91 (84.3)</td>
<td>108 (81.2)</td>
<td>153 (77.7)</td>
<td>0.375</td>
</tr>
<tr>
<td>No</td>
<td>46 (8.9)</td>
<td>5 (6.3)</td>
<td>6 (5.6)</td>
<td>13 (9.8)</td>
<td>22 (11.2)</td>
<td></td>
</tr>
<tr>
<td>Not sure</td>
<td>49 (9.5)</td>
<td>4 (5.1)</td>
<td>11 (10.2)</td>
<td>12 (9.0)</td>
<td>22 (11.2)</td>
<td></td>
</tr>
</tbody>
</table>

* p-values were generated using the chi square tests; ** NS, p-value not statistically significant because > 0.05

Table 3: The mothers’ ways of self management of a feverish child

<table>
<thead>
<tr>
<th>Variables</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temperature of feverish child</td>
<td></td>
</tr>
<tr>
<td>35 – 37</td>
<td>211 (40.7)</td>
</tr>
<tr>
<td>38 – 40</td>
<td>297 (57.2)</td>
</tr>
<tr>
<td>Don’t Know</td>
<td>11 (2.1)</td>
</tr>
<tr>
<td>Temperature to give antipyretics</td>
<td></td>
</tr>
<tr>
<td>35 ºC</td>
<td>1 (0.2)</td>
</tr>
<tr>
<td>36 ºC</td>
<td>6 (1.2)</td>
</tr>
<tr>
<td>37 ºC</td>
<td>199 (38.8)</td>
</tr>
<tr>
<td>38 ºC</td>
<td>269 (52.4)</td>
</tr>
<tr>
<td>39 ºC</td>
<td>33 (6.4)</td>
</tr>
<tr>
<td>40 ºC</td>
<td>5 (1.0)</td>
</tr>
<tr>
<td>Fever management</td>
<td></td>
</tr>
<tr>
<td>Give nothing</td>
<td>1 (0.2)</td>
</tr>
<tr>
<td>Give antipyretics</td>
<td>70 (13.8)</td>
</tr>
<tr>
<td>Cold sponges</td>
<td>15 (3.0)</td>
</tr>
<tr>
<td>Antipyretics + sponges + consult doctor</td>
<td>380 (75.0)</td>
</tr>
<tr>
<td>Take child to doctor</td>
<td>41 (8.1)</td>
</tr>
<tr>
<td>Preferred way to give antipyretic</td>
<td></td>
</tr>
<tr>
<td>Mouth</td>
<td>235 (45.2)</td>
</tr>
<tr>
<td>Anal</td>
<td>89 (17.1)</td>
</tr>
<tr>
<td>Both</td>
<td>196 (37.7)</td>
</tr>
<tr>
<td>Source of knowledge</td>
<td></td>
</tr>
<tr>
<td>Relatives / friends</td>
<td>146 (29.6)</td>
</tr>
<tr>
<td>Reading</td>
<td>123 (24.9)</td>
</tr>
<tr>
<td>Doctors/Nurses</td>
<td>183 (37.1)</td>
</tr>
<tr>
<td>Pharmacist</td>
<td>4 (0.8)</td>
</tr>
<tr>
<td>Others</td>
<td>37 (7.5)</td>
</tr>
</tbody>
</table>

40.7% of the mothers, at 38 ºC and above by 57.2% and 2.1% did not know when to consider their child feverish. The table also reveals that 52.4% of all mothers would give antipyretic medication when the body temperature is 38 ºC. About 39% of mothers initiated antipyretic treatment for a body temperature of 37 ºC, and 7.4% of mothers would wait till the temperature reached 39 ºC or more. When a child is feverish, 13.8% of mothers gave antipyretic, 3.0% of mothers applied sponge bathing, 8.1% stated they would take the child to a doctor immediately while three fourth of the mothers’ (75.0%) gave antipyretics, applied sponge bathing and consulted a physician as well. Oral medications were preferred by 45.2% of mothers, rectal medications by 17.1% and both by 37.7%. The mothers’ main sources of knowledge about fever in children were the doctors and nurses (37.1%), relatives and friends (29.6%), reading (24.9%), pharmacists (0.8%), and others (7.5%).

Table 4 shows mothers’ fears from fever. 41.7% of mothers thought that every child with high temperature should be referred to the hospital for treatment, 46.5% thought not, 11.7% were not sure. Feverish children were always awakened from sleep to administer antipyretics by 59.3% of mothers, sometimes by 36.6% and never by...
4%. 94.1% believed that fever can cause harm, approximately 60% believed that an untreated fever could lead to convulsions, 28.2% believed that it could lead to both convulsions and brain damage, 1.8 and 2.7% believed that brain damage and death respectively could be a result; only 5.9% mothers thought nothing would happen. The association between perceived consequences of fever and level of education was statistically highly significant (p < 0.005, Table 5). A significant association was also found between perceived consequences of fever and number of children (p < 0.05, Table 6).

**DISCUSSION**

A cross-sectional study conducted in the capital governorate of Kuwait sought information on mothers’ knowledge about fever in children, how they manage it at home and what particular fears they bear in mind about fever. It does have the limitation of excluding mothers’ who could not read Arabic.

Two thirds of mothers recognize fever in the child by non-measurement methods which were observing the child’s general look or touching him. This tactile temperature taking practice has been shown to be inaccurate with a high percentage of false-negative or false-positive fever determination[13]. Chaturvedi D[14] concluded that touch is not a valid screening test for fever. Measuring the temperature is obviously the most accurate method of detecting fever, but only one third mothers actually measure the child’s temperature at home to detect fever. It is recommended that a thermometer should always be used by a medical staff to record fever and caregivers must be motivated for the same[14-16].

The optimal method and the best anatomical site for the assessment of fever have been widely debated in recent years with the introduction of ear thermometers[9]. Mothers seems to prefer using at home thermometers which are less annoying to the child and easy to read regardless of their accuracy.
bacterial infection\cite{25}, and to clarify to mothers the misconception regarding treating fever with an antibiotic.

A common myth that has persisted since the time of Hippocrates is the association of fever with teething\cite{19}. It seems that this myth is still persisting as seen in our study results where more than 80% of mothers thought that teeth eruption causes fever. Parents and clinicians have traditionally attributed to teething many symptoms such as fever, pain, irritability, diarrhea, drooling and sleep disturbance, but a prospective cohort study carried out in Washington which investigated the relationship between tooth eruption, fever and teething symptoms provided no conclusive evidence that a relationship exists between the eruption of teeth and the experience of these symptoms, and a temperature greater than 38 °C or other serious symptoms in an infant should not be regarded by clinicians as due to teething and should be evaluated appropriately\cite{26}.

The normal body temperature varies with site and has a diurnal variation of about 0.5 °C. In adults the mean oral temperature is 36.8 °C. If it is 36 or 37 °C, it is accepted as normal. 40.7% of mothers would regard a temperature below 37 °C as indicative of fever. This shows that mothers do not know what temperature indicates fever. An almost similar number (38.8%) would treat inappropriately a normal temperature with an antipyretic. A survey of relatively well educated parents in the USA and two other studies also found that about one-fourth gave antipyretics to children when the temperature was within the normal range\cite{19,27,28}. In this study, more mothers preferred oral route rather than the rectal route.

The type of harm that mothers thought their children would suffer from was mainly convulsions; this was more apparent among the less educated mothers and those with more children. Limited knowledge and a bad past experience with a febrile child is a possible interpretation. Almost one-third of mothers thought that fever might lead to both brain damage and convulsions. The same fears were found among parents in several other

<table>
<thead>
<tr>
<th>Consequences of a feverish child</th>
<th>All Subjects</th>
<th>Number of Children</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N (%)</td>
<td>1 – 2 n (%)</td>
</tr>
<tr>
<td>Convulsion</td>
<td>301 (59.0)</td>
<td>100 (56.5)</td>
</tr>
<tr>
<td>Convulsion and brain damage</td>
<td>144 (28.2)</td>
<td>45 (25.4)</td>
</tr>
<tr>
<td>Other</td>
<td>35 (6.9)</td>
<td>22 (12.4)</td>
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<tr>
<td>Nothing</td>
<td>30 (5.9)</td>
<td>10 (5.6)</td>
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<td></td>
<td>p-value*</td>
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<td>1 – 4 n (%)</td>
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<td></td>
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<td>106 (56.1)</td>
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<td>p-value*</td>
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<td>0.026</td>
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</table>

* p-value was generated using the chi square test.

Table 6: The relationship between the number of children and the expected consequences of fever
High fever can cause a short “benign, febrile” seizure in 3 to 5 percent of all children, but the seizure does not injure the brain[30]. This event is difficult to prevent because febrile seizures usually occur during the first few hours of a fever and prophylactic administration of antipyretics does not decrease seizure recurrence[31,32]. Concerns about fever and its potential harmful effects may lead to parental behavior such as excessive monitoring and treatment[31]. This fear is translated into most children being awakened at night for antipyretics[21]. This causes unnecessary discomfort and distress to the child and considered intrusive to children during the time that they are recovering from their illness[33].

CONCLUSION
This study showed that mothers are often unaware of what body temperature indicates a fever and the way they deal with a feverish child was sometimes incorrect or inappropriate. We also noticed that a considerable number of them experienced fear and anxiety when their children developed fever. They believe that the fever could lead to serious complications and this probably forces them to rush to doctors. Only about one third of mothers indicated that doctors and nurses were their primary source of fever-related information. We would recommend that health care providers spend enough time with mothers attending a feverish child, explaining and answering their queries about fever, and providing them with adequate information that might reduce their fears. Use of a well-designed health education aid that presents evidence-based information on fever in a clear, consistent and entertaining manner would be more effective.

REFERENCES
Case Report

Neonatal Langerhan’s Cell Histiocytosis; Early Presentation with Delayed Diagnosis

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Kuwait Medical Journal 2007, 39 (4): 355-357

ABSTRACT

Neonatal Langerhan’s cell histiocytosis (LCH) is a rare disease which presents in the first four weeks of life with skin manifestations; although the diagnosis may be delayed till other organ involvement becomes apparent. We describe a four-month-old male infant who presented with skin lesions in the neonatal period and was diagnosed later, when involvement of lymph nodes, liver, spleen and bone became apparent. Due to the possibility of clinically unapparent involvement of other organ systems in neonatal LCH, thorough clinical, laboratory and imaging studies are mandatory for a comprehensive evaluation of all cases on presentation.

KEY WORDS: Langerhan’s cell histiocytosis, neonatal, skin lesions

INTRODUCTION

Langerhan’s cell histiocytosis (LCH) is a rare disorder with diverse clinical presentations and prognosis[1]. Its incidence is 2-5/1,000,000/year and is slightly more prevalent in boys[2]. Previously called Histiocytosis X, it was renamed LCH to differentiate it from reactive and neoplastic causes of histiocytosis[3]. LCH includes eosinophilic granuloma, Hand-schuller Christian and Letterer-Sive disease[4]. Neonatal LCH is defined as LCH presenting within the first four weeks of life irrespective of the age at diagnosis. Incidence is estimated as 1-2/1,000,000/year[5].

Baseline evaluation for a newly diagnosed patient requires search for all possible sites of involvement[6]. Treatment modalities of chemotherapy, radiotherapy, surgical intervention or combination of all these depends on the extent of the disease[7].

We present a male infant who had skin manifestations in the neonatal period and was diagnosed as LCH at four months of age only when involvement of other organ systems became apparent.

CASE REPORT

A four-month-old male infant from Srilanka who was said to be previously well until the parents noticed a neck swelling, low grade fever and pallor one week before presentation. He had history of multiple skin lesions appearing within the first month of age all over his body and face. He was a product of full term normal delivery, from non-consanguineous parents. There were no perinatal problems. He has a healthy elder brother. There was no family history of malignancy or blood diseases.

The patient on examination was alert, conscious, thriving well, but febrile and pale. There was bilateral proptosis more pronounced on the left and marked bilateral swelling of the neck. His growth parameters were at the 10th centile for age.

Skin examination revealed widespread vesiculo-pustular lesions especially prominent on the forehead, scalp, trunk and groin, together with dry scaly hypopigmented patches scattered all over the body (Fig. 1).

There was marked bilateral cervical lymphadenopathy with enlarged bilateral axillary and inguinal lymph nodes to a lesser extent. These nodes were all firm, non-tender, with no signs of overlying inflammation.

Chest examination showed tachypnea, mild subcostal retraction with bilateral equal air entry and no added sounds. Cardiovascular examination was normal. Liver was 3 cm and spleen 1 cm below their respective costal margins. There were no other masses felt on abdominal examination. Apart from mild hypotonia and head lag his CNS examination was normal.

Basic blood investigations showed normochromic normocytic anemia, with normal white blood cells and platelets. Blood chemistry, liver, renal functions, plasma and urine osmolality as well as coagulation studies were normal. In view of his extensive

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skin lesions with marked lymphadenopathy and hepato-splenomegaly LCH was suspected. A plain skull radiograph was done which showed multiple punched out osteolytic lesions (Fig. 2).

Chest X-ray showed a widened mediastinum while CT chest revealed large multinodular anterior mediastinal mass with bilateral hilar lymph nodes and extensive fibro-nodular infiltration of both lung parenchymas (Fig. 3).

There were also multiple osteolytic lesions in both scapulae and thoracic cage. CT abdomen showed diffuse hepato-splenomegaly with enlargement of the celiac, iliac and inguinal lymph nodes. Osteolytic lesions of the iliac bones and vertebrae were seen. CT head showed normal brain tissue, multiple osteolytic lesions of the skull base and left sphenoid wing and soft tissue swelling compressing and displacing the left optic nerve medially (Fig. 4).

Extensive infiltration of the upper neck and retropharyngeal space with multiple soft tissue nodules and osteolytic lesions of the jaw were seen. Lymph node, skin, and bone marrow biopsies were rejected by his father at that time only to be done in Sri Lanka where the father took his child. Bone marrow biopsy done there revealed a hypoplastic marrow. Lymph node excision biopsy showed infiltration with mononuclear and multinuclear Langerhan’s cells with numerous eosinophils.
Special stain S 100 was positive. He received two doses of vincristine and oral steroids. He was brought back to Kuwait where he was referred to the pediatric oncologist; he was treated as a case of LCH with multiorgan involvement. He received two cycles of vinblastine injections and oral steroids but unfortunately died of an intercurrent infection during the above treatment four months after diagnosis.

DISCUSSION

The variability in the presentation of neonatal LCH contributes to the frequent delay in diagnosis. When cutaneous involvement is the only obvious presenting sign 6-12 months may be required to determine the ultimate extent of the disease. Typical cutaneous lesions in neonatal LCH are scaly erythematous, seborrhoic like eruptions of brown to red papules especially prominent in intertriginous zones. Superficial ulcerations may occur. Weeping lesions may suggest eczema.

Sarah et al[8] followed up 19 cases in a retrospective validation cohort study who presented (as in our case) with skin lesions in the neonatal period and were subsequently diagnosed as LCH upon involvement of other organs. As in our case the most common initial skin lesions in their patients were crusted vesiculo-pustules. Those lesions were misdiagnosed as chronic dermatitis or as part of an infectious process. Twelve of the 19 patients had multisystem disease and two of them subsequently died.

When the diagnosis of neonatal LCH is suspected a comprehensive workup for systemic disease evaluation should be done. This includes careful physical examination as well laboratory and radiological investigations.

In a retrospective study done by Minkov[5], in which he studied 61 patients who presented in the neonatal period, only 20 cases were diagnosed within the first four weeks of life. Diagnosis was established later in the remaining 41 cases with median time from initial presentation to diagnosis being two months (range = 0 days - 23 months). In another retrospective study, in which the group of patients presented between 0-6 months of age, the average time for diagnosis was about six months[9]. Because of this delay in diagnosis, the true incidence of congenital/neonatal LCH may be expected to be higher.

A comprehensive evaluation of all cases is essential. Treatment depends on the extent of the disease, age at diagnosis, and presence of organ dysfunction. As in our case, most patients receive a combination of corticosteroids and chemotherapeutic agents (usually vinblastine or etoposide)[10]. Widely accepted prognostic factors are age, extent of organ involvement, and presence of organ dysfunction at diagnosis[10]. Awareness about the variety of ways this disease can present itself and its wide spread organ involvement is vital for all pediatricians who encounter this disease.

