EDITORIAL
Lung Cancer Screening: An insight
Adel K Ayed 267

REVIEW ARTICLE
Massive Bleeding in Trauma and Surgery: Role of rFVIIa
Mridul Panditrao, Minnu Panditrao, Mohammed Shamsah 269

ORIGINAL ARTICLES
Chylous Leakage after Donor Nephrectomy: A Rare Complication and a Nightmare for Surgeons
Mukesh Kumar Vijay, Preeti Vijay, Prasanna Kumar Mishra, Kaushik Sinha, Mrinal Kanti Ray, Pramod Kumar Sharma 277
Post-Infantile Presentation of Intestinal Malrotation
Ahmed M Kamal, Abdurrahman S Almulhim 281
The Role of Trace Elements in Helicobacter Pylori Infected Patients
Fatma Bozkurt, Serda Gulsun, Cemal Ustun, Mehmet Faruk Geyik, Salih Hsoglu 287
Squamous Intraepithelial Lesions Associated with HIV Infection and CD4+ Cell Counts in an Iranian Population
Farah Farzaneh, Esmat Barouti, Zohreh Amiri, Farzaneh Rahimi, Masoud Keyhobadi, Maryam Shahami 291
Papillary Microcarcinomas of the Thyroid Gland: Do We Need to be Aggressive in the Management?
Ali Alwadan, Jamila Al Senebani, Amil Al Qubati, Azzan Al Saadi 297
Related Factors for Rectosigmoid Hyperplastic Polyps: A Hospital-Based Study
Shih-Wei Lai, Kuan-Fu Liao 301

CASE REPORTS
Colo-Colic Intussusception in Amoebic Colitis: A Case Report
Seetharam Prasad, Lingadakai Ramachandra, Arunandichelvar Arumolichelvan 307
Unusual Presentation of Organic Foreign Body in Upper Aerodigestive Tract: Report of Two Cases
Mohammad Ibql Zea, Mohammad Hanif Beg, Maulana Mohammad Ansari 310
Small Cell Carcinoma Metastatic to the Appendix with Acute Suppurative Appendicitis
Meng Zhu, Li Qiu, Parajuly S Shyam 313
Caecal Carcinoma Presenting with Adult Intussusception
Mokhtar Eltair, Abdul Jaleel Poovathumkadavil, Abdul-Wahed Moshikh 317
Acute Bilateral Cataract in a Non-Complicated Type 1 Diabetic Youngster: A Case Report
Soliman El Gebely, Muath Al Nassar, Abdul Razzaq Al Shammeri 321
Atypical Presentation of Vibro Cholera
Mariam Al-Fadhli, Suha Abdul Salam, Mohammad Saraya 324
Short-lasting Unilateral Neuralgiform Headache Attacks with Conjunctival Injection and Tearing (SUNCT)
Syndrome Secondary to Pituitary Apoplexy
Sundus Al Duaij, Ahmad Al-Jazzaf, Mohamad Jawad 327
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Lung cancer is the leading cause of death in many countries and the most common cancer worldwide accounting for 1.2 million incident cases annually. The long term survival remains low despite advances in surgery, chemotherapy and radiotherapy\(^1\). Early stage of lung cancer is amenable for curative lung resection before local invasion or remote spread of the disease. By the time symptoms develop, the tumor is often at a late stage and that precludes the surgical option. Therefore, the prognosis is dismal (< 10% survival at 5 years)\(^1,2\).

Lung cancer is classified broadly into non-small cell lung cancer (NSCLC) which accounts for 80% of all lung cancers and small cell lung cancer (SCLC) for the remaining 20%. Individuals with early stage NSCLC can achieve cure through surgical resection and those people have the greatest potential to benefit from any screening program.

The incidence of lung cancer rises with age and it is uncommon before the age 40 years. The most important risk factor is smoking as 80 - 90% of all people diagnosed with lung cancer are smokers. Other risk factors include occupational hazards and previous scars due to chronic infections.

Because of the dilemma with a stage at diagnosis, there has been increased interest in testing methods like chest X-ray (CXR), sputum cytology, and low dose CT scanning (LDCT). The benefit of a screening test should include early detection of people with the disease and increasing one’s survival rate and the test should not harm the individual, especially people who are healthy and included in any study.

**Sputum cytology and CXR**

Sputum cytology and CXR have each been assessed in five randomized controlled trials (RCTs). The results suggest that neither CXR nor sputum cytology satisfy the criteria of a beneficial screening test. These studies showed that the combination of a CXR and sputum cytology did not decrease lung cancer mortality, nor did prolong the life expectancy of an individual with the disease. In addition, those studies did not address the harmful effects of these tests on individuals.

There were several problems concerning these trials. First, they did not use “no screening” as a comparison group and instead, compared intensive screening versus less frequent screening or CXR alone to CXR plus sputum cytology. Therefore, these trials did not assess whether screening was better than no screening. Second, the studies did not show improvement in disease specific or total mortality.

More sensitive studies of sputum for abnormalities suggestive of malignancy have been done. CXR screening every four months or six months in combination with sputum cytology has been assessed in two RCTs and CXR alone every six months as a single modality was assessed in a third RCT. In none of these studies, there was a control group (non-screening group), and the power of these studies to detect small decrease in mortality was limited. In addition, in none of these studies was CXR associated with a reduction in lung cancer mortality\(^1\).

**Low-dose CT Scanning (LDCT)**

LDCT is a scan that allows a low-resolution image of the lungs. There are several observational studies that evaluated LDCT is. Some studies concluded that LDCT associated with a reduction in lung cancer mortality. Others have concluded that these results may reflect the effect of bias. This conclusion is evidenced by detecting lung cancer at an early stage of the disease. However, some argue that the detection of lung cancer at an early stage of the disease does not necessarily mean improvement in life expectancy.

LDCT may be detecting nodules of histological cancer that are silent in their behavior, *i.e.*, it may lead to over diagnosis. So testing these types of individuals cannot increase their life expectancy. In addition, the debate whether surgical resection of screen-detected lung cancer changes the natural history of the disease.
continues. The debate is that the harmful effect of LDCT to the screened individuals may exceed the benefit. The harmful effect is due to high costs of screening, the follow-up, the morbidity and anxiety associated with false positive results\cite{1-3}.

**Evidence that LDCT reduces mortality for lung cancer**

In October 2010, the National Cancer Institute (NCI) announced that individuals who were randomized to screening with LDCT (26,722 persons) had less deaths from lung cancer than those assigned to screening with CXR (26,732). This study included 53,454 patients aged between 55 and 74 years and had a history of heavy smoking. They were screened once a year for three years and were followed for 3.5 additional years without screening. The rate of positive screening tests was 24.2\% with LDCT and 6.9\% with CXR over all the three years. A total of 96.45\% of the positive screening results in the LDCT and 94.5\% in CXR group were false positive results. The incidence of lung cancer was 645 cases per 100,000 persons in the LDCT and 572 cases per 100,000 person-years in CXR. At each year of screening, results suggestive of lung cancer were nearly three times as common in LDCT group than CXR group, and only 2 - 7\% of these results proved to be lung cancer. Cases discovered after LDCT were more likely to be early stage and less likely to be late stage than those discovered after CXR. There were 247 deaths from lung cancer per 100,000 person-years in LDCT and 309 deaths per 100,000 person-years in the CXR group, representing a relative reduction in mortality from lung cancer with LDCT of 20\%. The conclusion of this study was that screening with the use of LDCT scan reduces mortality from lung cancer compared with CXR group\cite{4,5}.

The major problem that will face a health service perspective by introducing LDCT screening for lung cancer would come from the increased number of false positive results. As a result, a high proportion of screening participants will undergo further follow-up, either by further CT or biopsy. The interpretation of positive results is also subjective to substantial variation. The difference in results is to some extent explained by the different definitions of a positive CT examination. In addition, even if the same definitions were used, variation may exist and precaution must be taken when generalizing data from country to country. Cost-effectiveness data from the NCI study is still not available to determine the amount of over-diagnosis bias, the estimate of cost for annual screening, and cost of further test for the false negative results. The cost also includes the diagnostic follow-up and treatment. The strategy for early detection of lung cancer before implementation will depend on the eligibility criteria of participants (target population), screening frequency, diagnostic follow-up, and treatment. We expect that a national screening program of annual LDCT would be very expensive and this can be most cost-effective, if very high-risk individuals alone are targeted\cite{6}.

However, a decision about the clinical effectiveness of LDCT screening for lung cancer is now answered by the controlled trial evidence that LDCT screening reduces mortality from lung cancer.

**REFERENCES**

Massive Bleeding in Trauma and Surgery: Role of rFVIIa

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ABSTRACT

Uncontrolled hemorrhage is the leading cause of death in trauma patients. It also constitutes a major cause of perioperative morbidity and mortality. The most of critically traumatized patients as well as many postoperative patients suffer profound bleeding accompanied by systemic coagulopathy. When the routine corrective measures have been exhausted and still there does not seem to be any respite, the anesthesiologists and intensivists are in great dilemma and panic attack of "what next"? rFVIIa (NovoSeven®), has already been approved and successfully recommended in many coagulopathies (both congenital as well as acquired) and abnormalities of platelet function (past or present refractoriness to platelet transfusion).

However, there are very few guidelines, if any, on its use for surgical / traumatic massive and uncontrolled bleeding. Because of the recent trends in rFVIIa usage in non-approved settings by physicians of various disciplines, significant concerns about its safety, efficacy and costs have arisen. In addition because of lack of randomized trials, the dosing is not yet standardized. An effort has been made to discuss its off label uses in massive bleeding, especially due to trauma and in the perioperative period. Also review of available guidelines has been mentioned along with recommendations.

KEY WORDS: recombinant activated factor VII, recommendations

INTRODUCTION

Traumatic injury is the leading cause of death worldwide among persons between 1 and 44 years of age[12], fourth leading cause of death in all age groups[13] and accounts for 10% of all deaths[4]. In fact, Global Burden Diseases (GBD) Study has classified the injuries as Group-3, along with other two broader categories of diseases; communicable, and non-communicable[5]. Despite improvement in care, uncontrolled bleeding contributes to 30 to 40% of trauma related deaths and is a leading cause of potentially preventable early in-hospital deaths[6-9].

PHYSIOLOGY OF BLEEDING AND HEMOSTASIS[10,11] As a physiological response to an injury, whether, traumatic or planned (surgical), especially, if there is an integumental (skin or mucus membrane) breach then logically hemorrhage is the result. American College of Surgeons13 (Advanced Trauma Life Support (ATLS) Team) has classified bleeding / hemorrhage in to four classes (Table1). This has further been modified recently to include some more parameters[11] (Table 2), Class I being, non-shock state, such as occurs when donating a unit of blood, whereas class IV being pre-terminal event requiring immediate therapy[13]. Massive hemorrhage may be defined as loss of total estimated blood volume (EBV) within a 24-hour period, or loss of half of the EBV in a 3-hour period. Bleeding secondary to surgical / traumatic cause is usually as a result of combination of vascular injury and coagulopathy[14].