REFERENCES

Case Report

Villous Adenoma Depletion Syndrome: Case Report

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ABSTRACT
Villous recto-sigmoidal tumors with severe fluid and electrolyte loss are rare. We report the case of a 90-year-old man with a 10 year history of mucous diarrhea. On admission he had pre-renal uremia, severe hyponatremia and hypokalemia. Colonoscopy showed a large rectal villous adenoma. Conservative treatment was followed by a complete, though temporary, recovery of the renal function. The McKittrick-Wheelock syndrome is a condition of severe water and electrolyte depletion due to colonic secretory villous adenoma. It can be a diagnostic challenge. Sodium loss may be the dominant feature.

KEYWORDS: acute renal failure, depletion syndrome, villous adenoma

INTRODUCTION
Villous adenomas of the colon comprise approximately 10% of all colonic adenomas and tend to occur in patients more than 60 years old. The incidence of invasive carcinoma in villous adenomas < 2 cm in size is about 10%, whereas villous adenomas > 2 cm in size have > 50% chance of having invasive carcinoma[1]. Villous adenomas are generally large and bulky and tend to be distal in location, resulting sometimes in constipation and rectal prolapse[2].

In 1954, McKittrick and Wheelock described a subset of patients with villous adenoma who had profuse watery diarrhea leading to excessive losses of fluid and electrolytes, dehydration, circulatory collapse, pre-renal azotemia and metabolic acidosis[3]. Since then several reports have described a syndrome with severe dehydration, hyponatremia, hypochloremia, hypokalemia and metabolic acidosis occasionally resulting in cardiovascular collapse, renal insufficiency and death.

The clinical picture results from the chronic fluid and electrolyte depletion in the watery mucous rectal discharge occasionally associated with these tumors.

To highlight the importance of the metabolic disturbance that may develop and the high index of suspicion required for diagnosis, a case of recurrent acute renal failure due to a large rectal villous adenoma is reported. The pathophysiology and management of the villous adenoma depletion syndrome are discussed.

CASE REPORT

A 90-year-old man presented to our emergency department with generalized weakness, drowsiness and vomiting for the previous seven days. He had no abdominal pain, but suffered from intermittent diarrhea (described as loose jelly-like stools occasionally streaked with blood) for the past 10 years.

Physical examination was unremarkable except for moderate signs of dehydration and mild disorientation. He had a heart rate of 80/min and a blood pressure of 100/60 mmHg. His abdominal examination was unremarkable. Rectal examination revealed mucous discharge with blood streaks, but no masses were felt.

Aggressive but meticulous fluid and electrolyte replacement was started. His electrolytes almost normalized over the next seven days. The results of the initial serum electrolytes and the ones done a week later after treatment are shown in Table 1.

At this stage the family members were informed about the importance of performing a colonoscopy. However, they refused to give consent. Hence the patient was discharged home. He was readmitted three weeks later with a similar picture and he was in acute renal failure.

Consent was obtained during this admission and a flexible colonoscopic examination was performed. This revealed a large friable polypoid mass that oozed out a mucinous solute; the mass extended from the first rectal valve to at least 15 cm. The rest of the colon was normal.

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Histopathologic examination of sections from colonoscopic biopsy material on light microscopy revealed villous adenoma morphology with mild dysplasia (Fig. 1). These pathological findings in a patient with severe fluid and electrolyte loss are consistent with a secretory villous adenoma.

Surgical resection was refused by the family; therefore a trial of nonsteroidal anti-inflammatory drug therapy (using diclofenac sodium 50 mg twice daily) was given. This had to be discontinued after a few days as the patient developed a severe allergic reaction. Since then the patient has required frequent admissions for the same problem with severe metabolic disturbances requiring intensive fluid and electrolyte management.

**DISCUSSION**

Colonic villous adenomas have a tendency to occur in the rectum and rectosigmoid regions. These adenomas are generally sessile and may be up to 10 cm in diameter. The malignant potential of adenomatous polyps increases with size, villous configuration, and degree of dysplasia[4]. Secretory villous adenomas differ from non-secretory villous adenomas on light microscopic and ultrastructural examination. These differences may to some extent clarify the secretory diarrhea associated with these villous adenomas. In non-secretory villous adenoma, mucous secretion is diminished, while in secretory villous adenoma, there is exaggerated mucous production. In these lesions, most of the adenomatous epithelium is composed of prominent, clear mucin-filled goblet cells. In addition, ultrastructural study of villous adenomas shows that secretory villous adenomas are hypersecretory, with atypical goblet cells that produce a mucin of abnormal composition[5].

The depletion syndrome characterized by cardiovascular collapse, acute renal failure, hyponatremia and a hypokalemic, hypochloremic metabolic acidosis is a rare complication of a rectal villous adenoma[3]. Characteristically there is watery, mucinous diarrhea with bowel actions as frequent as 20 times a day, not uncommonly for up to 15 years prior to the recognition of the cause[6]. At the onset the fluid and electrolyte losses are easily compensated by increased oral intake and renal regulation. As the tumor size increases these losses overwhelm compensatory mechanisms and the patient may seek medical attention[7]. One must keep in mind that digital examination of the rectum might miss even large tumors in many cases due to their soft, mucin-covered surface, often described as velvet-like. The mechanism of fluid and electrolyte loss is unclear. In a series of reported cases, secretory villous adenomas associated with the depletion syndrome were large, ranging from 7 to 18 cm in greatest dimension and were situated primarily in the rectum and occasionally in the sigmoid colon[8]. The large size allows for more surface area for secretion and their distal location limits the colon’s ability to reabsorb fluid resulting in the depletion syndrome[9]. Locally released prostaglandin E2 has been suggested as the secretagogue responsible for salt wasting[10]. Steven et al compared the rectal effluents from a secretory villous adenoma and infectious diarrhea. They discovered that immunoreactive prostaglandin E2 level were three-folds higher in the patients with a secretory villous adenoma. In an attempt to further categorize the presence of a secretagogue in the villous adenoma depletion syndrome, Jacob and colleagues had compared the cyclic nucleotide metabolism of a large secretory villous adenoma and infectious diarrhea. They discovered that immunoreactive prostaglandin E2 level were three-folds higher in the patients with a secretory villous adenoma. In an attempt to further categorize the presence of a secretagogue in the villous adenoma depletion syndrome, Jacob and colleagues had compared the cyclic nucleotide metabolism of a large secretory villous adenoma with a non-secretory villous adenoma, a solid carcinoma and their normal mucosa. The adenylate cyclase, cyclic AMP content, and cyclic AMP-dependent protein kinase ratios in the secretory tumor were increased as compared to these values in the non-secretory tumors and normal mucosae. They suggested that increased adenylate cyclase activity might be responsible for the massive

| Table 1: Biochemical parameters before and after treatment along with the normal values |
|---------------------------------------------|---------------------------------------------|---------------------------|
| **Biochemistry on presentation** | **Biochemistry after fluid and electrolyte repletion** | **Normal range** |
| Sodium | 108 mmol/l | 133 mmol/l | 134 - 144 mmol/l |
| Potassium | 3.0 mmol/l | 3.9 mmol/l | 3.60 - 5.10 mmol/l |
| Chloride | 62 mmol/l | 104 mmol/l | 94 - 115 mmol/l |
| Bicarbonate | 20.9 mmol/l | 19.6 mmol/l | 17.0 - 35.0 mmol/l |
| BUN | 66.5 mmol/l | 13.9 mmol/l | 2.5 - 7.2 mmol/l |
| Creatinine | 303 mmol/l | 96 mmol/l | 53 - 97 mmol/l |
| Serum osmolality | 94 mosm/kg | 284 mosm/kg | 280 - 300 mosm/kg |
| Urate | 1013 mmol/l | - | 150 - 430 mmol/l |
secretory diarrhea in patients with a secretory villous adenoma\textsuperscript{10}.

Whilst the mechanism remains unclear, its consequences are dramatic. Resultant losses can amount to 1.5 - 3.5 liters of fluid containing sodium 40-160 mmol/l (mean = 120 mmol/l), potassium 15-105 mmol/l (mean = 60 mmol/l) and chloride 30-165 mmol/l (mean = 123 mmol/l)\textsuperscript{12}. This results in a characteristic presentation with circulatory collapse, pre-renal uremia, hyponatremia, hypochloremia, hypokalemia and metabolic acidosis. The latter is particularly severe and often underestimated due to the co-existent metabolic acidosis\textsuperscript{7}. Rectal losses of sodium chloride are isotonic, whereas potassium losses are well in excess of plasma concentration with active secretion in the stool accounting for up to 150 mmol/day\textsuperscript{7}. This is crucial to the clinical presentation as chronic hypokalemia not only contributes to the patient’s symptoms, but also inhibits the normal compensatory mechanisms of electrolyte and water conservation.

A state of nephrogenic diabetes insipidus develops due to more than one mechanism; these include an inability to generate maximal medullary tonicity, impaired cellular responsiveness to antidiuretic hormone (ADH) and possible impaired release of ADH from the neurohypophysis\textsuperscript{7}. Reversal of the biochemical derangement is the cornerstone of successful management. Once resuscitated, immediate surgical resection of the tumor is the treatment of choice. Steven et al\textsuperscript{10} concluded that prostaglandin E2 is the mediator of fluid and electrolyte secretion by villous adenomas of the rectum. They suggested that the use of PG synthetase inhibitor (indomethacin) may facilitate the correction of severe fluid and electrolyte deficits in patients with large villous adenomas of the rectum. Another study\textsuperscript{13} on rabbit ileum demonstrated that indomethacin inhibited secretion of potential secretagogues, including cholera toxin and dibutylryl - cyclic adenosine monophosphate at sites that included the prostaglandin synthetic pathway. In 1989, Waddell et al\textsuperscript{14} reported regression of polyps in patients with familial polyposis using a nonsteroidal anti-inflammatory drug, sulindac. This observation has been confirmed in two subsequent studies by Labayle et al\textsuperscript{15} and Giardiello et al\textsuperscript{16}. Gowen, in 1996\textsuperscript{17} also showed a similar response in a patient with two villous adenomas of the colon using a long acting NSAID, piroxicam.

**CONCLUSION**

The reported case highlights the serious metabolic disturbances that occur in patients with villous adenoma. Lack of awareness of this complication might lead to a fatal outcome, as energetic replacement is required in the management of these patients. Treatment with NSAIDs would not eliminate the attendant risk of cancer and should not replace surgery as the mainstay of therapy.

**REFERENCES**

Case Report

Colloid Carcinoma of Colon Presenting as Intussusception in an Adult - Case Report

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ABSTRACT

Intussusception in adults is rare accounting for less than 5% of cases of intussusception. There is usually an underlying primary pathology. The presentation and clinical findings in adults are uniformly nonspecific making clinical diagnosis difficult. Diagnosis therefore, depends on a high index of suspicion and ancillary radiological aids.

KEY WORDS: adult, intussusception

INTRODUCTION

Adult intussusception is an uncommon clinical condition presenting with nonspecific symptoms\(^1,2\). There is usually an underlying pathology as compared to the same condition in the pediatric age group\(^2\).

Diagnosis therefore, depends on a high index of suspicion and ancillary radiological aids\(^3\). We present below the case of a 65 year-old male with colloid carcinoma of the colon presenting as intussusception.

CLINICAL PRESENTATION

A 65-year-old male Egyptian visitor presented with a five day history of abdominal pain and constipation. There was no background history of medical illness or previous surgery. The pain was described as cramp-like, off and on. There was no associated vomiting but he gave a positive history of constipation for five days. There was also a history of progressive abdominal distention with increasing discomfort.

On examination, he was mildly febrile (T- 37.5 °C), pulse was 84/min and BP was 120/80 mmHg. His chest was clinically clear with equal air entry bilaterally. Abdomen was distended and tympanic with vague periumbilical tenderness. There was no palpable distinct mass and bowel sounds were sluggish.

Laboratory results of complete blood count, liver function tests, serum urea, creatinine and electrolytes were all normal except for a total leucocyte count of 11,500/mm\(^3\). X-rays of abdomen (erect & supine) - showed distended colon with distal gases and ground glass opacity of the right upper abdomen.

Abdominal ultrasound scan showed a mass in the right upper quadrant - about 8 x 5 cm, sausage shaped with ‘pseudo kidney’ sign consistent with intussusception (Fig. 1). Water soluble contrast enema showed an obstructing lesion just distal to hepatic flexure with ‘claw’ sign (Fig. 2).

Laparatomy and possibility of colectomy and/or colostomy was discussed with the patient. Following a signed consent, he had surgery done. Operative findings were as follows: mass in right upper quadrant made up of distal ileum, cecum, ascending colon and proximal transverse colon.

Based on the patient’s age, the decision for a right hemicolectomy with primary anastomosis rather than reduction was made. The resection included the distal 10 cm of terminal ileum extending distal to mid transverse colon with the accompanying mesentery. The resected specimen on reduction showed a huge cecal mass with mucoid gelatinous appearance (Fig. 3).

Histology confirmed the diagnosis of colloid carcinoma of colon without mesenteric node involvement. Resection margins were also said to be free.

The patient’s postoperative period was uneventful and he was discharged on the eighth postoperative day. He was seen at the surgical outpatient two weeks later. At that time he remained well and was given a medical report to continue treatment in his native Egypt.

DISCUSSION

Intussusception in adults is rare accounting for about 5% of cases and 0.003 to 0.2 of hospital
admissions and 1% of cases of bowel obstruction\(^1\). In a series report from the University Hospital Geneva, Switzerland, only 10 cases of adult intussusception were reported over a 17 year period. Out of these, six had an underlying malignant pathology and all involved the large bowel\(^4\).

Intussusception in adults has an underlying primary pathology in up to 90% of cases as compared to pediatric cases in which 90% are idiopathic\(^1,2,5-8\). Intussusception is a pathologic condition in which a segment of bowel telescopes over a more distal segment. The basic anomaly is a difference in velocity of peristalsis between bowel segments.

Of the reported adult cases, 60% are due to malignant neoplastic conditions, mainly carcinomas and lymphomas while the remaining are due to benign neoplastic or inflammatory conditions; the commonest being lipomas\(^8,11,14\).

Diagnosis in adults is delayed and made difficult by the non-specific symptoms which include colicky abdominal pain, abdominal distention; which is mild unless complicated by obstruction, vomiting, constipation, diarrhea, bloody stool and fatigue. Clinical examination findings are also uniformly non-specific. Preoperative clinical diagnosis is usually an exception rather than the rule\(^1,2,5,9\).

Diagnosis is made by imaging studies like abdominal ultrasound scan, CT scan and contrast enema. The most reliable is the contrast enhanced CT scan of the abdomen. Classical findings include, alternating layers of low and high attenuation known as the ‘target’ sign\(^5,9\). Ultrasound findings which are severely limited by operator experience include ‘pseudo kidney’ sign, ‘target sign’ and ill defined abdominal masses\(^1,3,7\).

In our case, ultrasound alone gave a good clue to the diagnosis. Contrast enema only serves to confirm the findings of the above modalities. The typical finding with contrast enema is the ‘claw’ sign\(^13\).

Endoscopy has a limited role in the diagnosis of adult intussusception. The insufflation needed may complicate the clinical status of the patient. However, cases due lipomas in adults can be diagnosed and primarily treated by endoscopy\(^11,14\).

One area of major controversy in adult intussusception is whether or not to reduce it intra-operatively before resection. Resection is needed in 90% of cases due to the underlying primary pathology\(^4\). Advocates contend that this reduces the length of bowel resected and avoids the complications of extensive bowel resection.

The main disadvantage of this maneuver is the possibility of seedling with dissemination in cases of malignancy and bowel perforation. This is especially true as up to 60% have a primary
malignant etiology.

The recommendation is direct resection in patients with colon involvement especially in those above 45 years of age\textsuperscript{1,6,10,15}.

In our case, primary resection was done with good post-operative recovery and histological findings also confirmed a fair prognosis (Dukes B).

CONCLUSION

The diagnosis of adult intussusception is seldom made pre-operatively. Ultrasound in experienced hands can guide to the diagnosis, which can be confirmed by a CT scan or contrast enema.

ACKNOWLEDGMENT

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REFERENCES

Case Report

CHARGE Association with Schizencephaly in a Newborn Infant: A Case Report

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ABSTRACT

CHARGE association is an increasingly recognized non-random clustering of congenital malformations. We present a baby with readily recognizable clinical features that lead to a prompt diagnosis of CHARGE association. The baby also had a schizencephaly which makes us ponder that this could very well be a neural crest migratory disorder stressing the need for an expanded classification of “neurocrestopathies”. The recently recommended diagnostic criteria of CHARGE association are also reviewed.