STAGE I: VASOCONSTRICTION As a response to hemorrhage, all the mediators of vasoconstriction: noradrenaline, thromboxanes (TBXs) and mediators of RA system are released, causing intense vasoconstriction.

Effects: The first aid system can last from minutes to hours.
1. Vasoconstriction minimizes vessel diameter and slows bleeding
2. TBXsA2 leads to smooth muscle relaxation
3. The tamponade effect by the extravasated blood adds to vasoconstriction

STAGE II: PLATELET PLUG FORMATION A complex phase formed by three sub-phases
1. Platelet adhesion
2. Platelet release reaction
Platelets create extensions and come in contact with each other. They release their contents i.e., α granules & dense granules (growth factors, epinephrine, collagen, ADP, ATP, Ca++, 5HT)
3. 5HT & TBXs: potentiate vasoconstriction
4. Platelet aggregation: ADP increases platelet stickiness and they go on adhering with each other to create a platelet plug

STAGE III: COAGULATION CASCADE

This is the most complex of all the hemostatic processes. Liquid blood which is now exposed to the external environment gets converted into a gel or coagulum / clot made up of proteinous fibers – fibrin. In this network various elements of blood are trapped.

STAGE IV: FIBRINOLYSIS

For checking excessive clot formation and preventing its spread, factors like plasminogen, antithrombin III and protein C etc., influence this step.

Stage III: Phase of Coagulation / Coagulation Cascade: In this review, we shall concentrate on this phase in greater detail. The phase of coagulation can be further expanded in to three sub-phases\[13\] as per the activation of various coagulation factors:

1. Initiation phase (Fig. 1)\[15\]: As soon as vessel wall injury takes place tissue factor (TF) is exposed to the circulating endogenous factor VII which gets activated to VII A. Thus formation of TF / VII A complex takes place leading to the initiation of coagulation\[16,17\].

2. This complex activates the cells bearing TF to produce

3. Amplification phase (Fig. 2)\[15\]: The factor XA / VA complex activates and converts little amount of prothrombin to thrombin at subendothelial surface. This thrombin amplifies the process by activating V, VII and platelets\[18\]. The activated platelets bind factors VA, VIIA, IX A.

4. Propagation phase (Fig. 3)\[15\]: The thrombin activated platelets change their shape and expose negatively charged phospholipids to which factor VIIA / IXA complex binds, leading to factor X activation (XA) on the surface of activated platelets. This XA with VA again forms a complex and leads to activation of large amount of prothrombin resulting in a “Thrombin burst”. This thrombin is an enzyme that converts fibrinogen to fibrin and in addition activates factor XIII to XIIIA (fibrin stabilizing factor), so on and so forth and the process goes on till the whole area of the breach is completely “plugged in”.

As has already been pointed out, uncontrolled hemorrhage is the second leading cause of death from trauma, whether non-surgical or surgical. Most critically ill, traumatized patients suffer profound bleeding accompanied by systemic coagulopathy. The factors which ultimately decide the patient’s survival are; severity of injury\[19\], degree of coagulopathy prior to drug administration and co-existing acidosis\[20\].

<table>
<thead>
<tr>
<th>Class</th>
<th>Percentage loss of Blood Volume</th>
<th>Description</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Upto 15%</td>
<td>No Significant changes in vitals</td>
<td>No resuscitation required</td>
</tr>
<tr>
<td>II</td>
<td>15 – 30%</td>
<td>Mild tachycardia, narrow pulse pressure, skin pale and cool, Early signs of mental confusion</td>
<td>Volume resuscitation with crystalloids (Normal Saline / Ringer Lactate)</td>
</tr>
<tr>
<td>III</td>
<td>30 – 40%</td>
<td>Hypotension, moderate tachycardia decreasing peripheral perfusion, worsening mental status</td>
<td>Fluid resuscitation aggressively, Blood transfusion</td>
</tr>
<tr>
<td>IV</td>
<td>More than 40%</td>
<td>Left untreated, death ensues</td>
<td>Aggressive blood transfusion and other critical care support</td>
</tr>
</tbody>
</table>

1. Factor IX to IX A
2. Factor X to X A
The XA binds to VA on the cell surface.

3. Amplification phase (Fig. 2)\[15\]: The factor XA / VA complex activates and converts little amount of prothrombin to thrombin at subendothelial surface. This thrombin amplifies the process by activating V, VII and platelets\[18\]. The activated platelets bind factors VA, VIIA, IX A.

4. Propagation phase (Fig. 3)\[15\]: The thrombin activated platelets change their shape and expose negatively charged phospholipids to which factor VIIA / IXA complex binds, leading to factor X activation (XA) on the surface of activated platelets. This XA with VA again forms a complex and leads to activation of large amount of prothrombin resulting in a “Thrombin burst”. This thrombin is an enzyme that converts fibrinogen to fibrin and in addition activates factor XIII to XIIIA (fibrin stabilizing factor), so on and so forth and the process goes on till the whole area of the breach is completely “plugged in”.

Modified from Committee on Trauma\[11\], CNS = central nervous system

Table 1: American College of Surgeons, Advanced Trauma Life Support (ATLS) Team classification of hemorrhage\[12\]

<table>
<thead>
<tr>
<th>Parameter</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood loss (ml)</td>
<td>&lt; 750</td>
<td>750 - 1500</td>
<td>1500 - 2000</td>
<td>&gt; 2000</td>
</tr>
<tr>
<td>Blood loss (%)</td>
<td>&lt; 15%</td>
<td>15 - 30%</td>
<td>30 - 40%</td>
<td>&gt; 40%</td>
</tr>
<tr>
<td>Pulse rate (beats / min)</td>
<td>&lt; 100</td>
<td>&gt; 100</td>
<td>&gt; 120</td>
<td>&gt; 140</td>
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<tr>
<td>Blood pressure</td>
<td>Normal</td>
<td>Decreased</td>
<td>Decreased</td>
<td>Decreased</td>
</tr>
<tr>
<td>Respiratory rate (breaths / min)</td>
<td>14 - 20</td>
<td>20 - 30</td>
<td>30 - 40</td>
<td>&gt; 35</td>
</tr>
<tr>
<td>Urine output (ml / hour)</td>
<td>&gt; 30</td>
<td>20 - 30</td>
<td>5 - 15</td>
<td>Negligible</td>
</tr>
<tr>
<td>CNS symptoms</td>
<td>Normal</td>
<td>Anxious</td>
<td>Confused</td>
<td>Lethargic</td>
</tr>
</tbody>
</table>

Table 2: Classification of hemorrhage

Modified from Committee on Trauma\[11\], CNS = central nervous system
SO AS A NOVEL APPROACH: rFVIIa???

After taking into consideration in detail, the coagulation cascade, if this process can be augmented at the initial stage viz., at the Initiation phase with help of a recombinant activated factor VII (rFVIIa – NovoSeven®), the process can be circumvented.

rFVIIa is a recombinant protein, with a molecular weight of 50 kDa and has the same amino-acid sequence as native VIIa. When infused, its half-life is 2 - 3 h. The dose recommended for patients with Factor VIII and IX deficiencies complicated by inhibitors is 90 μg/kg. This dose was chosen as it consistently produces a plasma rFVIIa level > 10 U/ml, which is thought to be the level necessary for cessation of bleeding. When a lower dose of 35 μg/kg was compared with 90 μg/kg in a randomized trial of hemophiliacs undergoing surgery, bleeding was increased in the 35 μg/kg group. However, in a trial of rFVIIa for muscle and soft-tissue bleeding, 35 μg/kg was equivalent to 70 μg/kg. Dosing for other indications is arbitrary, with most reports using the 90 μg/kg dose. It does seem that lower doses are effective for select situations, such as intracerebral hemorrhage and warfarin reversal. There is some evidence of the use of mega doses (300 μg/kg) of rFVIIa for young hemophiliacs, which may lead to a rapid hemostatic response without the need for repeat dosing. However, these large doses raise concern about increasing the prothrombotic risk, and have not yet been studied in adults. The lack of an accepted method of monitoring rFVIIa hinders dosing decisions.

rFVIIa works locally at the site of vascular injury, in the presence of tissue factor TF (tissue factor dependent) activates or even in the absence of TF directly (tissue factor independent), converting factor X to Factor XA on the surface of activated platelets resulting directly in “thrombin burst” leading to stable hemostatic plug. Thus on the basis of available literature, rFVIIa has been approved and indicated for treatment of bleeding episodes and for the prevention of bleeding in those undergoing invasive procedures in patients diagnosed to have:

I. Congenital hemophilia with F VIII and IX inhibitors (Hemophilia A & B)
II. Acquired hemophilia
   a. especially, secondary to formation antibodies against inherent factor VIII. This affects adults, middle aged and both sexes are affected equally (as opposite to congenital hemophilia with young age group and male preponderance).
   b. Drug induced or penicillin, chloramphenicol, phenytoin
   c. Autoimmune conditions like rheumatoid arthritis, SLE, malignancies: solid or hematologic, lympho-proliferative
   d. Pregnancy related and post partum
III. Rarer bleeding disorders:
   a. Inherited FVII deficiency
   b. Congenital deficiencies of multiple coagulation factors.
c. Glanzmann’s thrombasthenia
d. Patients with Factor VII and XI deficiency
e. Bernard - Soulier syndrome.
f. Giant platelet syndrome

IV. Pre-procedural management in patients with end-stage liver disease

Until now, clear cut evidence in the form of large controlled trials confirming concrete evidence for the use of rFVIIa in surgical procedures is very sketchy. However, there are some trials where smaller number of patients receiving rFVIIa was compared with placebo. Thus, a larger multicenteric and multispecialty trial is yet to come forth. The available evidence which has come forward for the use of rFVIIa in various conditions is mentioned here. It is to be noted that this is mainly in the form of case reports, case series and not randomized controlled trials.

1. Perioperative and early postoperative bleeding is a common complication in gynecological surgery. Post menopausal patients (age range 58 - 72 yrs, n = 4) undergoing procedures like elective hysterectomies for benign fibroids, carcinomas of cervix, endometrium or uterine carcinomas or metastatic carcinomas of genital tract, who had episodes of profuse hemorrhage were given rFVIIa in the dose range of 17-70 μg/kg. In three patients, the bleeding resolved within 12 hours after a single dose. In the patients with metastatic disease, a 2nd dose was needed and complete resolution of bleeding took place within 12 hours after the 2nd dose.

2. For patients with hematological and / or oncological bleeding, platelet transfusion is the only most common intervention. It has its own limitations viz., allo-immunization, transmission of bacterial and viral infections, and a shorter shelf life. Pediatric patients (n = 8) undergoing surgical resection of brain tumors showed promising results and better outcome after the use of rFVIIa. In another report, rFVIIa was used to control massive postoperative hemorrhage in patients (n = 3) undergoing major thoracic surgery for lung cancer. A bolus of 90 μg/kg was given, while in two out of them it had to be repeated after two hours at 60 μg/kg. The clinical response was absolutely effective in arresting bleeding without hypercoagulability or thromboembolic phenomena.
3. Initially, conditions with increased thromboembolic risk, including trauma with or without disseminated intravascular coagulation (DIC), were considered a contraindication for the drug. The mechanism of action of rFVIIa suggests enhancement of hemostasis limited to the site of injury without systemic activation of the coagulation cascade. This was confirmed by one report[53]: seven massively bleeding, multi-transfused (median, 40 units (range, 25-49 units of packed cells), coagulopathic trauma patients were treated with rFVIIa (median, 120 μg/kg, range, 120 - 212 μg/kg) after failure of conventional measures to achieve hemostasis. Administration of rFVIIa resulted in cessation of the diffuse bleed, with significant decrease of blood requirements to two units (range, 1 - 2 units) of packed cells (p < 0.05); shortening of prothrombin time and activated partial thromboplastin time from 24 seconds (range, 20 - 31.8 seconds) to 10.1 seconds (range, 8 - 12 seconds, p < 0.005) and 79 seconds (range, 46 - 110 seconds) to 41 seconds (range, 28 - 46 seconds, p < 0.05), respectively; and an increase of FVII level from 0.7 IU/ml (range, 0.7 - 0.92 IU/ml) to 23.7 IU/ml (range, 18 - 44 IU/ml, p < 0.05). Three of the seven patients died of reasons other than bleeding or thromboembolism. The authors are convinced to conclude, that the use of the drug in trauma patients suffering from uncontrolled hemorrhage appears to be rational. The results of this report suggest that in trauma patients rFVIIa may play a role as an adjunctive hemostatic measure, in addition to surgical hemostatic techniques, and provides the motivation for controlled animal and clinical trials[53].

4. In a review of various case reports[53] for diverse indications and clinical situations, rFVIIa has been reportedly used in infants and elderly patients for cardiac surgery (n = 18). Either single bolus dose or divided doses were given. Bleeding significantly reduced in 16 out of 18, and was completely terminated in 9 out of 18 patients. rFVIIa had been administered before removal of an intra-aortic balloon pump.

5. Freiderich et al[54] recently reported their positive experience in the first prospective, randomized, double-blind, placebo-controlled trial of the use of rFVIIa in radical prostate surgery patients. A placebo treatment was compared with two doses (20 and 40 μg/kg) of rFVIIa. Blood loss was decreased in the rFVIIa groups (p < 0.01), and transfusions were eliminated in the higher dose group. Operative time decreased in the rFVIIa group (120 min versus 180 min, p < 0.05). No deleterious safety issues were identified, and in this group of older males those receiving rFVIIa did not develop the complications associated with hypercoagulopathy.

6. There are two very interesting reports[56,57] of two young females (both, 29-yr old) multipara, both essentially normal preoperatively, developed uterine atony, DIC and intra and post partum hemorrhage. The conventional treatment of uterotonic drugs, prostaglandins, transfusion of red cells (packed) as well as fresh frozen plasma failed to control bleeding. In one patient hysterectomy also could not stem the bleeding. In both patients 90 μg/kg of rFVIIa was given as final attempt to control the bleeding and save life. Surprisingly within 15 – 20 minutes of intravenous administration the bleeding stopped with resolution of coagulopathy and no side effects.

Recently an open non-randomized study was published[58]; a first of its kind where until November 2006 authors had administered rFVIIa to 38 parturients. Based upon experience with first 12 patients, they prepared guidelines for the use of rFVIIa. As a part of these guidelines, 26 patients who had PPH and received rFVIIA were compared to another group of 22 women who were treated during same time period without rFVIIa. They found that, the total amount of blood loss was signifcantly higher (11.3 ± 4.5 Vs 8.0 ± 3.1 l). The coagulation screen revealed significantly longer partial thromboplastin time (APTT) and prothrombin time (PT) values and significantly lower fibrinogen values in patients receiving rFVIIa. The need for red blood cells, platelets and fibrinogen concentrate was significantly higher in these women. Although the response was considered good in two-thirds of the women, several patients received rFVIIa with a poor or no response, as a result of arterial bleeding. So they concluded that, they did not gain any evidence to extend the use of rFVIIa into less severe cases of PPH. Furthermore, this policy would result in a profound increase in the overall costs of the treatment. Their recommendation was that, randomized placebo-controlled trials are urgently needed to optimize the use of rFVIIa in obstetric hemorrhage.

Similar words of caution are mentioned in one report[59] where authors are advising on randomized controlled trials and FDA approval for the use of rFVIIa in non-hemophiliac patients and ‘off the label’ indications.
On the other hand, a recent very lucid review, takes into consideration various factors playing a role in genesis, diagnosis and treatment of obstetric hemorrhage, confirming the role of rFVIIa in improving final outcome in the peri-partum hemorrhage cases.

Another report takes into consideration the role of rFVIIa in major obstetric hemorrhage. Authors report the use of recombinant activated factor in three cases of massive obstetric hemorrhage. Prolonged international normalized ratio (INR), activated partial thromboplastin time (APTT), and reduced fibrinogen were the trigger to use rFVIIa. It was effective to halt the process of coagulopathy, secure homeostasis and improve laboratory parameters in all three patients. They conclude that, rFVIIa is a potential hemostatic agent in massive obstetric hemorrhage. Its successful use has been reported in post-surgical bleeding and consumptive coagulopathy. It may abolish the need for hysterectomy, which has a devastating effect on the future fertility and psychological well-being of the patient.

Another path breaking effort, which is under way, is the creation of “NICE” (NovoSeven® In Critical Care Evaluation) Registry, wherein users of NovoSeven® are encouraged to register all cases of NovoSeven® usages in India. The indications for the use have been varied viz., obstetric bleeding (n = 28), liver diseases (n = 26), trauma (n = 25), thrombocytopenia (n = 20), upper GI / lower GI bleeds (n = 18), other surgeries (n = 16), intracerebral hemorrhage (n =15) and other conditions like anti-coagulation associated or other coagulopathies, cardiac surgeries, dengue etc. The reported evidence is that in nearly 65% patients bleeding stopped totally and in about 23% patients it was significantly reduced. Only about 12% patients refused to respond to it at all. When judged on the basis of survival, more than 70% patients were alive. So the report says that, they are finding the preliminary / interim data, encouraging. In addition, the latest evidence based guidelines are also posted on the website.

Although this may not be equated as the hard evidence from, say a randomized controlled trial, it has its own value in terms of ‘first step towards collection of data in ‘off-label’ use of rFVIIa, in India.

Thus, after having gone through all the available evidence about various recommended and ‘off the label’ (use that is not yet approved / recommended, but being used mainly based upon, anecdotal hearsay, random case reports and unrandomized open trials) it would appear that rFVIIa may be a useful weapon in combating uncontrolled hemorrhage of surgical and traumatic origin. However, lack of randomized controlled trials, exorbitant cost of the preparation and lack of standardization of dosage makes it very difficult to be used as a generalized and universal treatment modality. Even in that, there will be inherent ethical issues involved while conducting a randomized controlled trial in deciding which patients to be assigned to the ‘placebo / control’ group? What drug to be used as a placebo? How is it possible to justify use of a placebo in a patient who is on the brink of mortality due to massive bleeding? These issues need to be discussed at various levels and a consensus needs to be reached at.

RECOMMENDATIONS

The recommendations which can be made on the basis of available evidence are as follows:

Before considering the use of rFVIIa, patients should be resuscitated in accordance with the massive transfusion guidelines. These are as follows:

1. Full blood count, PT, APTT and fibrinogen should be checked regularly to guide replacement.
2. The use of rFVIIa should be considered, if bleeding continues when more than one blood volume has been transfused (approximately 10 units of red cells in an adult).
3. Adequate replacement with FFP, cryoprecipitate and platelets has been given.
4. No identifiable surgical source of bleeding has been found.
5. If it is felt that rFVIIa may be of benefit
6. It should normally only be requested by a consultant anesthetist.
7. It should normally be used only following discussion with a consultant hematologist.
8. One 4.8 mg vial should be given (50 - 100 ug/kg for a 50 - 100 kg patient). If bleeding does not diminish in 30 - 60 minutes, then a further 4.8 mg vial can be given. If bleeding continues after a second dose, there is little evidence to support the use of a third dose, and surgical exploration should be considered. It should be noted that there is a thrombotic risk associated with the use of rFVIIa and it should be used with caution in the following patient groups:
   i. Patients with a history of coronary artery disease
   ii. Patients with a history of arterial or venous thrombosis
   iii. Patients with cerebral vascular disease
   iv. Patients with DIC

CONCLUSIONS

There is general agreement that rFVIIa – NovoSeven®7 is safe and effective in hemophilia patients with inhibitors. Emerging data from anecdotal reports and completed or ongoing clinical trials suggest that rFVIIa is also effective in a variety of bleeding conditions in non-hemophilic patients. This has led some to use the term “universal” or “general”
hemostatic agent. Perhaps the use of this term is unfortunate since rFVIIa is not always effective in all hemorrhagic conditions. However, rFVIIa has been shown to be life-saving in many patients experiencing life-threatening hemorrhage. In such cases, the terms universal or general become irrelevant and the use of rFVIIa in such patients seems warranted even in the absence of controlled clinical trials. However, urgent, large, randomized controlled clinical trials are needed to define the appropriate role of this agent[58,59]. As aptly put in one of the reviews[64], “Challenges in the therapeutic use of a “so-called” universal hemostatic agent, rFVIIa should not become a routine and mundane modality but must be judiciously applied according to the necessity”.

REFERENCES

Chylous Leakage after Donor Nephrectomy: a Rare Complication and a Nightmare for Surgeons

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1Department of Urology, Institute of Post Graduate Medical Education and Research (IPGME & R), Kolkata, India
2Resident SNP Hospital, Kolkata, India
3Medica Superspeciality Hospital, Kolkata, India

ABSTRACT

Objective: To evaluate chylous drainage and its management in donor nephrectomy patients
Design: Retrospective study
Setting: Institute of Post Graduate Medical Education and Research (IPGME & R), Kolkata, and Medica Superspeciality Hospital, Kolkata, India
Subjects: Donor nephrectomy patients (open or laparoscopy procedure)
Intervention(s): The first case of chylous drainage which occurred after open donor nephrectomy was treated with conservative management for a prolonged period after browsing through literature. Later three cases which occurred after laparoscopic donor nephrectomy, were also managed conservatively.
Main Outcome Measure: Incidence and management of chylous ascites or drainage after open or laparoscopic nephrectomy

Results: In our institute, only four donor nephrectomy patients developed chylous drainage. Three were laparoscopic surgeries using the transperitoneal approach whereas one case was done using open retroperitoneal approach. Chylous drainage and its management are discussed.
Conclusion: Overall, our cases showed that chylous drainage can develop in laparoscopic transperitoneal procedures as well as in open retroperitoneal surgery, and that surgical dissection in the retroperitoneal area or the renal hilum is the most important risk factor for this complication. All our cases were well-treated only by conservative management and it has proven to be the main first line management for this condition.