KEY WORDS: CHARGE, choanal atresia, coloboma, neonatal, schizencephaly

INTRODUCTION

The CHARGE association is a rare disorder that arises during early development and affects multiple organ systems[1]. It is a non-random occurrence of congenital malformations that occurs together more frequently than one would expect on the basis of chance[2,3]. There are certain diagnostic signs which enable a clinician to clinch the diagnosis and involve a multidisciplinary team in the management of this unique condition[3,4].

CASE REPORT

A single live preterm, small-for-date, girl baby was born to a P>0 Bangladeshi mother at 39 +4 weeks by an emergency lower segment Cesarean section due to fetal distress and bradycardia. The cord was around the neck once. The mother was 33 years of age and the father was 40 years old. The parents were non-consanguineous. The mother had primary infertility for about 10 years. She had regular antenatal care at the local polyclinic and was referred to the hospital only at the time of labor. There was no history of any malformations in the family.

The baby’s Apgar Score was 3, 7 and 8 at one, five and ten minutes respectively. An endotracheal intubation was done immediately and intermittent positive pressure ventilation was performed. The baby responded to the resuscitation and had spontaneous breathing at about ten minutes of age. The baby became cyanosed immediately on extubation and had to be re-ventilated again.

A nasogastric tube could not be passed through both the nostrils. The weight was 1436 g, length was 43 cm and the head circumference was 28.5 cm, and they were all below the 3rd centile.

The baby had dysmorphic features. She had the distinctive ‘CHARGE’ facies (Fig. 1). A square facial appearance with a broad forehead with asymmetry and malar flattening was present. The philtrum was long, the nasal columella were prominent and the nostrils had a ‘pinched’ appearance. There was a high arched palate.

The ears were small, simple, asymmetrical, lowset and posteriorly rotated. There was increased width and decreased length of the ears. The ear lobes were absent, the antihelices were prominent and the conchae were triangular in shape (Fig. 2).

There was hypertelorism and the palpebral fissures were short. The baby had clenched hands and a short sternum. The labia majora appeared hypoplastic. The cardiovascular system and the abdomen were normal.

A nasal fibroendoscopic examination revealed bilateral posterior bony choanal atresia with a deflected septum. This was confirmed by a CT scan of the nasopharynx (Fig. 3) which revealed narrowing of the internal nostrils with no contrast passage into the nasopharynx due to osteo choanal atresia.

Under general anaesthesia the posterior bony septa formed by the vomer were removed. A 3 mm size ‘U’ shaped stent was positioned and repeated suction was performed to maintain the patency.
The baby had assisted ventilation for about five weeks. The baby subsequently had bronchopulmonary dysplasia and was gradually weaned off the oxygen.

The baby had sucking and swallowing difficulties due to velopharyngeal incoordination.

**Pertinent investigations**

CT scan of the nasopharynx (Fig. 3) showed narrowing of the internal nostrils with no contrast passage into the nasopharynx due to osteomembranous choanal atresia. MRI Brain (Fig. 4) showed atrophy involving the left parietal lobe. There was a prominent schizencephalic cleft in the left parietal lobe extending into the left frontal lobe.

CT scan of the petrous temporal bone showed defective development of the bony part of the anterior wall of the external auditory canal. The tympanic membrane was not adequately visualized. The ossicular chain of the middle ear was deformed and seemed to be attached to the anterior wall of the middle ear cavity.

On ophthalmologic examination, there was no evidence of any coloboma.

A chromosomal study revealed XX Chromosome and the integrity of the chromosomes was preserved.

A chest skiagram and an ECG were normal. An echocardiography showed the heart to be normal. An ultrasound of the abdomen showed no renal anomalies.

The baby had severe sucking and swallowing difficulties and had to be fed by gavage feeds. There was a global developmental delay. There was microcephaly. The head circumference was 30 cm at about three months of age and this was well below the 3rd centile. There was severe growth retardation.

Thus, this infant had a combination of congenital anomalies, *viz*, a distinctive CHARGE facies, bilateral posterior choanal atresia, characteristic ear abnormalities, retardation of growth and development, swallowing problems (velopharyngeal incoordination due to cranial nerve IX/X dysfunction), small labia, central nervous system malformation namely schizencephaly and the abnormal ossicular chain which is consistent with a diagnosis of CHARGE syndrome.

**DISCUSSION**

The CHARGE association is a non-random clustering of congenital malformations.

Although it was first described by Hall in 1979, it was Pagon *et al* in 1981 who first coined the acronym CHARGE association, the features of which were coloboma, heart defects, atresia choanae, retardation of growth, genital anomalies and ear anomalies. Pagon *et al* proposed that to make a confident diagnosis of CHARGE association, four of the six major features included in the acronym have to be present and these should include either coloboma or choanal atresia or both.

The CHARGE association has an estimated prevalence of 1:10,000.

In recent times, several consensus diagnostic criteria have been proposed which incorporate both major and minor features for CHARGE association both to enhance clinical diagnosis and facilitate research efforts.

Blake *et al* have proposed that CHARGE association should be considered, if there are one or two major characteristics and several minor characteristics.

The major criteria are coloboma, choanal atresia, cranial nerve involvement and characteristic ear abnormalities.

The minor characteristics occur less frequently or are less specific to CHARGE association. They are a distinctive characteristic facies, genital hypoplasia, cardio-vascular malformations, short stature, orofacial clefting and developmental delay. Our patient had three major characteristics namely bilateral bony posterior choanal atresia.
characteristic ear anomalies and severe sucking and swallowing problems due to velopharyngeal dysfunction caused by the involvement of the IX and X cranial nerves. She also had the distinctive facies, developmental delay and growth retardation as minor criteria. The labia majora appeared hypoplastic but this finding is unreliable in the neonatal period.

Bilateral posterior choanal atresia is an uncommon congenital anomaly (one case in 5000 - 8000 live births)\(^3\) and it should always alert pediatricians to the possibility of CHARGE association\(^3,4\). Choanal atresia is seen in about 50 - 60% of patients with CHARGE association\(^3,4\). Our patient had bilateral bony posterior choanal atresia.

Eye malformations in the form of coloboma of the iris, retina, choroid or disc occur in more than 80% of patients with CHARGE\(^3\). Our patient did not have any eye abnormalities.

Distinctive ear anomalies have been reported in 90% of patients with CHARGE association\(^3\). The characteristic ear is small with increased width and decreased length, asymmetrical with a prominent antihelix and a distinctive triangular concha. The ear lobe is absent. This pattern of ear anomalies is so distinctive that a preliminary diagnosis of CHARGE association can often be made on the basis of the ear shape alone\(^3,5\). Our patient had the distinctive external ears seen in classical CHARGE association.

Computed tomography of the temporal bone is often helpful in defining structural ossicular and / or inner ear anomalies\(^3,6,7\).

A computed tomography of the petrous bone in this baby revealed defective development of the bony part of the anterior wall of the external auditory canal. The tympanic membrane was not adequately visualized. The ossicular chain of the middle ear was attached to the anterior wall of the middle ear cavity.

Cranial nerve dysfunction is seen in about 70 - 90% of patients with CHARGE association\(^3,8,9\).

There could be anosmia (cranial nerve I) facial palsy (cranial nerve VII), sensorineural hearing loss (VIII) and severe swallowing difficulties (IX, X). Our baby had severe swallowing difficulties due to velopharyngeal in-coordination and needed gavage feeds throughout the period of hospitalization.

A characteristic distinctive facies is seen in 80% of patients with CHARGE association\(^3,5,9\).

The most frequent facial findings consist of a broad forehead, square face, high nasal bridge, full nasal tip, small mouth, facial asymmetry, ptosis, arched eyebrows and laterally protruding ears\(^3,9,10\). Our baby had the distinctive characteristic face seen in CHARGE association.

Congenital heart defects are seen in 75 - 80% of the patients with the CHARGE association\(^3\). Conotruncal and aortic arch anomalies are seen most commonly\(^3,10,11\). Our patient did not have any structural malformation of the heart.

Developmental delay was seen in 100% of the patients with CHARGE association\(^3\). Our baby had not attained head control till the age of four months.

There was severe growth retardation. The head circumference was well below the 3rd centile and had grown only one cm in four months. Microcephaly is one of the parameters predictive of poor intellectual outcome\(^12\). The other two parameters that are predictive of poor intellectual outcome are extensive bilateral ocular coloboma and brain malformations\(^12\).

Genital hypoplasia is seen in 70 - 80% of these children. Boys have micropenis and cryptorchidism and girls have hypoplastic labia\(^3\).

Tracheo-esophageal fistula and orofacial clefting are seen in 15 - 20% of the patients with CHARGE association\(^3\). However, these were not seen in our patient.

Renal anomalies are seen in 25% of children with CHARGE association\(^3\). These anomalies include horseshoe kidneys, hydronephrosis, renal hypoplasia, solitary or duplex kidneys and
ureteropelvic obstruction. This baby did not have any renal anomaly.

Central nervous system malformations in children with the CHARGE association have been well described in the literature. About 55% of these children have definite central nervous system malformations such as arhinencephaly, holoprosencephaly and other defects. The presence of central system malformations is most strongly associated with choanal atresia. This baby had a prominent shizencephalic cleft in the left parietal lobe extending into the left frontal lobe.

The term ‘schizencephaly’ designates the presence of clefts in the cortical hemispheres which result from flawed development of the cortical mantle during cell migration in the first trimester of pregnancy.

The etiology of CHARGE association remains speculative. A teratogenic causation was initially thought of but this has not been substantiated.

There is a crucial stage of embryogenesis, when failure to rupture the primitive bucconasal membrane (35th to 38th day) brings about choanal atresia. Conotruncal anomalies result from aberration in cephalic neural crest cell migration during the 4th and 5th weeks after conception. The cochlear duct begins to develop around the 36th day and the eyes develop between days 34 and 44 days post conception, which is also the time during which many cranial nerves are developing. All these malformations in CHARGE association occur early, during the first trimester.

Another interesting postulate is that CHARGE association seems to result from abnormalities in the development, migration and interaction of the cells of the cephalic neural crest and could belong to a class of the neurocrestopathies.

Interestingly, our baby had schizencephaly which is an important aftermath of a flawed development of the cortical mantle, a cell migratory disorder.

Thus, as many of the pathognomonic features of CHARGE association seem to arise secondary to an aberration in cephalic neural crest migration, this area needs to be explored further in establishing the etiology of this interesting condition.

Most cases of CHARGE syndrome have been sporadic occurrences in an otherwise normal family. There have been chromosomal imbalances seen in some patients. The chromosomal study in our patient was normal.

Tellier et al. noticed a significant increase in the mean paternal age at birth of patients with CHARGE association as compared with the normal population suggesting the possible role of a dominant mutation or a subtle chromosomal abnormality. Incidentally, our patient’s paternal age was forty years.

Infants with CHARGE association who survive early infancy have a better prognosis of growth and mental development. Extensive bilateral coloboma, microcephaly and brain malformations are predictive of poor intellectual outcome.

Aspiration is common during infancy due to incoordination of swallowing and gastro-esophageal reflux causing recurrent chest infection leading to increased respiratory morbidity and mortality.

Wyse et al. found that survival was poor with more than one of the following features, i.e. cyanotic heart disease, bilateral choanal atresia and tracheo-esophageal fistula.

Tellier et al. have proposed several criteria for poor survival including male gender, central nervous system and/or esophageal malformations and bilateral choanal atresia.

Since CHARGE association is a multisystem disorder involving various vital organs, a multidisciplinary approach involving specialists from different fields is mandatory in the proper management of these patients.

CONCLUSION

CHARGE association is a chronic and complex anomaly. The diagnosis should be considered in any neonate with bilateral choanal atresia, ocular coloboma, the classic CHARGE ‘ears’ and the distinctive characteristic CHARGE faces.

The recently recommended several diagnostic major and minor criteria should also be borne in mind and applied in establishing a diagnosis of CHARGE association.

The presence of a neural crest migratory disorder should alert the clinician to examine for the classic presentation of CHARGE association.

The management of this condition involves a multidisciplinary approach.

Early identification and prompt referral for medical, therapeutic and educational consultative services, regular follow up and a comprehensive intervention program would greatly enhance the morbidity and mortality in this multi-featured disorder characterized by a unique combination of diverse abnormalities.

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Case Report

Fulminating Shigella Encephalopathy (Ekiri Syndrome): A Case Report

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ABSTRACT

Neurological manifestation, particularly seizures and encephalopathy, are common in childhood shigellosis. Fulminating shigella encephalopathy (Ekiri syndrome) is a rare form of shigella associated encephalopathy characterized by a rapid, severe and fatal course with few dysenteric symptoms. Brain edema is a common finding in patients presenting with severe shigella encephalopathy. Shiga toxin production is not essential for development of shigella-associated neurological symptoms. Early recognition and proper management of cases of severe shigella encephalopathy may help to improve the outcome. We are reporting the case of a six and half year old male child with severe fulminating shigella-encephalopathy (Ekiri syndrome) who made a partial recovery. Brain magnetic resonance image (MRI) findings of this patient are reported. To the best of our knowledge, brain MRI studies were not reported before in the pediatric population with Ekiri syndrome; moreover, this is probably the first case of Ekiri syndrome to be reported in the Arab population.

KEY WORDS: brain edema, convulsions, Ekiri syndrome, encephalopathy, shigellosis

INTRODUCTION

Shigellosis is a common infectious disease especially in underdeveloped countries. The inflammatory process of acute shigella infection affects the colon and is characterized clinically by fever, cramping abdominal pain with frequent loose stools that might contain mucus, pus and blood.

Four serogroups (or species) of shigella have been described including group A (Shigella dysenteriae), group B (Shigella flexneri), group C (Shigella boydii) and group D (Shigella sonnei). These groups are further classified into serotypes and sub-serotypes.

Shigella organisms are highly virulent. A very small inoculum - as little as ten microorganisms - can cause disease in humans.[1]

Case history

A six and half year-old boy with unremarkable previous medical history presented with fever of 38.5 °C and repeated vomiting of one day duration.

During examination, he looked fully conscious, alert with stable vital signs (blood pressure of 105/60 mmHg and a heart rate of 110/min). His systemic review was unremarkable with no signs of meningeal irritation.

He was admitted to the hospital for observation and commenced on intravenous fluids and antipyretics.

Six hours later, the child started to pass frequent, loose, smelly motions that were not mixed with mucus or blood. By that time he was looking ill with depressed sensorium and high fever (39.5 °C).

Laboratory tests showed low serum sodium level of 129 mmol/l. Otherwise his electrolytes, sugar, liver enzymes, lactate and blood ammonia levels were all normal. Toxicology screening came negative.

Soon, the child developed two seizure episodes, 10 minutes apart; both were aborted by intravenous (iv) diazepam, and he was kept on continuous phenytoin infusion. Central nervous system (CNS) infection was suspected and the child was maintained on iv ceftriaxone and acyclovir. The child suddenly developed cardio-respiratory arrest. He was immediately resuscitated with endotracheal intubation and was shifted to the intensive care unit (ICU).

Brain computed tomography (CT) showed generalized brain edema (Fig. 1) that was managed with iv mannitol, hyperventilation and head elevation.

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Subsequent examination of the cerebrospinal fluid (CSF) was unremarkable with negative blood, urine and CSF cultures. Serology study for viruses was also negative. Stool cultures collected on admission grew *Shigella sonnei*.

Screening for metabolic disorders was negative. Electroencephalogram (EEG) showed a slow background activity with active focus of slow sharp waves in both temporo-parietal areas. *Shigella*-associated encephalopathy was assumed. CT brain on the sixth day after admission showed resolution of the brain edema with bilateral hypodense areas in both thalami and basal ganglia (Fig. 2). The child could be extubated on the eighth day after admission.

His level of consciousness slowly improved. Two weeks after admission, he was able to open his eyes spontaneously and showed a good response to verbal stimuli. However, he developed hypertonia and hyperreflexia with very poor muscle power. By

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**Fig. 1:** Non-enhanced CT brain at the level of mid-brain shows features of cerebral edema with effacement of CSF spaces

**Fig. 2:** Contrast-enhanced CT brain shows non-enhancing low attenuation areas in thalami and basal ganglia bilaterally

**Fig. 3 (a & b):** T2-weighted axial (3a) and coronal (3b) MRI brain images showing multiple lesions of high signal intensity in thalamic, basal ganglia and internal capsule regions bilaterally
that time he could be shifted to a general pediatric ward where an intensive physiotherapy program was started.

MRI brain done four weeks after admission showed multiple lesions in the area of basal ganglia, thalami and internal capsule bilaterally (Figs. 3 a & b).