KEY WORDS: laparoscopy, parenteral nutrition, somatostatin

INTRODUCTION

Chylous drainage results from either blockage or leakage of the lymphatics secondary to inadvertent trauma during surgery[1]. Most cases of traumatic chylous drainage resolve with conservative treatment but refractory cases may need surgical ligation of lymphatics[2,3]. We report four cases of chylous drainage following donor nephrectomy, three by laparoscopy and one by open procedure. The chylous drainage resolved with conservative management. A brief review of the literature on the management of post-operative chylous drainage is presented.

SUBJECTS AND METHODS

Donor nephrectomy patients, both by open retroperitoneal and laparoscopic transperitoneal approach performed in the department from August 2009 to January 2011 were evaluated for postoperative complications. The average number of living donor nephrectomies / year in the two medical centers is 110. Patients were evaluated for their age, clinical features, previous operation, trauma history, hemogram, renal function tests, electrolytes, site of kidney donation, diagnostic investigation and treatment. In open donor nephrectomy, the dissection of the kidney was straightforward and the surgical procedure did not differ from a standard donor nephrectomy. In the laparoscopic procedure, all were for left side and were performed using a three-port technique with the hand assisted port at midline below the umbilicus. This port was used for kidney retrieval. The kidney was successfully transplanted into the recipient using the standard technique. The donor’s initial postoperative period was unremarkable except for drainage of excessive fluid (650 ml average volume of drained fluid / day). Then gradually the clear fluid changed to milk-like fluid in the drainage tube with an increased volume (Fig. 1). Patients who developed
chylous drainage were evaluated for preoperative predisposing factors like congenital malformation or infection like viral or bacterial infection. Postoperative physical examination with laboratory investigation included serum sodium, potassium, urea, creatinine, hematocrit and WBC. Drainage fluid was examined for triglycerides, total protein with albumin and sent for bacteriologic culture. Ultrasound of abdomen was done when drainage was minimal and after removal of the drain tube (Table 1). Immediately after the diagnosis was established, the patient was kept fasting and received total parenteral nutrition. A low fat diet with medium chain triglycerides was started when the volume of the drainage dropped and drain tube was removed when there was complete cessation of chylous drainage and ultrasound showed no collection. Table 1 shows different variables and outcome of all patients including in the study.

RESULTS

Follow-up observations after one month on ultrasound found no recurrence of collection in the retroperitonium while on a normal diet. The patient returned to work and resumed a normal diet without any additional complications. Overall incidence of this rare complication in our two medical centers was 2.4 percent.

DISCUSSION

Chylous ascites or drainage is a rare condition. Its etiological factors can be broadly classified as congenital, infective, neoplastic and traumatic or postsurgical. The majority of cases are caused by diseases that interfere with abdominal or retroperitoneal lymphatic drainage. Amongst surgical procedures, vascular operations account for the majority of postoperative chylous ascites[2]. This complication may become evident within a few days following surgery or take several months[3].

The diagnosis can be confirmed by drainage fluid evaluation. The drainage is typically milky white and stains positive for fat with Sudan III. Its specific gravity is greater than 1.012 and has an alkaline pH. Cytology shows predominantly lymphocytes. Chemical analysis reveals high triglyceride levels that are 2 - 8 fold that of plasma (range 0.4 - 4 gm/dl) and protein content greater than 3 gm/dl. Serum abnormalities may include hypoalbuminemia, lymphocytopenia and anemia secondary to protein loss and malnutrition[1].

Management includes a combination of diuretics and restricted salt intake, a high protein, low fat, medium chain triglyceride diet, and parenteral nutrition[6]. Somatostatin has recently been shown to be effective in the treatment of this condition[4]. All our cases were well-managed conservatively.

Dietary intervention remains the mainstay of conservative treatment of chylous ascites and consists of a high protein, low fat, medium chain triglyceride diet. The rationale for using medium chain triglycerides is the fact that these bypass the lymphatic channels of the gut and enter directly into the portal venous system in contrast to long chain triglycerides which enter the portal venous blood through the lymphatics of the bowel. It has been recommended that medium chain triglycerides should be continued for several months after resolution of the ascites[4].

Total parenteral nutrition is an essential component in the management of chylous ascites / drainage and serves two important objectives; it fulfills the nutritional requirement of these patients and more importantly, it helps to decrease the production of lymph and allows the bowel to rest. The resolution of chylous ascites is reported to occur within 2 - 6 weeks in 60 - 100% patients with TPN alone, or in combination with medium chain triglycerides[6] but in our cases this occurred on eighth to sixteenth postoperative day. Although not all patients respond to TPN alone, this should be part of any conservative treatment plan.

Somatostatin is a naturally occurring peptide consisting of 14 to 28 amino acids. It is found in the central nervous system (CNS), gastrointestinal tract (GIT) and the pancreas. It decreases the intestinal absorption of fats, lowers triglyceride concentration in the thoracic duct and attenuates the lymph flow in the major lymph vessels. It also decreases splanchnic blood flow. Analogues now available are octreotide and lanreotide which are octapeptides with a much longer half life than somatostatin. Since somatostatin interferes with blood glucose regulation, close monitoring of blood glucose is recommended during its administration[6].

Other therapeutic measures include intravenous etilefrine, a sympathomimetic drug which acts by contracting the smooth muscle of the thoracic duct thereby decreasing the flow of chyle[6].
<table>
<thead>
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<th>Case 1</th>
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<td>2194</td>
<td>2686</td>
<td>2808</td>
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<td>Drain fluid total protein / albumin</td>
<td>47.7 / 31.9</td>
<td>56 / 42.6</td>
<td>48.2 / 38.6</td>
<td>52.8 / 40.4</td>
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<tr>
<td>Drainage dropped on</td>
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<td>7th POD</td>
<td>10th POD</td>
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<tr>
<td>Drainage stopped on</td>
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<td>9th POD</td>
<td>16th POD</td>
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<td>10th POD</td>
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</table>

GFR: Glomerular Filtration Rate, CT: Computerized tomography, Na: Sodium (mmol/l), K: Potassium (mmol/l), U: Urea(mg/dl), Cr: Creatinine (mg/dl), Hematocrit: %, Triglyceride: mg/dl, Total Protein / Albumin: g/lit, POD: Postoperative Day, USG Ultrasonography, WBC White Blood cell Count per cumm

# Including congenital malformation and viral or bacterial infection
In recent years, fibrin glue also has been used to treat chylous ascites. Fibrin glue was usually sprayed over the area of lymph leak as an adjunct treatment during operation. Molina et al[71] reported that a patient with chylous ascites after donor nephrectomy was treated laparoscopically with the assistance of fibrin glue. Fibrin sealants are considered to be the ideal physiological adhesive and the most effective tissue sealant. The effects of fibrin sealants mimic the final stages of coagulation, where thrombin releases fibrinopeptide A and B from the fibrinogen chain to form fibrin monomers, which then polymerize to form a fibrin clot at the site of application that in turn provides the matrix for subsequent wound healing. This physiologic product is biocompatible and does not incite foreign body reaction or inflammation. Huang et al have reported on managing chylous leak with percutaneous injection of fibrin glue. Their experience suggests that fibrin glue may be used alone to treat chylous ascites when ligation is impossible[8].

Surgical intervention is needed, if the lymphatic leak persists in spite of maximal conservative therapy for several weeks. This usually entails either direct suture ligation of the disrupted lymphatic channels or insertion of a peritoneo-venous shunt[8]. If surgical intervention becomes mandatory, either open or laparoscopic approach is possible. In some cases, the site of the fistula may be visible. Identification of the fistula may be helped by a fatty meal taken pre-operatively or by intra-operative injection of a contrast. Suture ligation of the lymphatics results in termination of the leak. Better outcomes of surgery are expected in patients with accurate localization of the leak. The main disadvantage of surgery is the hazard of re-operating on already compromised patients who are just recovering from major surgical trauma. Despite its disadvantages, surgical therapy remains an effective option for refractory cases[9]. If a definitive leak site cannot be identified, suturing of the retro-aortic tissues en-mass may resolve the lymphatic leak[3].

Peritoneo-venous shunting is an alternative to exploration in patients with rapid accumulation of ascitic fluid. This avoids nutritional depletion as the fluid is re-circulated. Shunts are associated with fewer complications than repeat paracentesis but complications like disseminated intravascular coagulation (DIC), fat embolism and fatal sepsis may occur[11]. Cope[10] describes a technique of catheterization of the cisterna chyli and major retroperitoneal lymphatic ducts by percutaneous transabdominal puncture and embolization of the leaking lymphatic trunk but the safety of this technique is yet to be established.

There is no consensus as regards the exact timing of operative intervention, but it is generally recommended that conservative therapy should be tried for at least 4 - 8 weeks[2].

CONCLUSION

Post-operative chylous drainage is a rare complication of open or laparoscopic donor nephrectomy surgery. The condition poses a difficult management problem. Most cases resolve with conservative treatment which usually involves a prolonged period of multimodal therapy aimed at decreasing lymph production and optimizing nutritional requirements along with other palliative measures. Refractory cases may need either open or laparoscopic ligation of the leaking lymphatic channels.

REFERENCES

Original Article

Post-Infantile Presentation of Intestinal Malrotation

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ABSTRACT

Objectives: To study intestinal malrotation presenting after the age of one year, analyze the spectrum of presentations and to predict risk of volvulus

Design: Retrospective study

Setting: Zagazig University Hospitals (Egypt) and King Fahd Hospital, Saudi Arabia

Subjects: All cases (54) of malrotation during April 2006 to April 2010

Intervention(s): Analysis of clinical, radiological and operative data

Main Outcome Measures: Presentation, significant associations and risk of volvulus

Results: The mean age was 4.8 ± 2.13 years. Presentations included acute volvulus (n = 27, 50%), chronic volvulus (4, 7.5 %), mesocolic hernia (4, 7.5 %), intussusception (5, 9%), exomphalos (5, 9%) and non-specific presentation (9, 17%). Associated anomalies were found in 19 cases (35%) with significant association of chronic volvulus and exomphalos.