Six weeks later, he was able to sit and stand with support, recognize his mother’s face and swallow fluids and soft food without choking or aspiration. He was then discharged home.

Ten weeks later, he could recognize most family members; he was able to say few words. Both muscle tone and reflexes were increased in the four limbs and this was more evident on the left side, with some dystonic movements in the upper limbs.

Muscle power improved in the right upper and lower limbs (grade of 3/5) while it remained poor on the left side (grade of 1/5). The patient was then lost to follow up.

DISCUSSION

Complications of shigella infection include both intestinal and extra-intestinal manifestations[2]. Hemolytic uremic syndrome and central nervous system (CNS) complications are among the most common extra-intestinal manifestations of shigellosis. Seizures and acute transient encephalopathy state (manifested by headache, delirium, lethargy, hallucinations, confusion, and depressed sensorium) are the most commonly reported neurological manifestations in pediatric population with shigellosis[1,3]. These may accompany or even precede the development of intestinal symptoms. The case may be misdiagnosed as a primary CNS disease, if the neurological symptoms appeared first[4].

Both seizures and shigella associated encephalopathy are usually benign, and are rarely followed by neurological sequelae[9].

A particularly fulminant form of acute shigella-associated encephalopathy known as Ekiri syndrome (Japanese: epidemic diarrhea) was first described in Japanese patients in the early 1900’s (before and immediately after the Second World War). The major clinical abnormalities were rapidly developing seizures and coma in patients with high fever and few dysenteric symptoms[6].

Only few cases of fulminant shigella encephalopathy (Ekiri syndrome) have been described in the second half of the last century. The largest series of this rare complication of shigellosis was reported by Goren et al[8], who studied 15 cases of fatal shigella encephalopathy during the years 1980 to 1990.

Having ruled out all other causes, acute fulminating encephalopathy (Ekiri syndrome) secondary to Shigella sonnei infection was a logical explanation for the sudden and severe neurological deterioration in our patient.

Cerebral edema is a common finding reported in most patients with shigella-associated encephalopathy, either by CT brain or at autopsy[2,7]. This was seen in the first CT brain of our patient (Fig.1). Focal or diffuse areas of low signal intensity were also reported in CT brain in cases of fulminating shigella encephalopathy[6]. This was seen as areas of low attenuation in the thalamic and basal ganglia regions bilaterally in the second CT brain of our patient done six days after presentation (Fig. 2). The same lesions persisted in the follow up MRI brain a month later. (Figs. 3 a & b).

The pathogenesis of shigella associated neurological dysfunction is not well understood. Shigatoxin, which is produced in appreciable amount by S. dysenteriae, was proved to be a neurotoxin in animal models. It acts on the neurons indirectly by inducing vascular endothelial damage in the brain and spinal cord with secondary neurological dysfunction. It also has cytotoxic activity, probably related to its ability to inhibit protein synthesis in mammalian cells[10].

The majority of shigella associated neurological findings were reported in patients with Shigella sonnei and Shigella flexneri[11]. Both species do not usually produce shiga toxin, as both are lacking the structural gene encoding shiga toxin production [12,13].

Moreover, shiga toxin was neither detected in the CSF of patients with shigella - associated neurological findings, nor produced in vitro by shigella strains isolated from these patients. These data suggest that the neurological manifestation of shigellosis in human may not be related to shiga toxin production[12].

Balter et al[14], studied the role of nitric oxide (NO) in shigella - related seizure in an animal models. NO is an important neurotransmitter in both peripheral and central nervous system. Overproduction of NO has been linked to neurotoxicity during ischemia. It also has a role in some form of neurodegenerative brain disease and in seizures induction[15].

In their study, Balter et al[14] found that Shigella dysenteriae infection elevate serum NO level, and this lowered the threshold of induced convulsions in mice. They hypothesized that NO may have a role in induction of neurological manifestation of human shigellosis by acting as a mediator to cytotoxins produced by different Shigella species and possibly by other enteric infections.

Khan et al[14] in a large study discussed the prognostic factors that affect the outcome in children
with shigellosis who presented with neurological manifestation. They found that patients who were unconscious and with documented seizures at presentation were at great risk of fatal outcome in shigella associated encephalopathy.

Although the mechanism that underlies neurological dysfunction in some cases of shigella enteritis is unclear, yet the syndrome exists as a well recognized clinical entity. It needs to be considered by pediatricians as a differential diagnosis in children presenting with acute encephalopathy of obscure origin.

Stool cultures are recommended in those patients with or without intestinal symptoms.

Early recognition and prompt and intensive measures to prevent or treat brain edema may improve the outcome.

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REFERENCES

Case Report

Autoimmune Polyglandular Syndrome (Type - III) : Case Report

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ABSTRACT

Autoimmune polyglandular syndromes are constellations of multiple glandular insufficiencies. There are four types - I, II, III and IV. Type II is the commonest. The case reported here has features of type III, which is a rare occurrence.

KEY WORDS: autoimmune polyglandular syndrome type-III, insulin resistance

INTRODUCTION

Autoimmune polyglandular syndromes (APS) are constellations of symptoms and signs of multiple glandular insufficiencies. Four types of APS exist. Type I, III, and IV are relatively rare while type II is more common[1]. Type III does not involve the adrenal cortex but two of the followings: autoimmune thyroid disease, type 1 diabetes mellitus (DM), rheumatoid arthritis, autoimmune liver disease, pernicious anemia, vitiligo and alopecia[2]. This case belongs to type III because of the presence of type 1 diabetes, hypothyroidism, rheumatoid arthritis and vitiligo along with a probable association of autoimmune hepatic involvement and is reported because of its rarity.

CASE REPORT

A 14-year-old Saudi girl was admitted to the Department of Medicine, King Khaled General Hospital, Hafr Al Batin, with the complaints of upper abdominal pain, vomiting and increase in respiratory rate of one day duration. She was a known case of type 1 DM with insulin resistance, deforming rheumatoid arthritis and hypothyroidism under therapy with raised hepatic transaminases-possibly due to autoimmune liver disease. She had not attained menarche but had all other signs of puberty. She was previously admitted one month ago for diabetic ketoacidosis (DKA) when her liver function tests were deranged in the form of raised transaminases with normal bilirubin level. Her viral markers were non-contributory. At discharge, she was put on 150 units of insulin per day. She had missed her morning dose of insulin on the day of present admission.

On clinical examination, her weight was a 58.5 kg. She was conscious, oriented, afebrile, severely dehydrated, having Kussmaul’s breathing with absence of pallor, cyanosis, icterus, thyromegaly, acanthosis nigricans and edema. She had vitiligo on extensor surface of both elbows and around the neck. Per abdomen examination showed epigastric and right hypochondrial tenderness. Respiratory, cardiovascular and central nervous system revealed no significant findings.

Investigations showed neutrophilic leucocytosis which reverted back to normal the next day. She had normal liver, renal and other biochemical parameters. Her blood gas analysis revealed severe high anion gap metabolic acidosis. Urine for acetone was positive. Her thyroid microsomal antibodies were positive. Sonography of abdomen failed to reveal any pathology. Her serum calcium, magnesium, phosphate, parathormone, cortisol, luteinizing and follicular stimulating hormone were all within normal range.

She was treated with standard protocol for DKA and broad spectrum antibiotics. She required 10 units of iv insulin per hour and subsequently more than 200 units of insulin per day when shifted to subcutaneous therapy. Insulin resistance was considered because of the high dose required. She was given a trial with metformin (500 mg) BID which lowered her insulin requirement significantly, but unfortunately, her hepatic transaminases went up and hence this oral anti-hyperglycemic agent was discontinued. Though used for a short period metformin helped in achieving a better glycemic control.

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DISCUSSION

Autoimmune polyglandular syndromes (APS) comprise a group of autoimmune disorders of the endocrine glands that result in failure of the glands to produce their hormones[31]. In 1980, Neufeld and Blizzard organized and classified these syndromes into four main types defined as polyglandular autoimmune disease, also termed autoimmune polyglandular syndromes-APS[3]. The polyglandular diseases are a series of organ-specific autoimmune illnesses characterized by the presence of circulating organ-specific antibodies, even in the absence of overt clinical disease[4,9]. Genetic factors are also involved in the pathogenesis of APS[4,6]. APS II and III are associated with HLA class II genes, with apparently distinctive HLA alleles for each. These APS are often observed in individuals in the same family, suggesting its inheritance could be due to an autosomal dominant trait with incomplete penetrance. HLA alleles are not seen in APS I and the mode of inheritance is autosomal recessive[10].

APS I is characterized by the classic triad of mucocutaneous candidiasis (90 to 100%), hypoparathyroidism (80 to 85%) and Addison's disease (70 to 75%) appearing in a chronological order[10]. For diagnosis at least two of the three major components need to be present[3,7]. It is a rare condition. Prevalence is one in 25,000 population[8]. Female to male ratio ranges from 0.8 - 1.5:1. It usually occurs in children.

APS II is characterized by the presence of autoimmune Addison's disease (100%) in association with either autoimmune thyroid diseases (originally described by Schmidt) and/or type 1 DM[2,3,9]. It is the most common type encountered clinically. Approximately 14 to 20 people per million population are affected. The female to male ratio is 4:1. It occurs primarily in adulthood[10].

APS III - in which a direct association of autoimmune thyroid disease (Hashimoto's thyroiditis, Grave's disease) and type 1 diabetes is found in absence of Addison's disease[1,2]. It is a very rare condition. The exact worldwide prevalence of APS III is unknown. There is no racial or ethnic difference, in frequency of percentage, reported. It is typically observed in middle-aged women but can occur in persons of any age. The hallmark of APS III is the absence of Addison's disease[10].

APS IV is a rare syndrome characterized by the association of autoimmune combinations not falling in the above categories[10]. For example, Addison's disease with one or more minor components (rheumatoid arthritis, autoimmune liver disease, primary gonadal failure, pernicious anemia, celiac disease, vitiligo, etc.) excluding other major components of APS I, II and III. In all the above types minor components are present in variable degrees.

The reported case is an adolescent girl with type 1 DM since the age of 11 years, who developed hypothyroidism at the age of 12 years and rheumatoid arthritis at the age of 10 years. She has vitiligo and probably autoimmune liver disease. The absence of goiter and the presence of microsomal antibodies in this patient probably denotes autoimmune atrophic thyroiditis. Insulin resistance in this patient could be due to anti-insulin antibodies which should be suspected in such patients with marked insulin resistance. Anti-insulin receptor antibody syndrome also known as type B insulin resistance (approximately 25 patients reported) is characterized by marked insulin resistance, hyperglycemia and acanthosis nigricans. Approximately, one third of patients also have other autoimmune diseases. The course of the DM is variable with occasional spontaneous remissions[11]. Although acanthosis nigricans was not present in this case, possible association of this syndrome could not be ruled out as only specialized laboratory facilities can quantify the anti-insulin receptor antibodies to facilitate this diagnosis. The combination of type 1 DM, hypothyroidism, rheumatoid arthritis, vitiligo and autoimmune liver disease suggest APS III in this patient. It is mandatory to consider other glandular hypofunction while evaluating patients with any type of endocrine hypofunction, because multiple glandular involvement is quite frequent. Screening (organ-specific autoantibodies or HLA typing) of their family members is equally important.

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Case Report

Late Onset Central Hypoventilation Syndrome with Hypothalamic Dysfunction in a Kuwaiti Girl

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ABSTRACT

Late onset central hypoventilation syndrome (LO-CHS) is now considered a well-established disease that develops in previously normal children after infancy and has been regarded as a distinct entity from the congenital central hypoventilation syndrome (CCHS). Both conditions are associated with neural crest tumours, but hypothalamic dysfunction (HD) is a feature of LO-CHS and not CCHS. We report a case of LO-CHS with HD (LO-CHS / HD) who presented in respiratory failure at the age of five years.

KEY WORDS: central hypoventilation, children, hypothalamic dysfunction

INTRODUCTION

Congenital central hypoventilation syndrome (CCHS) is characterized by abnormal autonomic control of breathing that results in severe hypoventilation occurring initially during sleep. It was first described in children by Mellins et al in 1970[1]. In most cases the onset of CCHS occurs in the neonatal period or during the early months of life[2]. A form of LO-CHS has been described in the literature. Katz et al[3] proposed that late onset central hypoventilation syndrome associated with hypothalamic dysfunction (LO-CHS/HD) is a distinct clinical syndrome. Both CCHS and LO-CHS have been associated with neural crest tumours and they generally occur in a histologically normal central nervous system (CNS). Both conditions have also been associated with PHOX2B gene mutation[4]. HD has been frequently associated with LO-CSH but not CCHS. We report on a case of LO-CSH/HD presenting in a five year-old Kuwaiti girl.

CASE REPORT

This Kuwaiti girl was five years old when she was first admitted to our pediatric department in coma, with marked hypoxemia and respiratory failure. She was successfully resuscitated and transferred to ICU for mechanical ventilation. Initial blood gas showed acute on top of chronic respiratory acidosis.

She was born at term weighing 3.2 kg to healthy non-consanguineous parents. She had no neonatal problems. Her five sisters and three brothers are alive and well. Child had normal growth and developmental milestones until the age of three years when her mother noticed that she became hyperphagic, eating almost all day with resultant rapid increase in weight (Fig. 1). She was seen by a pediatric endocrinologist who ruled out endocrinal causes of her obesity at that time.

Her mother also noticed that she was sleepier and she began to snore. Further history from the parents was suggestive of sleep disordered breathing. She had persistent snoring during sleep with frequent nocturnal arousal throughout the previous year. She had daytime hypersomnolence and depressed mood alternating at times with aggressive behaviour specifically in the past three months prior to her deterioration. The parents also reported recurrent unexplained fevers.

At the age of five years, following an upper respiratory tract infection while she was playing with other children at home she was found apnoeic and cyanosed. Mouth to mouth breathing was done and she was rushed to hospital where she was immediately intubated and mechanically ventilated for a week. She was notably obese with a weight of 40 kg (> 95th centile), and a height of 113 cm (75th centile) and her BMI was 31.5 kg/m² which was substantially above the 95th percentile for age. Otherwise her physical examination during that time was basically normal. Blood gas analysis showed pH 7.26, PaCO₂ 12.4 Kpa, PaO₂ 6.6 Kpa, and HCO₃ 40 meq/l. Apart from hyponatremia and low serum osmolality, her investigations showed normal serum potassium, urea, glucose,

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hematocrit, lactate, pyruvate and ammonia. Chest radiograph was also normal. Lateral X-ray neck showed enlarged adenoids. She had a normal ECG and her echocardiogram revealed normal pulmonary pressures and cardiac structure. CT scan of chest and upper abdomen as well as CT and MRI of the brain were normal. Following extubation she continued to show progressive hypoventilation evident clinically by drowsiness and biochemically by hypoxemia, CO₂ retention and raised bicarbonate. There were signs of partial upper airway obstruction due to enlarged tonsils and adenoids, therefore adenotonsillectomy was done. Child was then maintained on nocturnal nasal mask non-invasive ventilator, but six weeks later she became hypersomnolent, drowsy and markedly hypoxemic. An echocardiogram showed elevated pulmonary artery pressure. She was transferred to the ICU and mechanically ventilated accordingly together with diuretics. Her condition improved in four days. Tracheostomy was done and then she could be maintained and sent home on a bilevel positive airway pressure (BiPAP) machine which she was using when sleeping and all day while having viral illnesses. She also needed oxygen most of the time at home. When her thyroid function tests were rechecked, child was found to develop hypothyroidism (with a low TSH and T4). She was put on replacement therapy. Two years later, she developed diabetes insipidus and was also put on dDAVP (desmopressin) intranasally. PHOX2B direct sequencing of the exon 3 of the PHOX2B gene was done and showed no mutation. Despite all efforts to reduce her weight, she continued to add more due to her polyphagia and reduced activity. Her BMI reached 42.7 kg/m² by the age of eight years (Fig. 1). Viral illnesses continued to provoke worsening hypoventilation.

**DISCUSSION**

Both CCHS and LO-CHS are due to inadequate ventilation that is more manifest during sleep but eventually becomes compromised during night and day. This is caused by a markedly impaired response to hypercarbia and hypoxemia.

Both conditions occur in the absence of any cardiac, pulmonary, neuromuscular diseases or brain stem lesions. Imaging studies do not show any significant structural abnormalities as in our case.