Typical anatomical malrotation was seen in 21 (39%) cases with significant risk of volvulus (odds ratio 9.2). Nausea and vomiting, abdominal colic, and malnutrition were dominant in acute and chronic volvulus, mesocolic hernia and intussusception (p < 0.05).

Malnutrition and gastroesophageal reflux disease (GERD) were significantly associated with chronic volvulus (p < 0.05). Duodenal obstruction was significantly evident in acute volvulus while high cecum was dominant in intussusception. Prolonged ileus and persistent symptoms were significant in chronic volvulus and mesocolic hernia (p < 0.05), while wound infection and short bowel syndrome were significant in acute volvulus.

Conclusion: Malrotation in the post-infantile period has a wide spectrum and non-specific presentation. Risk of midgut volvulus is present, especially in typical cases, and trials must be done to predict the risk and avoid unnecessary surgery.

KEY WORDS: malrotation, mesocolic hernia, volvulus

INTRODUCTION

The clinical entities collectively referred to as malrotation, encompass a wide variety of anatomy, ages, and clinical presentations[1]. Malrotation results from the failure of one or more components of gut rotation or fixation, which in turn, may result in a narrowed mesenteric base about the origin of superior mesenteric artery (SMA). This anatomical arrangement predisposes the midgut to undergo volvulus, resulting in the potential catastrophic loss of intestine from the duodenum to the transverse colon[2].

Malrotation, however, consists of a spectrum of abnormalities of intestinal position and fixation ranging from normal to typical malrotation to complete non-rotation and all variations in between[3]. Complete malrotation presents in neonatal period with a typical picture of bilious vomiting and abdominal distension. After the neonatal period, and merging into childhood and adolescence, malrotation is incomplete or atypical with less dramatic presentation and a frequent misdiagnosis[4,5]. Atypical malrotation is usually concealed by other clinical manifestations such as gastro-esophageal reflux disease (GERD) or malnutrition[6]. However, even in this atypical group, it is not uncommon to be still exposed to the most fearful complication, midgut volvulus and gangrene[7].

It was usual for these atypical patients, whether diagnosed incidentally or intraoperatively, to have an elective Ladd’s operation. This strategy was supported by the fact that when complications occur, they are sudden and catastrophic with loss of a significant part of the intestine[8]. Opponents of this strategy rely on lower risk of complication of atypical malrotation, and low benefit of surgical intervention[9]. Early prediction of malrotation cases, more liable for complications, is still controversial and age cannot be a reliable
predictor. More accurate refinement of predictors may save vulnerable patients and prevent non-indicated surgeries.

In this research, we retrospectively reviewed cases of malrotation which presented in the post-infantile age period. The aim was to analyze clinical, radiological and operative features unique to this cohort.

PATIENTS AND METHODS

All cases over one year of age with intestinal malrotation that presented to the pediatric surgery units of Zagazig University Hospitals, Egypt and King Fahd Hospital, Hufof, Saudi Arabia during the four-year period between April 2006 and April 2010 were included. The study was approved by the local ethics committee. Diagnosis of malrotation was done after surgical confirmation and correction. Malrotation was considered, if one or more of the following operative criteria was documented:

- Midgut volvulus
- Presence of ligament of Treitz at right side of vertebrae
- Abnormal peritoneal bands extending from the ileum or right colon to the parietal peritoneum over duodenum (Ladd’s bands)
- Internal mesocolic hernia
- Fixation of the duodenum or upper jejunum to the cecum or right colon
- Visualization of the entire duodenum, especially the third and fourth parts at the base of mesocolon
- High position and abnormal mobility of cecum
- Presence of small intestine hiding the colon when the abdomen was opened

Cases of malrotation were anatomically classified into typical and atypical. Typical cases were those where the ligament of Treitz was found on the right side of vertebrae. Atypical cases were those with the ligament on the left of vertebrae. The study included cases which were diagnosed preoperatively, and those which were discovered incidentally during laparotomy for other causes, and were corrected accordingly.

We excluded cases which were diagnosed by radiography without surgery. Also, cases which were discovered incidentally without correction were not included.

The following data were collected:

- Patient’s demographic data
- Symptoms and signs both at presentation and within antecedent six months
- Associated anomalies
- Imaging signs
- Operative findings and procedures
- Post-operative course and complications

Follow-up was done for at least six months after surgery.

Statistical analysis: Continuous variables were described as the mean ± standard deviation (SD), and categorical variables were presented as numbers and percentages. Fisher exact test was used to compare categorical variables and significance was considered when p-value was < 0.05. Odds ratio was used for risk estimation and Pearson correlation coefficient for detection of association.

RESULTS

Over this four-year period, 54 cases with documented intestinal malrotation were recorded. Forty-five cases (83%) were diagnosed pre-operatively, while nine cases (17%) were found incidentally during other procedures and were managed accordingly. Presentation of malrotation included acute volvulus (27, 50%), chronic volvulus (4, 7.5 %), internal hernia (4, 7.5 %), and intussusception (5, 9%). Five cases were diagnosed during repair of exomphalos (9%) and remaining nine cases (17%) had non-specific presentation (Table 1). Thirty males and 24 females were managed with no significant difference (p-value = 0.370). The age range was 18 months to 11 years with a mean of 4.8 ± 2.13 years (variance 4.54). Acute volvulus and intussusception presentations were inversely correlated with age (Pearson correlation - 0.845 and - 0.810) while chronic volvulus and mesocolic hernia were positively correlated with age (Pearson correlation 0.7 and 0.67). Associated anomalies were found in 19 cases (35%) and their distribution is as shown in (Table 2). Associated anomalies were significantly more in chronic volvulus and with exomphalos (p = 0.001).

Anorexia and nausea were the most common symptoms (83%), followed by recurrent abdominal colic (81%) and biliary vomiting (75%), while GERD and abdominal distension were the least clinical signs (11%). Using upper gastrointestinal imaging (UGI), the most common radiologic signs included duodenal...
obstruction (Fig. 1) in 29 cases (54%), followed by right side ligament of Treitz in 21 cases (39%). High cecum was seen by gastrografin enema in 11 cases. This study was done only in 18 cases in whom UGI was not sufficient for diagnosis. Whirl sign was documented in nine cases by computed tomography (CT) which was done in 41 cases.

Table 3 shows the operative findings. High and mobile cecum was seen in 45 cases (83%) and Ladd’s bands were seen in 44 cases (81%) (Fig. 2). Acute volvulus occurred in 27 cases (50%) (Fig. 3). Operative signs which were unique to chronic volvulus in our series included congestion of mesenteric vessels and enlarged mesenteric lymph nodes (Fig. 4). Furthermore, edema of mucosa and chylous ascites (in one case) were found. Mesocolic hernia (Fig. 5) was seen in four cases (7.5%). We had 21 (39%) cases with typical anatomical malrotation by radiological and operative criteria, and 18 of them (86%) had volvulus. In the remaining 33 (61%) atypical cases, 13 cases (41%) had volvulus. Typical malrotation was a risk factor for volvulus (odds ratio 9.2).

Beside Ladd’s operation, resection anastomosis was done in five cases (9%). Four of them were extensive, and appendectomy was done in 42 cases. No mortality was recorded, and seven cases were lost in follow-up before six months. Postoperative complications included prolonged ileus (more than three days) in 15 cases (28%) and sepsis in one case (2%). Persistence of symptoms occurred in seven cases (13%) in whom, no intestinal resection was done.

Analysis of the relation between presentation and patient’s data were plotted in Table 4. For clinical picture, nausea and vomiting, abdominal colic, and malnutrition were dominant in acute and chronic volvulus, internal hernia and intussusception (p < 0.05). Malnutrition and GERD were significantly associated with chronic volvulus (p < 0.05). For radiological criteria, duodenal obstruction was significantly evident in acute volvulus while high cecum was dominant in intussusception but the relation was insignificant (p > 0.05). Prolonged ileus and persistant symptoms were significantly more with chronic volvulus and internal hernia cases (p < 0.05), while wound infection and short bowel syndrome were significantly more in acute volvulus.

DISCUSSION

Intestinal malrotation can occur in patients at any age and, in contrast with traditional teaching, nearly half of these patients may present during adulthood. An increased awareness of this entity and an understanding of its varied presentation at different ages may reduce time to diagnosis and improve patient outcome[11].
The diagnosis of malrotation is easily made in neonatal and infantile period because of biliary vomiting and rapid progress. Malrotation beyond infantile period is associated with multiplicity of symptoms which are non-specific and consequently are associated with delays in diagnosis\[12\]. Some series stated that midgut volvulus occurred in 45 to 80% of neonates, but only in 14% adults\[13\]. This was disputed by other investigators and the risk of developing midgut volvulus at any age has been documented\[14\]. Also, the potential to develop sudden midgut volvulus with intestinal gangrene after many years of undiagnosed abdominal pain was found to be not uncommon\[15\]. This high risk of volvulus combined with the difficulty of diagnosing malrotation in older children mandates scrutiny and high suspicion while manipulating these cases.

In our series and according to anatomical malrotation classification in relation to site of ligament of Treitz\[1\], typical anatomical malrotation was.