Etiology of both conditions is not fully understood though PHOX2B gene mutation has been recently associated with these conditions. In our patient there was no gene mutation as it was the case in four out of nine LO-CHS patients studied by Trochet et al. CCHS is a rare condition with an estimated incidence of one per 200,000 live births and a median age of diagnosis of 3.5 months as shown in the French registry of CCHS by Trang and his group. Incidence of LO-CHS is not exactly known but in a large series of 188 patients with central hypoventilation only nine of them were LO-CHS. Hyponatremia with inappropriate ADH secretion as well as hypothalamic dysfunction including hyperphagia, hypersomnolence, thermal dysregulation, emotional lability, and endocrinopathies have been frequently associated with LO-CSH but not CCHS. Our case has eventually demonstrated all of the above one after the other with evolving hypothyroidism and diabetes insipidus both of which required treatment. Neural crest tumours such as ganglioneuroma, ganglioneuroblastoma and neuroblastoma are known associations of CCHS and some cases of the LO-CHS (four out of eleven in one series). Our case did not show any of these tumours until now, as they may declare themselves years after the onset of hypoventilation and hypothalamic dysfunction. Children with

![Fig. 1: The patient's growth chart in years showing a normal height (over the 90th - 95th centile, dotted line) with an outstanding increase in weight (solid line)](image-url)
LO-CHS/HD typically have normal growth and development until 1.5 - 4 years of age after which they tend to have voracious appetite resulting in gross obesity. Respiratory failure with hypercarbia ensues. This may be precipitated by anesthesia or hypertrophy of tonsils and adenoids. Our patient came in respiratory failure at the age of five years, but she had polyphagia and obesity since she was three and her sleep disordered breathing was also noticed when she was four years old. Her symptoms improved only partially and temporarily when adenotonsillectomy was done.

Our patient was initially intubated and ventilated but following extubation she continued to show progressive hypoventilation and so was put on nocturnal nasal mask non-invasive ventilator that she could tolerate only for few weeks. She then had to undergo tracheostomy and was put on BiPAP machine. These sorts of ventilatory options are all well described in the literature[9-11].

Using such options for home ventilation these children can have a good long term medical and psychosocial outcome[12]. Nevertheless early diagnosis, appropriate management and diligent effort on the part of the parents remain of utmost importance in dealing with these children.

REFERENCES

Low Carbohydrate Ketogenic Diet Enhances Cardiac Tolerance to Global Ischaemia

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Acta Cardiol. 2007; 62:381-389

The cardio-protective effects of a low carbohydrate ketogenic diet following global ischaemic injury as compared to rats fed a normal and high carbohydrate diet for a period of 19 weeks, were investigated. The reperfusion recovery of coronary flow was highly significant in the low carbohydrate ketogenic diet group. Although the initial reperfusion recovery of the pressure developed in the left ventricle, Pmax was similar in all groups, after 15 minutes, the momentum for faster recovery was maintained in the low carbohydrate ketogenic diet group. Ultrastructural observations of the cardiac muscles have shown that there was a decrease in the number of mitochondria in rats fed a high carbohydrate diet and an increase in the number of mitochondria in those fed a low carbohydrate ketogenic diet as compared to the normal diet group. This study demonstrates that a low carbohydrate ketogenic diet is cardio-protective functionally.

Introduction: Ischaemia and reperfusion lead to cell death. These pathways are regulated and hence are subjected to therapeutic intervention. Previously, we have shown that a low carbohydrate ketogenic diet (LCKD) reduces the risk factors for heart disease in obese patients. This study is aimed at understanding the cardio-protective effects of LCKD following global ischaemic injury in rats.

Materials and Methods: Rats weighing 190-250 g were divided into normal diet (ND), LCKD and high carbohydrate diet (HCD) groups consisting of six animals in each group. Specific diets were given to each group for a period of 19 weeks. Changes in body weight, ultrastructure of the cardiac muscles and the cardio-protective effects of the LCKD group as compared to the ND and HCD groups were investigated in rats following global ischaemic injury.

Results: Electron microscopic studies have shown that there was a decrease in the number of mitochondria in rats fed a high carbohydrate diet and an increase in the number of mitochondria in those fed a low carbohydrate ketogenic diet as compared to the normal diet group. Rats on LCKD had a remarkable tolerance to ischaemia and a faster recovery of cardiac function following reperfusion. The initial reperfusion recovery of the pressure developed in the left ventricle, Pmax was similar in all groups. However, after 15 minutes, the momentum for faster recovery was significantly maintained in the LCKD group (P < 0.05). The reperfusion recovery of coronary flow was highly significant (P < 0.05) in the LCKD regime. The increase in left ventricle end diastolic pressure, coronary vascular resistance and the changes in body weight were not significant between the experimental groups.

Discussion and Conclusion: This is a unique study showing ultrastructural variation in cardiac muscle in relation to cardio-protective function in rats fed a low carbohydrate ketogenic diet. This study suggests that the LCKD is cardio-protective functionally. The underlying mechanism of the cardio-protective effect of an LCKD needs to be elucidated.
Discrepancy in Antimicrobial Susceptibility Test Results Obtained for Oral Streptococci with the Etest and Agar Dilution

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A total of 270 viridans group streptococci (VS) isolated from healthy children, identified to the species level, were tested for their susceptibilities to penicillin, imipenem, erythromycin, and vancomycin. A total of 270 isolates and 1,080 organism-antibiotic combinations were evaluated. The overall susceptibility rates of all isolates obtained by the Etest (ET) versus agar dilution (AD) were 60.4% versus 61.8% for penicillin, 63.8% versus 63.9% for erythromycin, 90.6% versus 96% for vancomycin, and 99.1% versus 96.0% for imipenem, respectively. Major discrepancies occurred in the testing of the susceptibility of Streptococcus mutans to vancomycin, with 59.5% (ET) versus 100% (AD), followed by S. salivarius, with 84.1% versus 100%; S. oralis, with 82.1% versus 96.4%; and S. mitis, with 90% versus 100%, respectively. There were also differences in the rates of susceptibility of S. mutans, 66.5% (ET) versus 85.1% (AD), and S. intermedius, 82.9% versus 72.1%, respectively, to penicillin. General agreement between the results of ET and AD was obtained for 973 organism-antibiotic combinations, i.e., 90.1%. Very major errors were found for 6.8% of isolates, and major errors were found for 3.2% of isolates; the minor errors were negligible. Agreement between the results of the two methods was 98.7% for penicillin, 94.6% for vancomycin, 96.9% for imipenem, and 99.9% for erythromycin. The highest rate of very major errors was for vancomycin, at 5.4%. The ET appears to be as efficient as AD for susceptibility testing of VS, except for vancomycin, where very major errors in the results were relatively high.

Butyrylcholinesterase Activity and Lymphocyte Subpopulations in Peripheral Blood of Kuwaiti Women Experiencing Recurrent Spontaneous Abortion

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J Reprod Immunol. 2007 Sep 18; [Epub ahead of print]

This study has evaluated the hypothesis that activity of the detoxifying enzyme butyrylcholinesterase (BuChE) correlates with levels of serum anti-cardiolipin antibodies (ACA) and T lymphocytes in peripheral blood of women experiencing recurrent spontaneous abortion (RSA). Peripheral venous blood from 16 non-pregnant, RSA-afflicted women and 8 healthy non-pregnant women was analyzed for frequency of T lymphocyte subpopulations by two-color flow cytometry and for serum BuChE using butyrylthiocholine iodide/spectrophotometry. RSA-afflicted women with high serum ACA, but not those with normal ACA levels, exhibited significantly increased percentages of CD4+CD25+ cells (p<0.01) and CD4+HLA-DR+ cells (p<0.05) relative to healthy women. CD4+CD25+(high) cells were significantly lower (p<0.05), while CD4+CD25+(low) cells were significantly higher (p<0.01), in women with elevated ACA compared to healthy women and to RSA women with normal ACA. Relative to healthy, non-pregnant subjects, serum BuChE activity in RSA patients was elevated, both for those with normal ACA (p<0.01) and elevated ACA levels (p<0.01). Among healthy controls, a significant positive correlation was observed between frequency of CD3+NK cells and BuChE activity (p<0.01), but not for RSA-afflicted subjects. A positive correlation between BuChE activity and frequency of CD4+CD25+ cells, as well as CD4+CD25+(high) cells, was observed in the RSA-afflicted subject group with elevated ACA (p<0.05), which may be related to induction of BuChE by toxic metabolites resulting from pathogenic T cell activity. It is concluded that, among RSA patients, high serum ACA correlates with elevated levels of activated T cells and reduced CD4+CD25+(high)/CD4+CD25+(low) cells in comparison to healthy women or those afflicted with RSA but with normal ACA. BuChE activity is observed to be elevated in RSA patients irrespective of serum ACA status.
Factors Associated with Quality of Life of Outpatients with Breast Cancer and Gynecologic Cancers and Their Family Caregivers: A Controlled Study

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ABSTRACT

Background: Quality of life (QOL) issues are of interest in cancer because effective methods of treatment and detection have led to an increase in the number of long-term survivors. The objectives of the study were: to assess the subjective QOL of stable Sudanese women cancer outpatients and their family caregivers, using the WHO 26-item QOL Instrument; compare with matched general population groups, as well as diabetic and psychiatric patient groups; examine patient-caregiver concordance in ratings; and assess the variables associated with their QOL, with a view to identifying factors that can enhance quality of care.

Methods: Responses of oncology outpatients with breast cancer (117), cervical cancer (46) and ovarian cancer (18) (aged 44.6, SD 11.5) were compared with those of their family caregivers and matched general population groups. Data were analyzed by univariate and multivariate statistics.

Results: The cancer groups had similar QOL domain scores, which were significantly lower than those of their caregivers, but higher than the control group as well as those of psychiatric and diabetic patients studied previously. Patients who were married, with higher education, better employment, and with longer duration of illness had higher QOL. Patients on radiotherapy and their caregivers had higher QOL scores. Correlations between patient’s ratings and caregiver impression of patient’s QOL were high. Caregiver impression was a significant predictor of patient’s and caregiver’s QOL. Other predictors for the patient were: currently feeling sick and duration of illness; for the caregiver: feeling sick, relationship to patient, and age.

Conclusion: Cancer patients in stable condition and with psychosocial support can hope to enjoy good QOL with treatment. The findings constitute an evidence base for the country’s cancer care program, to boost national health education about prognosis in cancer. Families living with women cancer patients are vulnerable and need support if the patient is recently diagnosed, less educated, single, not formally employed; and the caregiver is female, parent, younger, less educated, unemployed and feels sick. Clinicians need to invest in the education and support of family caregivers. The patient-caregiver dyad should be regarded as a unit for treatment in cancer care.

Beneficial Effects of Ketogenic Diet in Obese Diabetic Subjects

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Mol Cell Biochem 2007; 302:249-256

Objective: Obesity is closely linked to the incidence of type II diabetes. It is found that effective management of body weight and changes to nutritional habits especially with regard to the carbohydrate content and glycemic index of the diet have beneficial effects in obese subjects with glucose intolerance. Previously we have shown that ketogenic diet is quite effective in reducing body weight. Furthermore, it favorably alters the cardiac risk factors even in hyperlipidemic obese subjects. In this study the effect of ketogenic diet in obese subjects with high blood glucose level is compared to those with normal blood glucose level for a period of 56 weeks.
**Materials and Methods:** A total of 64 healthy obese subjects with body mass index (BMI) greater than 30, having high blood glucose level and those subjects with normal blood glucose level were selected in this study. The body weight, body mass index, blood glucose level, total cholesterol, LDL-cholesterol, HDL-cholesterol, triglycerides, urea and creatinine were determined before and at 8, 16, 24, 48, and 56 weeks after the administration of the ketogenic diet.

**Results:** The body weight, body mass index, the level of blood glucose, total cholesterol, LDL-cholesterol, triglycerides, and urea showed a significant decrease from week 1 to week 56 (P < 0.0001), whereas the level of HDL-cholesterol increased significantly (P < 0.0001). Interestingly these changes were more significant in subjects with high blood glucose level as compared to those with normal blood glucose level. The changes in the level of creatinine were not statistically significant.

**Conclusion:** This study shows the beneficial effects of ketogenic diet in obese diabetic subjects following its long-term administration. Furthermore, it demonstrates that in addition to its therapeutic value, low carbohydrate diet is safe to use for a longer period of time in obese diabetic subjects.

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**Increasing Severity of Haematuria with Successive Pregnancies in a Woman with Renal Angiomyolipoma**

**Objective:** To report a case of a 31-year-old woman with renal angiomyolipoma (RAML) who presented with progressive massive haematuria with successive pregnancies.

**Clinical Presentation:** A 28-year-old woman presented with mild haematuria in the third trimester of her second pregnancy. This was due to bleeding from a left RAML. Patient became pregnant for a third time. The RAML increased in size and patient bled more during the third trimester. After delivery she refused partial nephrectomy or renal embolisation. In the third trimester of the fourth pregnancy, she presented with massive haematuria, shock, severe anaemia (haemoglobin of 6gm/l) and required a total of 26 units of blood transfusion during a 4-week period. She required emergency Caesarian section at 36 weeks and simple nephrectomy 3 months postpartum.

**Conclusion:** The risk of profuse haemorrhage from RAML may increase with successive pregnancies in women with RAML. This anomaly should be treated in between pregnancies by either angioembolisation or resectional surgery.

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**Different Responses to Angiotensin-(1-7) in Young, Aged and Diabetic Rabbit Corpus Cavernosum**

We evaluated the ability of angiotensin-(1-7) [Ang-(1-7)] to produce relaxation of the corpus cavernosum of New Zealand White rabbits. The reactivity of corpus cavernosal strips isolated from young rabbits (8-10 months old) was assessed in organ-bath chambers. Cumulative concentration response curves for Ang-(1-7), angiotensin II (Ang II), carbachol and sodium nitroprusside (SNP) were established. Ang-(1-7) (10(-12) to 10(-5)M) produced a concentration-dependent relaxation of the corpus cavernosal strips with a pD(2) value of 9.8+/-0.3. Ang-(1-7)-induced maximal relaxant response was reduced by 48+-/-2%, 57+-/-3% and 76+-/-2% in the presence of A-779 (10(-6)M), a selective Ang-(1-7) receptor (AT(1-7)) antagonist, nitro-l-arginine methyl ester (l-NAME) (10(-4)M),
an inhibitor of nitric oxide (NO) synthase, or iberiotoxin (5 x 10(-8)M), an inhibitor of calcium-activated potassium (BK) channels, respectively. In contrast, Ang II-induced contraction was increased in the presence of A-779. Carbachol-, SNP- and Ang-(1-7)-induced relaxations were significantly reduced whereas Ang-II induced contraction was significantly increased in the cavernosum strips from older (18-24 months old) and diabetic rabbits compared to the young. Pre-incubation of the cavernosum strips obtained from young, older or diabetic rabbits with Ang-(1-7) resulted in a significant attenuation of Ang II-induced contraction. In conclusion, these results demonstrate that Ang-(1-7) can produce nitric oxide-dependent relaxation of the corpus cavernosum through activation of AT(1) and BK channels. Older and diabetic animals showed impaired Ang-(1-7)-mediated relaxation suggesting that aging and diabetes related erectile dysfunction (ED) may be partly due to decreased Ang-(1-7)-mediated relaxation of the corpus cavernosum. Acute pre-incubation with Ang-(1-7) was effective in attenuating Ang II-induced contraction of rabbit corpus cavernosum suggesting that the possible role of Ang-(1-7) in treatment of ED should be investigated.

Relationship of Depression, Disability, and Family Caregiver Attitudes to the Quality of Life of Kuwaiti Persons with Multiple Sclerosis: A Controlled Study

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BMC Neurol 2007; 7:31

Background: Assessment of subjective quality of life (QOL) of persons with multiple sclerosis (MS) could facilitate the detection of psychosocial aspects of disease that may otherwise go unrecognized. The objectives of the study were to (i) compare the QOL ratings of relapsing remitting (RRMS) and progressive (PMS) types of MS with those of a general population group and the impression of their family caregivers; and (ii) assess the association of demographic, clinical, treatment, depression, and caregiver variables with patients’ QOL.

Methods: Consecutive clinic attendees at the national neurology hospital were assessed with the 26-item WHOQOL Instrument, Beck’s Depression Inventory and Expanded Disability Scale. Caregivers rated their impression of patients’ QOL and attitudes to patients’ illness.

Results: The 170 patients (60 m, 109 f) consisted of 145 (85.3%) with RRMS and 25 with PMS, aged 32.4 (SD 8.8), age at onset 27.1 (7.7), EDSS score 2.9 (1.8), and 76% were employed. The patients were predominantly dissatisfied with their life circumstances. The RRMS group had higher QOL domain scores (P < 0.001), and lower depression(P > 0.05) and disability (P < 0.0001) scores than the PMS group. Patients had significantly lower QOL scores than the control group (P < 0.001). Caregiver impression was significantly correlated with patients’ ratings. Depression was the commonest significant covariate of QOL domains. When we controlled for depression and disability scores, differences between the two MS groups became significant for only one (out of 6) QOL domains. Patients who were younger, better educated, employed, felt less sick and with lesser side effects, had higher QOL. The predictors of patients’ overall QOL were disability score, caregiver impression of patients’ QOL, and caregiver fear of having MS.

Conclusion: Our data indicate that MS patients in stable condition and with social support can hope to have better QOL, if clinicians pay attention to depression, disability, the impact of side effects of treatment and family caregiver anxieties about the illness. The findings call for a regular program of psychosocial intervention in the clinical setting, to address these issues and provide caregiver education and supports, in order to enhance the quality of care.
Forthcoming Conferences and Meetings

Compiled and edited by
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Women’s Health-2007
Dec 01-02, 2007
Kiev, Ukraine
Contact: Meeting Organiser
Tel: 00-38-0-632-776-465; Fax: 00-38-0-445-331-270
E-Mail: markov@nbscience.com

Minimally Invasive Techniques in Gynaecology
Dec 03-06, 2007
Norderstedt, Germany
Contact: European Surgical Institute, Hummels buetteler Steindamm 71, D-22851 Norderstedt, Germany
Tel: 49-0-4-052-973-200; Fax: 49-0-4-052-973-209
E-Mail: info@esi-online.de

Controversies in Women’s Health
Dec 06-07, 2007
San Francisco, CA, United States
Contact: UCSF Office of Continuing Medical Education, 3333 California Street, Room 450, San Francisco, CA 94111
Tel: 415-476-4251 / 415-476-5808; Fax: 415-476-0318 / 415-502-1795
E-Mail: info@ocme.ucsf.edu

4th Pan Arab Contience Society Congress
Dec 06-08, 2007
Doha, Qatar
Contact: Prof. Sherif Mourad
Tel: 20-105-355-353; Fax: 20-24-553-443
E-Mail: msmourad@tedata.net.eg

Ultrasonography: Fundamentals in Critical Care
Dec 07-10, 2007
Scottsdale, AZ, United States
Contact: ACCP Customer Relations
Tel: 800-343-2227
E-Mail: accp@chestnet.org

Obstetrics and Gynecology-2007
Dec 08-09, 2007
Kiev, Ukraine
Contact: Meeting Organiser
Tel: 00-38-0-632-776-465; Fax: 00-38-0-445-331-270
E-Mail: markov@nbscience.com

Urology Update for the Non-Urologist
Dec 08-15, 2007
Miami, FL, United States
Contact: Eileen Tener
Tel: 813-333-6878
E-Mail: etener@cruiseplanners.com

Problems of Hospital Infections
Dec 13-14, 2007
Kiev, Ukraine
Contact: Dr Markov
Tel: 00-380-445-331-270; Fax: 00-380-445-331-270
E-Mail: dr@nbscience.com

Problems of Chronic Obstructive Pulmonary Diseases
Dec 13-14, 2007
Kiev, Ukraine
Contact: Dr Markov
Tel: 00-380-445-331-270; Fax: 00-380-445-331-270
E-Mail: dr@nbscience.com

The Medical Management of HIV/AIDS
Dec 13-15, 2007
San Francisco, CA, United States
Contact: UCSF Office of Continuing Medical Education, 3333 California Street, Room 450, San Francisco, CA 94111
Tel: 415-476-4251 / 415-476-5808; Fax: 415-476-0318 / 415-502-1795
E-Mail: info@ocme.ucsf.edu

Homeopathy – 2007
Dec 15-16, 2007
Kiev, Ukraine
Contact: Meeting Organiser
Tel: 00-38-0-632-776-465; Fax: 00-38-0-445-331-270
E-Mail: markov@nbscience.com

Infectious Diseases in the Adult Patient: A Primary Care Update
Dec 24-28, 2007
Sarasota, FL, United States
Contact: Eva or Cristina
Tel: 1-866-267-4263 (toll free), 1-941-388-1766; Fax: 1-941-365-7073
E-Mail: mail@ams4cme.com
New Era Cardiac Care 2008: Innovation and Technology
Jan 10-13, 2008
San Diego, CA, United States
Contact: Karen S. Morgan
Tel: 1-805-534-0300; Fax:1-805-534-9030
E-Mail: Info2008@amainc.com

STD Intensive
Jan 15-17, 2008
Cincinnati, OH, United States
Contact: CME Office
Tel: 1-800-207-9399 / 513-558-7277; Fax: 513-558-1708 / 513-558-1756
E-Mail: uccme@uc.edu

CTA@ISET: The Future of Cardiac and Vascular Imaging
Jan 19-20, 2008
Hollywood, FL, United States
Contact: Complete Conference
Tel: 888-334-7495 / 305-279-2263
E-Mail: Questions@ccmcme.com

Medicolegal Risk Management from Both Sides of the Aisle
Jan 21-25, 2008
Sarasota, FL, United States
Contact: Eva or Cristina
Tel: 1-866-267-4263 (toll free), 1-941-388-1766; Fax: 1-941-365-7073
E-Mail: mail@ams4cme.com

12th Annual Update in Gynecologic Urology 2008
Jan 24-26, 2008
Dawn Beach, Netherlands
Contact: Polly Grieger
Tel: 866-798-6338; Fax: 219-548-8619
E-Mail: polly@meetingachievements.com

Teaching Conference in Clinical Cardiology and Neurology
Jan 25-26, 2008
Miami, FL, United States
Contact: Donna Fye
Tel: 305-243-6491; Fax: 305-243-6136
E-Mail: tcccn@crme.med.miami.edu

Two Day Hepatitis Meeting
Jan 26-27, 2008
Athens, Greece
Contact: Tonia Epifani
Tel: 302-106-984-291; Fax: 302-106-984-294
E-Mail: tnt@tnt-executive.gr

STD Intensive
Jan 28-Feb 01, 2008
Cincinnati, OH, United States
Contact: CME Office
Tel: 1-800-207-9399 / 513-558-7277; Fax: 513-558-1708 / 513-558-1756
E-Mail: uccme@uc.edu

International Congress of Neonatology
Jan 30-Feb 02, 2008
Luxor, Egypt
Contact: Kamel BARGAOUI
Tel: 33-607-686-118
E-Mail: kamel@medicom-international.com

4th Asian Pacific Congress of Heart Failure
Jan 31-Feb 03, 2008
Melbourne, Australia
Contact: APCHF 2008 Congress Managers
Tel: 61-292-650-700; Fax: 61-292-675-443
E-Mail: apchf@tourhosts.com.au

15th International Union Against Sexually Transmitted infections (IUSTI) - Asia Pacific Congress on Sexually Transmitted Infections and HIV/AIDS
Feb 03-06, 2008
Dubai, United Arab Emirates
Contact: A. D’Silva
Tel: 97-143-624-717; Fax: 97-143-624-718
E-Mail: iusti@index.ae

1st International conference on Drug Design and Discovery
Feb 03-06, 2008
Dubai, United Arab Emirates
Contact: Ms Zakia Kazmi
Tel: 00-97-142-237-651; Fax: 00-97-142-237-687
E-Mail: zakia@agnmakconsultants.com

Practical Updates in Anesthesiology
Feb 04-08, 2008
Puerto Vallarta, Mexico
Contact: Jenny J. Mace
Tel: 734-936-4235; Fax: 734-936-9091
E-Mail: jenmace@umich.edu

STD Intensive
Feb 05-07, 2008
Denver, CO, United States
Contact: CME Office
Tel: 1-800-207-9399 / 513-558-7277; Fax: 513-558-1708 / 513-558-1756
E-Mail: uccme@uc.edu
Cardiovascular Disease Prevention Symposium
2008
Feb 07-09, 2008
Coral Gables, FL, United States
Contact: Julie Zimmett
Tel: 786-596-2398; Fax: 786-596-2769
E-Mail: juliez@baptisthealth.net

Society of Cardiovascular Anesthesiologists 11th Annual Comprehensive Review and Update of Perioperative Echocardiography
Feb 10-16, 2008
San Diego, CA, United States
Contact: SCA, P.O. Box 11086, 2209 Dickens Road, Richmond, VA 23230-1086, US Tel: 804-282-0084; Fax: 804-282-0090
E-Mail: sca@societyhq.com

New Horizons in Anesthesiology
Feb 10-18, 2008
Steamboat Springs, CO, United States
Contact: Office of Continuing Medical Education
Tel: 404-727-5695; Fax: 404-727-5667
E-Mail: cme@emory.edu

STD Part Time Intensive
Feb 12-14, 2008
Cincinnati, OH, United States
Contact: CME Office
Tel: 1-800-207-9399 / 513-558-7277; Fax: 513-558-1708 / 513-558-1756
E-Mail: uccme@uc.edu

CRITICARE-2008
Feb 13-17, 2008
Bhopal, India
Contact: Organising Secretary
Tel: 91-552-742-212-15; Fax: 91-552-742-689
E-Mail: criticarebhopal@gmail.com

The 1st International and The 6th National Congress on Quality Improvement in Clinical Laboratories
Feb 14-17, 2008
Tehran, Iran
Contact: Dr. Mir Majid Mossalaeie
Tel: 982-188-915-262; Fax: 982-188-902-968
E-Mail: mossalaei@iqicl.org

7th Genoa Meeting on Hypertension, Diabetes and Renal Diseases
Feb 21-23, 2008
Genoa, Italy
Contact: Ms. Barbara Rossi
Tel: 00-39-010-583-224; Fax: 00-39-0-105-531-544
E-Mail: genoameeting@aristea.com

International Symposium on Cardiovascular and Neurovascular Medicine (ISCNM) in conjunction with International Heart Failure Symposium
Feb 22-24, 2008
Hong Kong, China
Contact: Wingman Wong
Tel: 85-22-632-3194; Fax: 85-22-144-5343
E-Mail: cardiology@cuhk.edu.hk

Microbicides 2008
Feb 24-27, 2008
New Delhi, India
Contact: Conference Secretariat/Indian Council of Medical Research
Tel: 911-126-589-493; Fax: 911-126-885-886
E-Mail: m2008@microbicides2008.com

35th International Congress of the Egyptian Society of Cardiology
Feb 25-29, 2008
Cairo, Egypt
Contact: Mrs Fatheya Al-Said
Tel: 20-101-773-104; Fax: 20-26-374-749
E-Mail: egy_congress@link.net

Emergency Medicine: An Evidence-Based Approach to Adult Care
Feb 25-29, 2008
Sarasota, FL, United States
Contact: Eva or Cristina
Tel: 1-866-267-4263 (toll free), 1-941-388-1766; Fax: 1-941-365-7073
E-Mail: mail@ams4cme.com

Internal Medicine: Current Clinical Topics for the Primary Care Setting
Mar 01-31, 2008
Sarasota, FL, United States
Contact: Eva or Cristina
Tel: 1-866-267-4263 (toll free), 1-941-388-1766; Fax: 1-941-365-7073
E-Mail: mail@ams4cme.com

Perioperative Management
Mar 02-05, 2008
Marco Island, FL, United States
Contact: Office of Continuing Medical Education
Tel: 410-955-2959; Fax: 410-955-0807
E-Mail: cmenet@jhmi.edu

The 14th World Congress of Anaesthesiologists
Mar 02-07, 2008
Cape Town, South Africa
Contact: Barbara Quantz
Tel: 00-32-26-417-470; Fax: 00-32-26-417-471
E-Mail: Info@optionsglobal.com
Infectious Diseases: Adult Issues in the Outpatient and Inpatient Settings
Mar 04-10, 2008
Sarasota, FL, United States
Contact: Eva or Cristina
Tel: 1-866-267-4263 (toll free), 1-941-388-1766; Fax: 1-941-365-7073
E-Mail: mail@ams4cme.com

2nd International Conference on Hypertension, Lipids, Diabetes and Stroke Prevention
Mar 06-08, 2008
Prague, Czech Republic
Contact: Jo Jackson
Tel: 41-229-080-488; Fax: 41-227-322-850
E-Mail: strokeprevention08@kenes.com

Society of Cardiovascular Anesthesiologists 13th Annual Update on Cardiopulmonary Bypass
Mar 09-15, 2008
Whistler, BC, Canada
Contact: SCA
Tel: 804-282-0084; Fax: 804-282-0090
E-Mail: sca@societyhq.com

Cardiovascular Risk Reduction and Mature Women's Health
Mar 10-20, 2008
New York, NY, United States
Contact: Cindy Smyth
Tel: 1-877-536-6736
E-Mail: vacations@kennedyseminars.com

STD Intensive
Mar 11-13, 2008
Denver, CO, United States
Contact: CME Office
Tel: 1-800-207-9399 / 513-558-7277; Fax: 513-558-1708/513-558-1756
E-Mail: uccme@uc.edu

Total Endovascular Series Lower Extremity 1 Symposium
Houston, TX, United States
Contact: Kristen Brought
Tel: 713-965-0566; Fax: 713-960-0488
E-Mail: tes@meetingmanangers.com

16th Annual Meeting of The Asian Society for Cardiovascular Surgery
Mar 13-16, 2008
Singapore, Singapore
Contact: Kelly Chan
Tel: 63-464-402; Fax: 63-464-403
E-Mail: mice@themeetinglab.com

24th Annual Cardiovascular Conference
Mar 16-20, 2008
Lake Louise, AB, Canada
Contact: Dr. Peter Klinke
Tel: 1-877-595-1884 (toll free); Fax: 250-595-5367
E-Mail: peterklinke@vhif.org

Family Medicine: An Evidence-Based Approach to Patient Care
Mar 17-21, 2008
Sarasota, FL, United States
Contact: Eva or Cristina
Tel: 1-866-267-4263 (toll free), 1-941-388-1766; Fax: 1-941-365-7073
E-Mail: mail@ams4cme.com

STD Intensive
Mar 17-21, 2008
Cincinnati, OH, United States
Contact: CME Office
Tel: 1-800-207-9399 / 513-558-7277; Fax: 513-558-1708/513-558-1756
E-Mail: uccme@uc.edu

The 6th Annual Scientific Conference of Saudi Thoracic Society
Mar 18-20, 2008
Riyadh, Saudi Arabia
Contact: Professor Mohamed Al-Hajjaj
Tel: 00-96-612-488-966; Fax: 00-96-612-487-431
E-Mail: saudithoracicsociety@gmail.com

28th International Symposium on Intensive Care and Emergency Medicine
Mar 18-21, 2008
Brussels, Belgium
Contact: Natercia Tavares
Tel: 32-25-553-631; Fax: 32-25-554-555
E-Mail: nta@intensive.org

Breast Imaging Update
Mar 21-23, 2008
San Francisco, CA, United States
Contact: UCSF Office of Continuing Medical Education, 3333 California Street, Room 450, San Francisco, CA 94111
Tel: 415-476-4251 / 415-476-5808; Fax: 415-476-0318 / 415-502-1795
E-Mail: info@ocme.ucsf.edu

12th Pan Arab Conference on Diabetes PACD12
Mar 25-28, 2008
Cairo, Egypt
Contact: Mahmoud Ibrahim, MD
Tel: 2-0-122-131-868; Fax: 2-0-22-723-693
E-Mail: mahmoud@arab-diabetes.com
The 2nd Scientific Symposium of Al-Wali Hospital - Anorectal Diseases Today and Tomorrow  
Mar 25-27, 2008  
Aden, Yemen  
Contact: Dr Abdulhakim Al-Tamimi  
Tel: 00-967-733-422-323; Fax: 00-96-72-395-353  
E-Mail: abotammam11@yahoo.com

**Cardiac Surgery** Update and Progress - CSUP  
Mar 29-Apr 05, 2008  
Lech-Zürs, Austria  
Contact: E&E PCO  
Tel: 43-18-674-944-0; Fax: 43-18-674-944-9  
E-Mail: office@ee-pco.com

3rd British Society of Cardiovascular Magnetic Resonance Meeting  
Apr 02, 2008  
Leeds, England, United Kingdom  
Contact: Michelle Glenville  
Tel: 44-1-865-391-215  
E-Mail: Info@bscmr.org

22nd European Immunogenetics and Histocompatibility Conference  
Apr 02-05, 2008  
Toulouse, France  
Contact: Mogens Thomsen  
Tel: 33-561-322-061; Fax: 33-561-322-084  
E-Mail: thomsen@toulouse.inserm.fr