Table 4: Patient data and presentations

<table>
<thead>
<tr>
<th>Sex:</th>
<th>Patients n(%)</th>
<th>Acute volvulus n = 27 (%)</th>
<th>Chronic volvulus n = 4 (%)</th>
<th>Mesocolic hernia n = 5 (%)</th>
<th>Intussusception n = 5 (%)</th>
<th>Exomphalos n = 5 (%)</th>
<th>Non specific n = 9 (%)</th>
<th>p-value</th>
</tr>
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<tbody>
<tr>
<td>Male</td>
<td>30 (56)</td>
<td>17 (63)</td>
<td>2 (50)</td>
<td>3 (75)</td>
<td>3 (60)</td>
<td>3 (60)</td>
<td>2 (22)</td>
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<tr>
<td>Female</td>
<td>24 (44)</td>
<td>10 (37)</td>
<td>2 (50)</td>
<td>1 (25)</td>
<td>2 (40)</td>
<td>2 (40)</td>
<td>7 (78)</td>
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</tr>
<tr>
<td>Age: 1.5 – &lt; 3.9</td>
<td>12 (22)</td>
<td>7 (27)</td>
<td>-</td>
<td>-</td>
<td>5 (100)</td>
<td>-</td>
<td>-</td>
<td></td>
</tr>
<tr>
<td>3.9- &lt; 6.3</td>
<td>25 (46)</td>
<td>12 (44)</td>
<td>1 (25)</td>
<td>-</td>
<td>-</td>
<td>5 (100)</td>
<td>7 (78)</td>
<td>0.1063</td>
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<tr>
<td>6.3 – &lt; 8.7</td>
<td>9 (17)</td>
<td>5 (19)</td>
<td>2 (50)</td>
<td>1 (25)</td>
<td>-</td>
<td>-</td>
<td>1 (11)</td>
<td></td>
</tr>
<tr>
<td>8.7—11</td>
<td>8 (15)</td>
<td>3 (10)</td>
<td>1 (25)</td>
<td>3 (75)</td>
<td>-</td>
<td>-</td>
<td>1 (11)</td>
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<td>Congenital anomalies</td>
<td>19 (35)</td>
<td>5 (19)</td>
<td>4 (100)</td>
<td>2 (50)</td>
<td>3 (60)</td>
<td>5 (100)</td>
<td>4 (44)</td>
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</tr>
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<td>Clinical presentation:</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Anorexia and nausea</td>
<td>45 (83)</td>
<td>27 (100)</td>
<td>4 (100)</td>
<td>4 (100)</td>
<td>5 (100)</td>
<td>2 (40)</td>
<td>3 (33)</td>
<td>0.001</td>
</tr>
<tr>
<td>Abdominal colic</td>
<td>44 (81)</td>
<td>27 (100)</td>
<td>4 (100)</td>
<td>4 (100)</td>
<td>5 (100)</td>
<td>-</td>
<td>4 (44)</td>
<td>0.009</td>
</tr>
<tr>
<td>Biliary vomiting</td>
<td>41 (75)</td>
<td>20 (74)</td>
<td>4 (100)</td>
<td>4 (100)</td>
<td>5 (100)</td>
<td>1 (20)</td>
<td>7 (78)</td>
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<td>Constipation</td>
<td>21 (56)</td>
<td>14 (52)</td>
<td>2 (50)</td>
<td>2 (50)</td>
<td>3 (60)</td>
<td>-</td>
<td>-</td>
<td>0.266</td>
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<tr>
<td>Malnutrition</td>
<td>9 (17)</td>
<td>1 (4)</td>
<td>4 (100)</td>
<td>3 (75)</td>
<td>-</td>
<td>-</td>
<td>1 (11)</td>
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<tr>
<td>GERD</td>
<td>6 (11)</td>
<td>2 (8)</td>
<td>2 (50)</td>
<td>-</td>
<td>-</td>
<td>2 (22)</td>
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</tr>
<tr>
<td>Abdominal distension</td>
<td>6 (11)</td>
<td>2 (8)</td>
<td>-</td>
<td>3 (75)</td>
<td>1 (20)</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Radiological criteria:</td>
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<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Duodenal obstruction</td>
<td>29 (54)</td>
<td>25 (93)</td>
<td>3 (75)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1 (11)</td>
<td>0.005</td>
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<td>Treitz ligament:</td>
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<td></td>
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<td>0.0122</td>
</tr>
<tr>
<td>Rt. to vertebrae</td>
<td>21 (36)</td>
<td>15 (56)</td>
<td>3 (75)</td>
<td>-</td>
<td>-</td>
<td>1 (20)</td>
<td>2 (22)</td>
<td>0.1041</td>
</tr>
<tr>
<td>At vertebrae</td>
<td>18 (34)</td>
<td>6 (22)</td>
<td>-</td>
<td>3 (75)</td>
<td>2 (40)</td>
<td>1 (20)</td>
<td>6 (66)</td>
<td>0.3638</td>
</tr>
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<td>Lt. to vertebrae</td>
<td>15 (28)</td>
<td>6 (22)</td>
<td>1 (25)</td>
<td>1 (25)</td>
<td>3 (60)</td>
<td>3 (60)</td>
<td>1 (11)</td>
<td>0.0875</td>
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<tr>
<td>High cecum</td>
<td>11 (20)</td>
<td>3 (11)</td>
<td>2 (50)</td>
<td>1 (25)</td>
<td>5 (100)</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Whirl sign</td>
<td>9 (17)</td>
<td>6 (22)</td>
<td>3 (75)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>0.2335</td>
</tr>
<tr>
<td>Post-operative complications:</td>
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<tr>
<td>Paralytic ileus</td>
<td>15 (28)</td>
<td>5 (19)</td>
<td>4 (100)</td>
<td>4 (100)</td>
<td>-</td>
<td>1 (20)</td>
<td>1 (11)</td>
<td>0.0176</td>
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<tr>
<td>Wound infection</td>
<td>9 (17)</td>
<td>6 (22)</td>
<td>-</td>
<td>-</td>
<td>2 (40)</td>
<td>-</td>
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<td>0.0233</td>
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<td>Persistent symptoms</td>
<td>7 (13)</td>
<td>-</td>
<td>4 (100)</td>
<td>2 (50)</td>
<td>-</td>
<td>-</td>
<td>1 (11)</td>
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<td>Bronchopneumonia</td>
<td>6 (11)</td>
<td>4 (16)</td>
<td>-</td>
<td>1 (25)</td>
<td>1 (20)</td>
<td>-</td>
<td>-</td>
<td>0.3343</td>
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<tr>
<td>Short bowel syndrome</td>
<td>6 (11)</td>
<td>6 (22)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Abdominal sepsis</td>
<td>1 (2)</td>
<td>1 (4)</td>
<td>-</td>
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<td>-</td>
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</table>
associated with high risk of volvulus (odds ratio 9.2), but more controlled studies are needed to analyze this suggestion. Also, out of 27 cases with acute volvulus in our study, only five cases needed intestinal resection. In contrast to neonatal period, volvulus in older pediatric age appears to be slowly progressing and could be salvaged, if judicious assessment was done at presentation.

We had four cases with chronic volvulus and positive correlation with age. Unique features were mesenteric vessels congestion and lymph nodes enlargement. These features were attributed to the long period of incomplete obstruction with increased venous and lymphatic pressure. The latter can explain lymphatic exudate seen in one case. In our series, chronic volvulus was significantly associated with malnutrition and persistent symptoms after surgical correction. This also can be explained by the chronic exudation of protein in lymph and luminal dilatation due to chronic obstruction. Chronic volvulus was mentioned before, and was accused for complications including biliary and pancreatic obstruction, chylous ascites, and mesenteric vein thrombosis\textsuperscript{[16]}. Also, diarrhea and malabsorption in chronic volvulus were attributed to bowel lymphedema resulting from lymphatic obstruction\textsuperscript{[13]}. Few cases of malrotation and chylous ascites were documented in the literature, and it was postulated that lymphatic obstruction from midgut volvulus can lead to the leakage of chyle into the peritoneum\textsuperscript{[17]}. Even in asymptomatic patients, the finding of chylous ascites during hernia repair was supposed to be a signal of hidden malrotation\textsuperscript{[18]}

In this study, all preoperatively discovered cases were diagnosed by upper gastrointestinal imaging (UGI) and contrast enema studies. Other imaging modalities, e.g., ultrasound (US) and computed tomography (CT) scan were supplementary, especially in acute presentations. Whirl sign was seen in CT scans of nine cases. All of them had acute volvulus. Abnormalities in the orientation of the superior mesenteric artery (SMA) and superior mesenteric vein (SMV) on ultrasonography in patients with malrotation has been suggested to be an alternative way to establish this diagnosis\textsuperscript{[19]}. However, it has been shown by other authors that inversion of the SMV / SMA relationship can also be seen in patients with normal midgut rotation\textsuperscript{[20]}. Furthermore, not all cases of malrotation have abnormal SMV / SMA orientation on US\textsuperscript{[21]}. Because of the lower sensitivity and specificity of US compared with UGI, and because of the fact that US cannot estimate the length of the mesenteric base (which determines the risk of midgut volvulus), upper gastrointestinal imaging has remained the gold standard diagnostic modality for malrotation\textsuperscript{[22]}. Demonstration of the third duodenal segment (D3) in retroperitoneal location with CT scan has been recently proposed as a method for excluding malrotation\textsuperscript{[23]}, but needs more confirmation and was not recorded in our cases. Although CT scan was of high diagnostic accuracy in emergent cases in our series, it was of no added benefits in elective circumstances of malrotation.

Five cases were discovered during management of intussusception without antecedent diagnosis of malrotation. In these cases, the only anatomical sign of malrotation was high mobile cecum. It was suggested that malrotation by its nature is associated with a mobile right colon, which may be a prerequisite for intussusception\textsuperscript{[24]}. Hydrostatic reduction of intussusception would theoretically mask underlying malrotation and some authors attributed recurrence after air reduction to hidden malrotation\textsuperscript{[25]}

Another unique variety of malrotation in our series was mesocolic hernia which was found in four cases, and was restricted to older children (above 6 years of age) with positive correlation with age. All cases were of the left variety according to Willwerth’s classification\textsuperscript{[26]}.

It was observed in the four cases of mesocolic hernia that no acute obstruction happened, and also, that there was paucity of the other morphologic criteria of malrotation. This is compatible with the embryologic explanation of mesocolic hernia which is attributed to lack of fixation after successful rotation. The restriction of these cases to old children may be explained by the time needed for herniation and time needed for the vague symptoms to be explained as mesocolic hernia.

Seven cases were recorded in our series in which operation was not beneficial with persistent nausea, vomiting, and malnourishment. All cases of chronic volvulus and half cases of mesocolic hernia were included in this postoperative complication. Chronic obstruction with dilated loops appears to be the underlying pathology of persistent symptoms. The association between malrotation and pseudo-obstruction was mentioned before\textsuperscript{[27]}. Most retrospective studies suggest that following operations for intestinal malrotation, the patients do well\textsuperscript{[10]}, but a group of patients were found not to have any benefit from operation and neuropathic rather than myopathic intestinal dismotility was found\textsuperscript{[28]}. Also, malrotation was found to be a feature of congenital megacystis-microcolon hypo-peristalsis syndrome and congenital absence of argyrophil neurons\textsuperscript{[29]}. Both conditions are characterized by functional and anatomical abnormalities of the gut, and it was suggested that there is an association between malrotation, abnormal innervation and functional abnormalities of the gut.

Esophagus also could be implicated with dysmotility which accompanies malrotation and some authors suggested that malrotation is an important factor responsible for delayed gastric emptying in GERD\textsuperscript{[30]}. We had six cases with GERD in this series,
but malrotation stigmata were more prominent than reflux. Also, after correction of malrotation, no sufficient follow up was done to trace effect of malrotation correction on associated GERD.

CONCLUSION

Intestinal malrotation is a congenital anatomic anomaly with risk of volvulus and loss of segments of intestine. The clinical picture and risk of volvulus are clearly evident in neonates and infants. In the post-infantile period, malrotation has wide spectrum and non-specific presentation. Risk of midgut volvulus is significant especially in typical cases and trials must be conducted to predict risk of volvulus without doing unnecessary operations. Age appears to be of weak predictive value for midgut volvulus, and other classifications need to be approved by controlled studies.

REFERENCES

The Role of Trace Elements in Helicobacter Pylori Infected Patients

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²Department of Infectious Diseases and Clinical Microbiology, Elazig Education and Research Hospital, Elazig, Turkey
³Department of Infectious Diseases and Clinical Microbiology, Duzce University, Duzce, Turkey
⁴Department of Infectious Diseases and Clinical Microbiology, Dicle University, Dicle, Turkey

Objective: To evaluate the effect of trace elements in patients with Helicobacter pylori associated chronic gastritis

Design: Prospective study

Settings: Clinical services of the clinical microbiology and infectious diseases and gastroenterology clinics at Dicle University, Turkey

Subjects: A total of 92 patients with variable severity of chronic gastritis (45 Helicobacter pylori positive and 47 Helicobacter pylori negative gastritis) and 90 age and sex matched healthy subjects were included in the study conducted between October 2006 and November 2008.

Intervention: Histopathologic examination, culture of Helicobacter pylori and urease tests were performed for each patient. The atomic absorption spectrophotometer was used in the measurement of trace elements in the serum.

Main Outcome Measures: Serum copper and zinc levels were significantly elevated in patients with Helicobacter pylori associated gastritis compared to Helicobacter pylori negative gastritis and healthy controls (p < 0.0001). Serum copper, zinc and Cu / Zn levels in patients with Helicobacter pylori negative chronic gastritis was not significantly different from the serum levels in healthy controls (p > 0.05).

Conclusions: Our results suggest a relationship between Helicobacter pylori associated chronic gastritis and the elevation of trace element levels in serum. This study confirms that the elevation of trace element levels in serum (Cu and Zn levels) will be helpful in the diagnosis of Helicobacter pylori associated chronic gastritis in the absence of invasive procedures, and is useful in predicting the severity of infection in patients with chronic gastritis.

KEY WORDS: chronic gastritis, copper, Helicobacter pylori, zinc

INTRODUCTION

Nowadays, Helicobacter pylori (HP) is considered to be the bacterium responsible for the most frequent and persistent chronic infection worldwide, involving half of the entire world population. Untreated, the infection lasts for the whole life[1]. HP plays an important role in the initiation of gastrointestinal diseases, particularly peptic and duodenal ulcers, as well as gastric cancer and lymphoid tissue lymphoma[2].

Most infectious diseases are accompanied by a change in levels of several trace elements in the blood. However, it is not known whether changes in the gastrointestinal uptake of trace elements contribute to this event[3]. These metals are important for the metabolism of HP (Ni, Cu, Zn, Fe) and during the treatment of HP[4]. One of the accepted mechanisms leading to ulcer formation is colonization of HP in the gastric mucosa that stimulates excess production of reactive oxygen species and elements[5].

This prospective study was performed to evaluate the effect of trace elements in the diagnosis of HP-positive gastritis.

SUBJECTS AND METHODS

This study was carried out on 92 patients (45 HP positive, 47 HP negative patients) with variable severity of chronic gastritis (CG) and 90 age and sex matched healthy subjects as controls. Esophago-gastro-duodenoscopy was performed on all patients and healthy subjects. All patients were hospitalized in the clinical services of the Clinical Microbiology, Infectious Diseases and Gastroenterology Clinics at Dicle University, Turkey, between October 2006 and November 2008. Histopathology tests, culture and urease tests were used in the detection of HP.

Both groups had a detailed history taken and underwent a thorough clinical examination.

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Complete blood examination, complete urine examination and routine biochemical tests were measured in all subjects. Gastric biopsies were taken from 11 sites (antrum, five; corpus, five; and cardia, one).

The trace element levels were measured in all serum samples by using Unicam 929 Atomic Absorption Spectrophotometer. 5 ml of venous blood was taken from the antecubital vein after overnight fasting from all subjects (n = 182). The blood was centrifuged at 5200 rpm for 10 minutes. Then the blood samples were stored in deep-freezer, at -80 °C. At the time of study, serum samples were diluted with deionized water. Cu, Zn and Mg levels were measured in all serum samples by using Unicam 929 Atomic Absorption Spectrophotometer.

Informed consent was obtained from all patients who participated in our study. This study was approved by the Ethics Committee of the Dicle University. The study protocol conforms to the ethical guidelines of the 1975 declaration of Helsinki.

Statistics
All data were statistically analyzed and presented as mean and standard deviation (SD). Statistical analysis was performed using SPSS 17.0 for Windows Version program. A p-value < 0.05 was considered statistically significant. Analysis of variance (ANOVA) followed by Dunnett’s test was used in order to analyze for significant differences between groups.

RESULTS
Out of 182 patients, 92 (50.55%) were male and 90 (49.45%) were female (mean age = 48 ± 10.2 years). Out of the 45 HP positive patients, 23 (51%) were male and 22 (49%) were female (mean age = 49.4 ± 16.9 years). Out of the 47 HP negative patients, 24 (51%) were male and 23 (49%) were female (mean age = 46.1 ± 7.7 years).

In comparison of trace element levels in HP positive and HP negative patients, serum Cu and Zn were significantly higher in patients with HP positive CG as compared to HP negative patients (p < 0.0001). The ratio of Cu / Zn levels was also significantly elevated in HP positive CG patients as compared to HP negative patients (p < 0.013). The comparison of serum trace element levels in HP positive and negative ulcerative patients is shown in Table 1.

In comparison of trace element levels in HP positive and healthy controls, serum Cu, Zn and the ratio of Cu / Zn levels were significantly higher in HP positive CG patients as compared to healthy controls (p < 0.0001).

There was a tendency toward higher concentrations of Cu and Zn in HP positive CG patients versus healthy and HP negative patients. The comparison of serum trace element levels in HP positive CG and control patients is shown in Table 2.

In comparison of trace element levels in HP negative CG patients and healthy controls, there was no significant difference regarding serum Cu, Zn and the ratio of Cu / Zn levels between HP negative CG patients and healthy controls (p > 0.05). The comparison of serum trace element levels in HP negative CG patients and healthy controls is shown in Table 3.

DISCUSSION
Trace elements, especially Zn and Cu play an important role in organism and host defense. Zinc and copper metabolism of the host is markedly altered in all infections or inflammations[6]. Our data confirmed that trace elements were more altered in severe inflammations compared to milder infections in patients with HP associated CG. Serum zinc and copper levels were more significantly increased in HP positive CG patients as compared to HP negative patients and healthy controls.

<table>
<thead>
<tr>
<th>Trace elements</th>
<th>HP+</th>
<th>HP-</th>
<th>p- value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cu (μg/dl) ± SD*</td>
<td>92.6 ± 24</td>
<td>54.5 ± 12.8</td>
<td>0.0001</td>
</tr>
<tr>
<td>Zn (μg/dl) ± SD</td>
<td>76.8 ± 29.4</td>
<td>53.3 ± 11.7</td>
<td>0.0001</td>
</tr>
<tr>
<td>Cu / Zn (μg/dl) ± SD</td>
<td>1.37 ± 0.6</td>
<td>1.07 ± 0.3</td>
<td>0.013</td>
</tr>
</tbody>
</table>

*mean and standard deviation; HP= Helicobacter pylori

<table>
<thead>
<tr>
<th>Trace elements</th>
<th>HP+</th>
<th>Control</th>
<th>p- value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cu (μg/dl) ± SD*</td>
<td>92.6 ± 24</td>
<td>57 ± 17.3</td>
<td>0.0001</td>
</tr>
<tr>
<td>Zn (μg/dl) ± SD</td>
<td>76.8 ± 29.4</td>
<td>55.8 ± 12.5</td>
<td>0.0001</td>
</tr>
<tr>
<td>Cu/Zn (μg/dl) ± SD</td>
<td>1.37 ± 0.6</td>
<td>1.04 ± 0.3</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

*mean and standard deviation; HP= Helicobacter pylori

<table>
<thead>
<tr>
<th>Trace elements</th>
<th>HP-</th>
<th>Control</th>
<th>p- value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cu (μg/dl) ± SD*</td>
<td>54.5 ± 12.8</td>
<td>57 ± 17.3</td>
<td>0.71</td>
</tr>
<tr>
<td>Zn (μg/dl) ± SD</td>
<td>53.3 ± 11.7</td>
<td>55.8 ± 12.5</td>
<td>0.59</td>
</tr>
<tr>
<td>Cu/Zn (μg/dl) ± SD</td>
<td>1.07 ± 0.3</td>
<td>1.04 ± 0.3</td>
<td>0.939</td>
</tr>
</tbody>
</table>

*mean and standard deviation; HP= Helicobacter pylori

Table 1: Comparison of serum trace element levels in HP positive and negative CG patients

Table 2: Comparison of serum trace element levels in HP positive CG patients and healthy controls

Table 3: Comparison of serum trace element levels in HP negative and healthy controls
Studies suggesting that abnormal Cu and Zn metabolism may play a predictive role in the pathogenesis of CG and development of its complications makes this subject of current interest. Trace elements, which are co-factors of enzymes in antioxidant defense system, are often investigated in many diseases, such as HP (+) or HP (-) CG. In these studies, contradictory results are reported in terms of plasma or serum levels of trace elements. Dovhanj et al found Zn levels in HP positive ulcerative patients high compared to HP negative ulcerative patients and healthy controls. They also found that serum Cu levels were not altered in HP positive ulcerative patients. Winfried et al reported that Cu and Zn play an important role in the pathogenesis of HP and Zn intake in HP(+) subjects was significantly higher than that in HP (-) subjects because of intensive need of HP for Zn. Akcam et al found serum Zn levels higher in HP positive ulcerative patients compared to HP negative patients and healthy controls. However, their findings were not statistically meaningful. This finding was probably due to the fact that their study group comprised of children and 65% of their study group had Zn deficiency. Ugwuja et al reported that Zn levels were decreased in HP positive pregnant women who had gastritis as compared to HP negative patients and healthy controls. Their study population comprised of pregnant women and in pregnancy there is an increased body metabolism. They also used a different method in HP detection.

Poo et al reported that serum Cu and Cu/Zn ratio were elevated in HP positive ulcerative patients and this finding is compatible with our study. They found Zn levels decreased in HP positive CG patients, which was not our finding. Their findings differ from ours due to the fact that their patient groups were comprised of advanced benign and malignant disease.

Many studies reported that chronic infections and inflammations affect body metabolism and cause alterations of Cu and Zn levels. This elevation might be due to release of copper from intracellular to the extracellular environment because of bacterial invasion, though release of some antioxidants by neutrophils may cause increased levels of Zn and Cu as a consequence of cellular damage. Moreover, it was thought that elevated levels of minor acute phase reactants, such as ceruloplasmin, could be a reason for the increased serum Cu levels in infections.

We showed that the elevation of trace element levels in serum (Cu, Zn and Cu/Zn levels) is a leading finding in HP patients with CG. In addition, since serological examinations do not require invasive measures, this will pose an additional advantage in diagnosis.