Australasian Society for Infectious Diseases  
Annual Scientific Meeting  
Apr 02-05, 2008  
Coolum, QLD, Australia  
Contact: Daliah Frank  
Tel: 61-282-040-770; Fax: 61-292-124-670  
E-Mail: conferenceinfo@ashm.org.au

Reproductive Endocrinology and Infertility  
Apr 03-04, 2008  
San Francisco, CA, United States  
Contact: UCSF Office of Continuing Medical Education, 3333 California Street, Room 450, San Francisco, CA 94111  
Tel: 415-476-4251 / 415-476-5808; Fax: 415-476-0318 / 415-502-1795  
E-Mail: info@ocme.ucsf.edu

The Houston Aortic Symposium: Frontiers in Cardiovascular Diseases  
Apr 04-06, 2008  
Houston, TX, United States  
Contact: Cindy Brown  
Tel: 760-720-2263; Fax: 760-720-6263  
E-Mail: cbrown@promedicacme.com

New Horizons in Anesthesiology  
Apr 06-11, 2008  
Cozumel, Mexico  
Contact: Office of Continuing Medical Education  
Tel: 404-727-5695; Fax: 404-727-5667  
E-Mail: cme@emory.edu

1st International Congress on Prehypertension & Cardiometabolic Risk  
Apr 09-12, 2008  
Prague, Czech Republic  
Contact: Jo Jackson  
Tel: 41-229-080-488; Fax: 41-227-322-850  
E-Mail: prehypertension@kenes.com

CARDIO ATHENA 2008 - International Meeting on Cardiovascular Medicine  
Apr 11-12, 2008  
Athens, Greece  
Contact: Mrs. Penelope Mitroyianni  
Tel: 302-107-257-693; Fax: 302-107-257-532  
E-Mail: Info@erasmus.gr

7th Cardiology Update 2008  
Apr 17-19, 2008  
Athens, Greece  
Contact: Lilian Sait  
Tel: 00-302-107-753-180; Fax: 00-302-107-753-101  
E-Mail: lsait@ath.forthnet.gr

Evivenice 2008 - Venice Course on Extreme Vascular Interventions  
Apr 17-19, 2008  
Venice, Italy  
Contact: OSC Healthcare  
Tel: 00-39-0-51-224-232; Fax: 00-39-0-51-226-855  
E-Mail: info@evivenice.com

Apr 30-May 03, 2008  
Prague, Czech Republic  
Contact: ESC Central Office  
Tel: 32-25-820-852; Fax: 32-25-825-515  
E-Mail: esccentraloffice@contraception-esc.com

40th Annual Meeting of the Society for Obstetric Anesthesia and Perinatology  
Apr 30-May 04, 2008  
Chicago, IL, United States  
Contact: SOAP Headquarters  
Tel: 216-447-7863; Fax: 216-642-1127  
E-Mail: soaphq@soap.org
**Cardiology, Pulmonary and Critical Care Medicine:** A Collection of the Most Useful Topics  
May 01-31, 2008  
Sarasota, FL, United States  
Contact: Eva or Cristina  
Tel: 1-866-267-4263 (toll free); Fax: 1-941-365-7073  
E-Mail: mail@ams4cme.com

**3rd International Romanian Congress of Anti-Aging Medicine**  
May 02-04, 2008  
Bucharest, Romania  
Contact: Catalin Enachescu  
Tel: 40-723-034-834, Fax: 40-214-130-212  
E-mail: congress@theantiaging.ro

**Cytokines 2008**  
May 10-15, 2008  
Kololi, Gambia  
Contact: Anthony F. England, Ph.D.  
Tel: +31 30 214 5715  
E-Mail: england@mangosee.com

**The 6th International Workshop on Drug Delivery Systems for Nanomedicine: Nanostructures and their Biomedical Applications**  
May 13-16, 2008  
Trest, Czech Republic  
Contact: Monika Fialová  
Tel: 42-0-261-174-305; Fax: 42-0-261-174-307  
E-Mail: monika.fialova@czech-in.cz

**Obstetric Anaesthesia 2008**  
May 14-16, 2008  
Belfast, Ireland  
Contact: Meeting Secretariat  
Tel: 44-2-087-411-311; Fax: 44-2-087-410-611  
E-Mail: www.oaameetings.info

**Seminar on Legal-Medical Issues**  
May 16-31, 2008  
Fort Lauderdale, FL, United States  
Contact: Eileen Tener  
Tel: 813-333-6878  
E-Mail: etener@cruiseplanners.com

**XVI World Congress of Cardiology**  
May 18-21, 2008  
Buenos Aires, Argentina  
Contact: Meeting Organiser  
E-Mail: congress@worldheart.org

**Cardiology Essentials and Case Studies**  
May 21-Jun 02, 2008  
Civitavecchia, Italy  
Contact: Eileen Tener  
Tel: 813-333-6878  
E-Mail: etener@CruisersParadise.com

**18th Annual Anatomic Pathology Updated Course**  
May 24-29, 2008  
Bethesda, MD, United States  
Contact: Ricky Giles  
Tel: 202-782-2637; Fax: 202-782-5020  
E-Mail: came@afip.osd.mil

**IV International Symposium of Hypertension HTA 2008 and II International Workshop of Vascular Risk**  
May 26-29, 2008  
Santa Clara, Cuba  
Contact: Emilio F. González, MD., PhD.  
Tel: 53-42-281-351; Fax: 53-42-281-449  
E-Mail: hta2008@uclv.edu.cu

**The 2nd Asia-Pacific Congress of Pediatric Cardiology and Cardiac Surgery**  
May 27-30, 2008  
Jeju Island, Republic of Korea  
Contact: Song Yi KIM  
Tel: 82-3452-7291; Fax: 82-3452-7292  
E-Mail: pccs2008@intercom.co.kr

**Emergency Medicine: An Evidence-Based Approach for Improving Outcomes**  
Jun 01-30, 2008  
Sarasota, FL, United States  
Contact: Eva or Cristina  
Tel: 1-866-267-4263 (toll free); Fax: 1-941-365-7073  
E-Mail: mail@ams4cme.com

**DVD - Dermatology: Recognition and Management for Primary Care, Volume III**  
Jun 01-30, 2008  
Sarasota, FL, United States  
Contact: Eva or Cristina  
Tel: 1-866-267-4263 (toll free), 1-941-365-7073  
E-Mail: mail@ams4cme.com

**43rd Congress of the Polish Society of Otolaryngologists**  
Jun 04-07, 2008  
Lodz, Poland  
Contact: Marcin Durko M.D  
Tel: 48-426-785-785; Fax: 48-426-785-785  
E-Mail: sekretariat@orl2008.pl

**The 1st International Congress of Infection in Transplantation and Cancer**  
Jun 10-12, 2008  
Tehran, Iran  
Contact: Meeting Organiser  
Tel: 00-982-122-424-205-10; Fax: 00-982-122-424-206  
E-Mail: info@idtmrc.ac.ir
Forthcoming Conferences and Meetings
December 2007

Infectious Disease Update
Jun 16-27, 2008
Harwich, England, United Kingdom
Contact: Eileen Tener
Tel: 813-333-6878
E-Mail: etener@CruisersParadise.com

Update on the Management of Thromboembolic Disorders
Jun 22-26, 2008
Sacramento, CA, United States
Contact: Office of Continuing Medical Education
Tel: 916-734-5390 / 866-263-4338 / 866-CME-4EDU
E-Mail: gwenn.welsch@ucdmc.ucdavis.edu

4th Asian Interventional Cardiovascular Therapeutics
Jun 25-27, 2008
Bangkok, Thailand
Contact: Mr. Pong
Tel: 66-27-180-060-5; Fax: 66-27-180-065
E-Mail: thaiheart@thaiheart.org

Primary Care, Part 1: A Comprehensive Review in Adult Medicine
Jul 01-31, 2008
Sarasota, FL, United States
Contact: Eva or Cristina
Tel: 1-866-267-4263 (toll free), 1-941-388-1766; Fax: 1-941-365-7073
E-Mail: mail@ams4cme.com

The 1st World Congress on Controversies in Cardiovascular Disease Diagnosis, Treatment and Interventions (C-Care)
Jul 03-06, 2008
Berlin, Germany
Contact: Ms. Ruthi Yahav
Tel: 972-3-56-66-166; Fax: 972-3-56-66-177
E-Mail: ccare@comtecmed.com

The 14th World Congress on Heart Disease, International Academy of Cardiology Annual Scientific Sessions 2008
Jul 16-29, 2008
Toronto, ON, Canada
Contact: Meeting Secretariat, 14th World Congress on Heart Disease, International Academy of Cardiology, Annual Scientific Sessions 2008, PO Box 17659, Beverly Hills, CA 90209, USA
Tel: 1-310-657-8777; Fax: 1-310-659-4781
E-Mail: Klimedco@ucla.edu

The XVII International AIDS Conference
Aug 03-08, 2008
Mexico City, Mexico
Contact: General Info
Tel: 41-227-100-800
E-Mail: info@aids2008.org

XXIInd European Conference on Philosophy of Medicine and Health Care
Aug 20-23, 2008
Tartu, Estonia
Contact: Dr. Bert Gordijn, Secretary of the ESPMH, Dept. of Ethics, Philosophy and History of Medicine 137, Radboud University Nijmegen Med. Centre, PO Box 9101, 6500 HB Nijmegen, The Netherlands
E-Mail: b.gordijn@efg.umcn.nl or d.verhaar@efg.umcn.nl

Urology Update for the Non-Urologist
Aug 22-29, 2008
Seward, AK, United States
Contact: Eileen Tener
Tel: 813-333-6878
E-Mail: etener@CruisersParadise.com

6th International Congress on Autoimmunity
Sept 03-07, 2008
Porto, Portugal
Contact: Jo Jackson
Tel: 41-229-080-488; Fax: 41-227-322-850
E-Mail: autoimmunity@kenes.com

6th Advanced Symposium on Congenital Heart Disease in the Adult
Sep 26-27, 2008
Thessaloniki, Greece
Contact: Ms Artemis Thoma
Tel: 00-302-310-265-898 Fax: 00-302-310-240-669
E-Mail: thesis@thesis-pr.com

The Medical Management of HIV/AIDS
Dec 11-13, 2008
San Francisco, CA, United States
Contact: UCSF Office of Continuing Medical Education, 3333 California Street, Room 450, San Francisco, CA 9411
Tel: 415-476-4251 / 415-476-5808; Fax: 415-476-0318 / 415-502-1795
E-Mail: info@ocme.ucsf.edu

Cardiology & Infectious Disease
Jul 28-Aug 09, 2008
Oslo, Norway
Contact: Dr. Martin Gerretsen
Tel: 1-888-647-7327; Fax: 1-888-547-7337
E-Mail: cruises@seacourses.com
WHO Facts Sheet

1. New Guide on Palliative Care Services for People Living with Advanced Cancer
2. New WHO Pocket-Charts will save Lives by Predicting Heart Attack and Stroke
3. New Standard for Documenting the Health of Children and Youth
4. Basic Surgery Skills to Save Lives and Prevent Disability
5. New Guidance on Insecticide-Treated Mosquito Nets

Compiled and edited by
Babichan K Chandy


1. NEW GUIDE ON PALLIATIVE CARE SERVICES FOR PEOPLE LIVING WITH ADVANCED CANCER

WHO released its first guide on planning palliative care services for people living with advanced stages of cancer. The guide, which is based on consultations with more than 70 leading cancer experts in the world, has identified highly effective low-cost public health models to care for terminally ill cancer patients, especially in developing countries.

The guide, ‘Palliative Care: Cancer Control Knowledge into Action, WHO Guide for Effective Programmes’ was launched on the occasion of World Hospice and Palliative Care Day, 6 October, 2007.

Palliative care is an approach that improves the quality of life of patients and their families facing life-threatening illness by providing pain-relief and management of other distressing and debilitating symptoms. Palliative care services are appropriate from the time of diagnosis of a life-threatening illness and throughout the course of the illness. Preliminary estimates show that each year, 4.8 million people who suffer from moderate to severe pain caused by cancer do not receive treatment.

“Everyone has a right to be treated, and die, with dignity. The relief of pain - physical, emotional, spiritual and social - is a human right” said Dr Catherine Le Galès-Camus, WHO Assistant Director-General for Noncommunicable Diseases and Mental Health. “Palliative care is an urgent need worldwide for people living with advanced stages of cancer, particularly in developing countries, where a high proportion of people with cancer are diagnosed when treatment is no longer effective.”

The new guide is aimed primarily at public health planners. It provides guidance on how to conduct a national situation analysis and response review, mapping the burden of cancers in advanced stages against palliative care services available, and recommending plans for low-cost public health models to close any gaps.

“Simple and low-cost public health models of palliative care can be implemented to reach the majority of the target population, particularly in developing countries where the majority of cases are diagnosed in late stages”, said Dr Benedetto Saraceno, Director a.i. for Chronic Diseases and Health Promotion. “These models consider the integration of palliative care services in the existing health system, with a special emphasis on community- and home-based care.”

In 2005, 7.6 million people died of cancer out of 58 million deaths worldwide. More than 70% of all cancer deaths occur in developing countries, where resources available for prevention, diagnosis and treatment of cancer are limited or nonexistent. Based on WHO projections, cancer deaths will continue to rise with an estimated 9 million people dying from cancer in 2015, and 11.4 million dying in 2030.

Yet many of these deaths can be avoided. More than 40% of all cancers can be prevented. Others can be detected early, treated and cured. Even with late stage cancer, the suffering of patients can be relieved with good palliative care.

For more information contact: Dr Cecilia Sepulveda, Senior Adviser, Essential Practices and Palliative Care, WHO, Geneva. Tel:+41.22.791.3706, Mobile: +41 79 574 7063, E-mail: sepulvedac@who.int
2. NEW WHO POCKET-CHARTS WILL SAVE LIVES BY PREDICTING HEART ATTACK AND STROKE

A new book of pocket-charts that will help health workers to identify people at risk of heart attacks and strokes and save lives by prescribing the most appropriate treatment is published by the World Health Organization (WHO). The charts can be adapted for use in any setting, in any country, with any patient.

The “Pocket Guidelines for Assessment and Management of Cardiovascular Risk” can be carried and used by any health care worker and is available in six languages. The guide contains easy-to-use charts that can predict the risk of a heart attack or a stroke and could help health workers to save and improve the lives of people in all countries.

“This is a real breakthrough. Now, health care workers everywhere - whether they are in a high-tech medical center in a big city, or riding a bicycle to visit patients in the countryside - can use a simple assessment and treatment tool to prevent heart attacks and strokes,” said the WHO Director-General, Dr Margaret Chan. “Primary health care workers now have a new tool to assess and manage people at risk of heart attacks and strokes. This brings cardiovascular care to the places and people who need it most.”

This is the first cardiovascular disease risk-prediction system that can be used worldwide and is also specially designed for use with people everywhere, including in low-resource settings. It is an important innovation that will help health workers to target limited health care resources at people who are at higher risk of developing heart attacks and strokes. These guidelines will be distributed to health workers in the form of pocket guides that have been produced for each of the WHO regions (risk profiles are different for different parts of the world). The pocket guides are available in hard copy and on the WHO website http://www.who.int/cardiovascular_diseases/resources/publications/en/index.html

“We are never prepared for the sudden death of a family member or a friend from a heart attack or stroke”, said Dr Catherine Le Galès-Camus, WHO Assistant Director-General for Noncommunicable Diseases and Mental Health. “Cardiovascular diseases are increasing towards epidemic proportions in developing countries - they already account for one-third of global deaths, and almost 10 percent of the global burden of disease, and are likely to become the developing world’s leading cause of death in 2010. There is reason for hope, however, given that huge potential exists to control this emerging epidemic. These risk charts are a major new tool for providing the best health care to all the world’s people”.

To ensure that the pocket guide gets into the hands of the health care workers who should use it, WHO will be collaborating with national Ministries of Health and health-focused nongovernmental organizations to organize ‘training of trainers’ workshops and distribution of the pocket guide.

The risk-prediction charts integrate the following risk factors when predicting the risk of a heart attack or stroke in the 10 year period following the patient assessment:

- Age, Sex, Tobacco use, Blood pressure, Diabetes status, Blood cholesterol

The pocket guide also incorporates management recommendations, based on the risk of developing heart attacks and strokes, in the following areas:

- Smoking cessation, Dietary changes, Physical activity, Weight control, Alcohol intake, Antihypertensive drugs, Lipid lowering drugs, Hypoglycaemic drugs, Antiplatelet drugs, Anticoagulant treatment, Revascularization surgery, Drugs that are not recommended.

Background: Cardiovascular disease (CVD) is the number one cause of death globally, causing one third of all deaths. In 2005, 11.8 million people died of heart attacks and other heart diseases, and 5.7 million died of stroke. Around 80% of these deaths were in low- and middle-income countries. By 2015, an estimated 20 million people will die from CVD annually, mainly from heart attacks and strokes. Socioeconomic costs of premature deaths and disability, and escalating costs of medical care make it all the more urgent to take measures to prevent and control this burgeoning epidemic in low- and middle-income countries where health care resources are limited.

Urbanization and globalization promote tobacco use, unhealthy diet and physical inactivity. These risk factors result in increased risk of people developing heart attacks and strokes because the result is raised levels of blood pressure, blood glucose, blood cholesterol and body weight. These, in addition to increasing age, are major risk factors that determine an individual’s chances of having a heart attack or stroke. This is known as the cardiovascular risk.

Until now, individuals have often been assessed and treated based on a single cardiovascular risk factor such as high blood pressure, high blood lipids or diabetes. This approach can result in committing a patient who has only a small cardiovascular risk to many years of drug therapy or, conversely, neglecting to treat those with an overall higher cardiovascular risk. Most importantly, the single
risk factor approach is not cost effective and is not affordable for many low-income and middle-income countries.

For successful prevention and control of the CVD epidemic, the combination of population-based and individual-based strategies are needed to lower the cardiovascular risk of populations and individuals. Population-wide strategies such as tobacco control and promotion of a healthy diet and physical activity are very cost effective in all countries. Cost effective interventions are also available to treat those who have survived heart attacks and strokes. However, treating risk factors such as high blood pressure and blood lipids is cost effective for low-income and middle-income countries only if interventions are targeted at high risk individuals.

In many low-income and middle-income countries, national and state health care budgets and per capita health expenditures are suboptimal. It is imperative, therefore, to use the limited resources that are available as effectively and efficiently as possible. This requires the prioritization of cost-effective approaches and the targeting of those patients who are most likely to benefit from interventions. In any population, those people who are most likely to benefit from cost-effective CVD interventions are the people with the highest cardiovascular risk.

The World Health Organization, in collaboration with the International Society of Hypertension (ISH), has developed cardiovascular risk prediction charts that enable cardiovascular risk assessment and prediction in non-western populations.

Many health care systems in low-income countries do not have the basic infrastructure facilities to support resource intensive risk prediction tools, particularly in primary health care. The WHO/ISH charts use easily measurable indicators of risk to quantify the 10-year risk of developing heart attacks and strokes. These indicators of risk include gender, age, systolic blood pressure, smoking status, diabetes and total blood cholesterol. For use in low-resource settings, where blood cholesterol measurement is not routinely available, alternative charts have been developed that predict risk without blood cholesterol. Also, in many low-resource settings, urine sugar levels may be used as a surrogate marker for diabetes.

Although the risk-prediction charts and pocket guides are simple to use, short training sessions will be required to introduce the charts into regular health care practice. The charts are ready for use now, and will be updated over time. Like all risk-prediction tools, the accuracy of this tool for specific populations can be improved over the long term by making minor adaptations as data are collated for individual populations. Technical assistance will be provided, through the WHO-ISH collaboration, to compare this new tool with other risk prediction methods, to further improve accuracy, and to adapt the CVD risk-prediction charts to suit very specific country contexts.

For more information contact: Shanthi Mendis.
Senior Adviser, Cardiovascular diseases, Chronic Disease and Health Promotion, Tel: +41 22 791 3441, mobile: +41 79 505 7455 E mail: mendiss@who.int

3. NEW STANDARD FOR DOCUMENTING THE HEALTH OF CHILDREN AND YOUTH

WHO published the first internationally agreed upon classification code for assessing the health of children and youth in the context of their stages of development and the environments in which they live.

The International Classification of Functioning, Disability and Health for Children and Youth (ICF–Cy) confirms the importance of precise descriptions of children’s health status through a methodology that has long been standard for adults. Viewing children and youth within the context of their environment and development continuum, the ICF-Cy applies classification codes to hundreds of bodily functions and structures, activities and participation, and various environmental factors that restrict or allow young people to function in an array of daily activities.

The rapid growth and changes that occur in first two decades of life were not sufficiently captured in the International Classification of Functioning, Disability and Health (ICF), the precursor to the ICF-Cy. The launch of the ICF–Cy addresses this important developmental period with greater detail. Its new standardized coding system will assist clinicians, educators, researchers, administrators, policy makers and parents to document and measure the important growth, health and development characteristics of children and youth.

Children who are chronically hungry, thirsty or insecure, for example, are often not healthy and have trouble learning and developing normally. This classification provides a way to capture the impacts of the physical and social environment so that these can be addressed through social policy, health care and education systems to improve children’s well-being.

“The ICF-Cy will help us get past simple diagnostic labels. It will ground the picture of children and youth functioning and disability on a continuum within the context of their everyday life and activities. In this way it enables the accurate and constructive description of children’s health.
and identifies the areas where care, assistance and policy change are most needed,” said Ros Madden, Australian Commission on Safety and Quality in Health Care, and, Chair of the Functioning and Disability Reference Group of the WHO Family of International Classifications (WHO-FIC) Network.

The ICF–CY has important implications globally for research, standard setting and mobilizing resources. “For the first time, we now have a tool that enables us to track and compare the health of children and youth between countries and over time,” said Nenad Kostanjsek of WHO’s Measurement and Health Information team. “The ICF–CY will allow countries and the international community to take informed action to improve children’s health, education and rights, by treating their health as a function of the environment that adults provide.”

The classification also covers developmental delay. Children who achieve certain milestones later than their peers may be at increased risk of disability. Using this classification, health practitioners, parents and teachers can describe these delays precisely in order to plan for health and educational needs and frame policy debates.

The children and youth version of the International Classification of Functioning, Disability and Health (ICF-CY) is launched today in Venice, with international praise:

• “The publication of the ICF-CY by the WHO provides, for the first time, a standard language to unify health, education and social services for children,” said Dr. Margaret Giannini, Director of the Office of Disability, U.S. Department of Health and Human Services.

• “This approach offers a scientific basis for describing each child’s functional abilities using a shared language. Further, the ICF-CY has important implications for educational policy, research, and service designs for children and youth with disabilities,” said Mary Ruth Coleman Ph.D., President Council for Exceptional Children (2007).

• “The ICF-CY is a tool that can be shared by clinical services as well as by schools, community agencies and government entities. Further, with the visibility of an international WHO standard, the ICF-CY can serve to affirm the universal needs and rights of children,” said Rune J. Simeonsson, Chair, WHO Work group on ICF-CY Children and Youth; University of North Carolina.

• “The approach of focusing on how children and youth function physically, socially and mentally within the context of their development and environment has important implications for special education,” said Yutaka Oda, President, National Institute of Special Education, Japan.

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4. BASIC SURGERY SKILLS TO SAVE LIVES AND PREVENT DISABILITY

The World Health Organization (WHO) is expanding its programme to train health care staff in low- and middle-income countries in essential emergency, basic surgery and anaesthesia skills. The programme, which already exists in 22 countries, will boost the capacity of first-level health facilities (rural or district hospitals and health centres) to deal with simple but essential surgery in a growing number of developing regions.

In many cases, death and permanent disability can be avoided through simple surgical interventions following road traffic injuries, interpersonal violence or war, abdominal emergencies, pregnancy complications, congenital abnormalities, fractures, burns, or the consequences of acute infections.

Together, these conditions cause the loss of approximately 11% of total lost years of healthy life (according to the World Health Report 2002). Injuries alone kill more than 5 million people every year, accounting for nearly one in every 10 deaths worldwide.

The WHO Emergency and Essential Surgical Care Project trains health staff in simple surgical procedures, anaesthesia and emergency care. After training and with the help of basic equipment, health care staff are able to perform surgical procedures that save lives and prevent disability.

“The initiative signifies a shift in the way we think about surgery,” explains Dr Luc Noel, in charge of clinical procedures at WHO. “Until recently, surgery was a neglected health issue in developing countries because it was assumed to be too expensive and sophisticated.”

Surgical intervention has become a common component in the management of patients with HIV/AIDS. Some complications associated with HIV infection (such as abscesses, anorectal disorders, lymphadenopathies, lipoatrophy or mild forms of Kaposi’s sarcoma) are also diagnosed and treated with simple surgical interventions. Current evidence shows that basic surgical and anaesthetic services should be integrated into primary healthcare packages.

“Why should a child die from appendicitis, or a mother and child succumb to obstructed labour, when simple surgical procedures can save their lives?” said Dr Meena Cherian, who heads the surgery programme at WHO.
The quality of emergency and essential surgical care is often constrained by inadequate basic equipment for interventions that are simple but vital, such as resuscitation, giving oxygen, assessing anaemia and inserting a chest drain.

Other barriers to the timely and appropriate delivery of basic surgical services in low and middle income countries include poor infrastructure and insufficient numbers (and training) of health-care professionals.

In most developing countries, adequate surgical services are found only in tertiary centres in urban areas. Furthermore, the migration of health professionals leaves a shortage at primary-health facilities, where services are provided by non-specialist or even non-medical personnel, many of whom are inadequately trained.

However, a number of isolated, local initiatives have shown that even with only basic training and technologies, many lives can be saved or improved.

For instance, clubfoot (a congenital deformity of the foot, marked by a twisted position of the ankle, heel and toes) can greatly impede mobility in children; if untreated, clubfoot can lead to severe disability and loss of productive life. Clubfoot is estimated to occur in 1-2 per 1000 live births, which translates into well over one hundred thousand cases worldwide per year. Clubfoot diagnosed at birth or soon after can often be treated using a minimally invasive technique called the Ponseti method.

The Ponseti method involves multiple manipulations and plaster castings early in a child’s life. Proper implementation of the Ponseti method results in a dramatic decrease in the number of clubfoot cases that require surgery. These techniques have been quite effective in the industrialized world; they require minimal resources and can be implemented by health personnel in primary health care facilities. Recent programmes in Africa, India and South America are training local health care professionals in the Ponseti technique. In Uganda, over one hundred professionals have been trained, resulting in effective treatment of 95% of new cases of clubfoot.

WHO will present future actions of the Emergency and Essential Surgical Care Project to stakeholders and partners at a meeting of the Global Initiative for Emergency and Essential Surgical Care in Dar-es-Salaam, Tanzania, on 24-25 September. At the meeting, WHO will also seek support from multilateral donors to expand the initiative.

WHO established the Global Initiative for Emergency and Essential Surgical Care in 2005 to improve access to and quality of surgical care in the developing world. A broad partnership of internationally recognized organizations and individuals, the GIEESC counts 22 countries representing all WHO regions among its members.

Stakeholders include doctors (surgeons, anaesthetists, paediatricians, obstetricians, nurses), economists, donors, non-governmental organizations, professional societies. A meeting co-hosted by WHO, the World Bank, Global Health Sciences, the Rockefeller Foundation and the Karolinska Institute (Sweden) was held in June 2007 to promote access to surgical services in resource-constrained countries in sub-Saharan Africa.

For more information contact: Daniela Bagozzi, WHO, Geneva, Communications Officer, Health Technology & Pharmaceuticals, Tel: +41 22 791 4544, Mobile: +41 79 475 5490, E-mail: bagozzid@who.int

5. NEW GUIDANCE ON INSECTICIDE-TREATED MOSQUITO NETS

The World Health Organization (WHO) issued new global guidance for the use of insecticide-treated mosquito nets to protect people from malaria. For the first time, WHO recommends that insecticidal nets be long-lasting, and distributed either free or highly subsidized and used by all community members.

Impressive results in Kenya, achieved by means of the new WHO-recommended strategy, show that free mass distribution of long-lasting insecticidal nets is a powerful way to quickly and dramatically increase coverage, particularly among the poorest people.

Previously, WHO’s guidelines focused primarily on providing insecticide-treated mosquito nets for use by children under five years old and pregnant women. However, recent studies have shown that by expanding the use of these nets to all people in targeted areas, increased coverage and enhanced protection of vulnerable groups can be achieved, while protecting all community members. In areas of high transmission of malaria, where young children and pregnant women are the most vulnerable, WHO now recommends making their protection the immediate priority while progressively achieving full coverage.

In Kenya, from 2004 to 2006, a near ten-fold increase in the number of young children sleeping under insecticide-treated mosquito nets was observed in targeted districts, resulting in 44% fewer deaths than among children not protected by nets, according to preliminary data from the Government of Kenya. This is the first demonstration of the impact of large-scale distribution of insecticide treated mosquito nets under programme conditions, rather than in research settings, where, in different parts of Africa, reduction observed in overall mortality.
has ranged from 14% up to 60%.

These achievements can be attributed to three principal ingredients which all need to be present for malaria control efforts to succeed: high political commitment from the government, strong technical assistance from WHO, and adequate funding from bilateral and multilateral donors.

“WHO’s new evidence-based guidance provides a road map for ensuring that life-saving long-lasting insecticidal nets are more widely available and used by communities, and are more effective in protecting poor women and children,” said Dr Margaret Chan, the Director-General of the World Health Organization. “The collaboration between the Government of Kenya, WHO, and donors serves as a model that should be replicated throughout malarious countries in Africa.”

In 2001, the Ministry of Health of Kenya developed the new national strategy for malaria control targeting increased coverage of insecticide treated mosquito nets. In 2006, President Mwai Kibaki launched an effort funded by a US$ 17 million grant from the Global Fund to Fight AIDS, Tuberculosis and Malaria, to distribute 3.4 million long-lasting insecticidal nets free of charge to children in 45 of Kenya’s 70 districts through two campaigns. The Division of Malaria Control of Kenya, working with an international research team, has been monitoring the coverage and impact of this intervention.

Between 2002 and 2006, with a GBP 6 million grant from the United Kingdom Department for International Development, WHO has advocated for and supported the Kenyan Government to undertake free mass distribution, provided technical support for the preparation of two Global Fund proposals, and provided a full-time logistician to support planning and implementation of free net distribution. WHO’s contribution also included helping to outline delivery mechanisms and pricing strategies to reach coverage targets, sharing knowledge and lessons learnt related to net distribution, and strengthening partnerships. Two WHO staff work full-time on supporting the Kenyan Government’s malaria control programme.

“The Government of Kenya is strongly committed to achieving improved and equitable health outcomes for all Kenyans, particularly women and children. The incredible gains in Kenya have been made possible with donor funds, which enabled us to buy these nets, and WHO’s technical support, which helped ensure that they reached those who most need them,” said Charity Ngilu, Minister of Health of Kenya.

Insecticide-treated nets are mosquito nets treated with insecticides which repel, disable or kill the vector mosquitoes which transmit malaria. Conventional insecticide treated mosquito nets need to be re-treated regularly, while long-lasting insecticidal nets (LLINs) are designed to be effective without re-treatment for the life of the net.

The new WHO guidance on nets recommends that campaign-like mass distribution strategies be complemented by delivery through routine health services to achieve and maintain high levels of coverage.

At around US$ 5 per net, LLINs are a simple and cost-effective intervention against malaria. Until recently, progress in scaling up insecticide treated mosquito nets has been slow in many countries, due in part to the inability of the international community to reach a consensus on how to deliver them to achieve and sustain high coverage. Approaches have included commercial channels, social marketing, and free or subsidized distribution through routine public health services or campaigns.

In some cases, a small co-payment may motivate health workers to distribute long-lasting insecticidal nets, thus boosting coverage, but the new WHO guidance stresses that cost should not be a barrier to access. Thus far, only free distribution has enabled rapid achievement of high population coverage and elimination of inequities in net use, as has been demonstrated in Kenya.

“This data from Kenya ends the debate about how to deliver long-lasting insecticidal nets,” said Dr Arata Kochi, head of the WHO’s Global Malaria Programme. “No longer should the safety and well-being of your family be based upon whether you are rich or poor. When these nets are easily available for every person, young or old, malaria is reduced.”

Malaria, which is preventable and treatable, still kills more than one million people each year, mainly African children under five years of age.

For more information contact: Valerie Crowell, HIV/AIDS, Tuberculosis and Malaria, Technical Officer, WHO, Geneva, tel: +41 22 791 1204, email: crowellv@who.int  The new WHO guidance can be found here: http://www.who.int/malaria/itnguidelines.html
# Yearly Author Index

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