CONCLUSION
Our study was of a different nature due to the fact that we found serum Copper, Zinc and Cu/Zn levels significantly increased in patients with HP positive CG as compared to HP negative chronic gastritis and healthy individuals.

The present study shows that serum Cu and Zn were altered in HP positive patients and provides confirmatory results, indicating that trace element levels are disturbed in HP infected CG patients as compared to non-infected patients. Serum trace element measurements may have the potential to be used in the evaluation of treatment success.

More extensive studies should be carried out in terms of serum trace elements in chronic and severe cases in order to understand their role better in the pathogenesis, diagnosis and treatment of these disorders.

ACKNOWLEDGMENT
The authors who have taken part in this study declare that they do not have any conflict of interest with respect to this manuscript.

REFERENCES


Squamous Intraepithelial Lesions Associated with HIV Infection and CD4+ Cell Counts in an Iranian Population

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5Shemiran Health Center, Shaheed Beheshti Medical University, Tehran, Iran

ABSTRACT

Objective(s): To evaluate the association between cervical squamous intraepithelial lesions (SIL) and the human immunodeficiency virus (HIV) infection and CD4 counts among an Iranian population

Design: Case-control study

Setting: North and East Tehran Health Centers, related to Shaheed Beheshti Medical University, Iran

Subjects: Two hundred forty seven women including 58 HIV infected cases and 189 healthy controls recruited between 2007 and 2010.

Intervention(s): none

Main Outcome Measure(s): Cytology-based cervical Pap smears and hematologic findings were compared between cases and controls

Results: The prevalence of abnormal smear was significantly higher in the study group (36.2%, 15 LSIL + 6 HSIL) compared with controls (3.2%, 6 ASCUS) (p < 0.001, OR = 2.4, 95% CI 1.2 - 4.6). The mean of CD4 count was significantly lower in cases with abnormal smear compared with cases with normal smear (573.0 ± 306.9 Vs 383.7 ± 123.6; p = 0.042).

Conclusion(s): Our results suggest the need for undertaking a serious effort towards the provision of gynecological care and cervical cancer screening at the same health center as HIV care, in Iranian HIV infected women.

INTRODUCTION

Cancers underlying the human immunodeficiency virus (HIV) infection have been associated with increasing incidence of some malignancies behind the setting of immunosuppression. Kaposi’s sarcoma, non-Hodgkin’s lymphoma and cervical cancer which are called as AIDS-defining cancers, have been found to be associated with HIV infection. The incidence of several other malignancies, such as anal, liver, lung and skin cancer, and Hodgkin’s disease have been more common in HIV positive patients[1].

The role of AIDS in the etiology of cervical cancer has not been well-identified. A number of co-factors such as smoking and sexually transmitted infections have been identified to be associated with the development of high-grade cervical intraepithelial neoplasia (CIN) and cervical cancer[2,3]. Several large studies have found that immunosuppressive patients including HIV positive women are at high risk of incident and persistent human papilloma virus (HPV) infection and CIN[4-6].

Some cohort studies suggested that CIN and cervical cancer in HIV positive women has a much worse prognosis and more aggressive clinical course, higher rate and shorter intervals to recurrence and death from the cancer[7]. There is also a correlation between degree of HIV-related immunosuppression as determined by absolute CD4+ counts and the prevalence of HPV infection[8].

On the basis of previous guidelines and recommendations, cervical cancer screening among immunosuppressive women particularly those who are HIV-positive must be emphasized and done with closer intervals; for example, two Pap smears six months apart after the initial HIV diagnosis should be done and, if results of both are normal, they should undergo annual cytologic screening[9].

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Iranian women with AIDS disease are now being registered by the Family Health Center close to their home and are accessing the newest antiretroviral therapy. Thus, these women may live long enough for progression of HPV-induced cervical neoplasia[10]. Kolahdoozan et al. reported in 2010 that cervical cancer is the fifth most common cancer in Iranian women[11]. Therefore, it is becoming increasingly necessary to provide some data documenting the background prevalence of cervical neoplasia for these high-risk women and the national protocol for regular cervical cancer screening services for these women and to link screening and treatment in such a manner that it ensures compliance.

This study was undertaken among HIV infected women attending the North and East Tehran Health Centers, with a goal to determine SIL according to liquid based cytology (LBC) results and to assess its relation to the patients' immune status to develop and evaluate the appropriateness of cervical cancer screening protocols for HIV positive women living in Iran.

SUBJECTS AND METHOD
Case and control groups
This case-control observational study was conducted between July 2007 and June 2010. All HIV infected women, registered in North and East Tehran Health Centers, receiving highly active antiretroviral therapy (HAART) were asked to participate in the research. Non-pregnant women registered at the same centers were also been invited to participate as a control group. This study was approved by Reproductive Health Research Center and Shaheed Beheshti Medical University, Tehran Ethics Committee. After explanation of the study and clinical procedures, all women provided written informed consent. Eligibility criteria for both groups were good mental and physical condition with no signs of sexually transmitted infections (e.g., cervico-vaginal discharge). Pregnant individuals, women who had a history of previous diagnosis or treatment of cervical neoplasia or cancer, or had undergone hysterectomy were excluded. Eligibility criteria for cases included prior documented evidence of HIV infection, receiving the treatment for six months or less, and current absence of acute illness.

Study procedure
A short questionnaire established socio-demographic, past medical history and other characteristics known to be associated with increased risk of cervical cancer. Height and weight were measured, and body mass index (BMI) was calculated (BMI = weight (kg) / [height (m)]^2).

Peripheral blood samples for estimating CD4+ lymphocyte cell counts were collected. A trained gynecology oncologist conducted a physical and pelvic examination in all women and collected specimens from the ectocervix and endocervix for Pap smear test. The specimens were sent to the cytopathology laboratory of the Taleghani Hospital at the Shaheed Beheshti Medical University on the same day. After cervical specimens were collected, colposcopic exams were performed on all women by the same gynecology oncologist. If any suspicious abnormality was indicated by colposcopy or cytology results, lesions were further evaluated by biopsy, endocervical curettage, or loop electrical excision. Although, those who had abnormal cervical smear were recalled for more investigation including colposcopy, compliance of women with an abnormal smear result, was incomplete (approximately 70%, e.g., prisoners, etc...) and as a result we used cytology to define end points in our analysis. As low-grade SIL sometimes are high-grade lesions when evaluated by biopsy, and cytology has some false-negative results[12,13], we used “any SIL” as our main end point.

Laboratory tests
Cytological analyses were undertaken in the cytopathology laboratory of the Hospital. Upon arrival, the specimen vials (pre-labeled with a unique identifying number) were prepared and assessed with a ThinPrep® 3000 processor. All samples were screened and diagnosed by a certified senior cytopathologist according to the Bethesda system guidelines[14]: normal (no squamous cell abnormality), atypical squamous cells of undetermined significance (ASC-US), atypical squamous cells - high grade (ASC-H), low-grade squamous intraepithelial lesions (LSIL), high-grade squamous intraepithelial lesions (HSIL), and suspicious for squamous cell carcinoma (SCC). All results were reviewed by a board certified senior cytopathologist. The cytopathologist as well as cytopathologist, were blinded to the clinical profile and colposcopic and histological findings to ensure unbiased reporting.

Statistical analysis
Data were analyzed by a Statistical Package for Social Sciences (SPSS software version 17). The frequencies of abnormal smears were determined using Fishers Exact test and odds ratios (OR) determined with their associated 95% confidence intervals (CI) and compared between cases and controls. The number of women with low CD4 counts less than 400 was compared between cases and controls as well as between cases with normal and abnormal smear using independent sample t-test. Other numeric variables are presented as the mean (± standard deviation) and were compared using t-test or Mann Whitney U
December 2011

Table 1: Categorical characteristics in cases compared with controls

<table>
<thead>
<tr>
<th>Variables</th>
<th>Cases N = 58 (%)</th>
<th>Controls N = 189 (%)</th>
<th>p-value</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Past medical history</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight loss</td>
<td>18 (31)</td>
<td>15 (7.9)</td>
<td>&lt; 0.001</td>
<td>5.2</td>
<td>2.4 – 11.2</td>
</tr>
<tr>
<td>Chronic cough</td>
<td>10 (17.2)</td>
<td>3 (1.6)</td>
<td>&lt; 0.001</td>
<td>12.9</td>
<td>3.4 – 48.8</td>
</tr>
<tr>
<td>Fever</td>
<td>4 (6.9)</td>
<td>–</td>
<td>0.003</td>
<td>4.5</td>
<td>3.6 – 5.7</td>
</tr>
<tr>
<td>Chronic diarrhea</td>
<td>10 (17.2)</td>
<td>3 (1.6)</td>
<td>&lt; 0.001</td>
<td>8.7</td>
<td>1.02 – 74.36</td>
</tr>
<tr>
<td>Vaginal discharge</td>
<td>14 (48.3)</td>
<td>37 (58.7)</td>
<td>0.38</td>
<td>0.8</td>
<td>0.53 – 1.26</td>
</tr>
<tr>
<td>PCB</td>
<td>2 (3.4)</td>
<td>9 (4.8)</td>
<td>0.77</td>
<td>0.7</td>
<td>0.08 – 6.67</td>
</tr>
<tr>
<td>AUB</td>
<td>4 (6.9)</td>
<td>12 (6.3)</td>
<td>0.92</td>
<td>1.1</td>
<td>0.21 – 5.60</td>
</tr>
<tr>
<td>BV</td>
<td>16 (27.6)</td>
<td>3 (1.6)</td>
<td>0.001</td>
<td>17.4</td>
<td>2.28 – 132.57</td>
</tr>
<tr>
<td>TV</td>
<td>2 (3.4)</td>
<td>5 (2.6)</td>
<td>0.67</td>
<td>1.1</td>
<td>1.7 – 0.67</td>
</tr>
<tr>
<td>Candidiasis</td>
<td>20 (34.5)</td>
<td>132 (69.8)</td>
<td>&lt; 0.001</td>
<td>0.7</td>
<td>0.58 – 0.82</td>
</tr>
<tr>
<td>Herpes</td>
<td>6 (10.3)</td>
<td>3 (1.6)</td>
<td>0.006</td>
<td>2.3</td>
<td>5.9 – 10</td>
</tr>
<tr>
<td>UTI</td>
<td>12 (20.7)</td>
<td>51 (27)</td>
<td>0.61</td>
<td>0.8</td>
<td>0.34 – 1.74</td>
</tr>
<tr>
<td>Other history and conditions</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hx of hospitalization</td>
<td>16 (27.6)</td>
<td>18 (9.5)</td>
<td>0.001</td>
<td>3.6</td>
<td>1.7 – 7.7</td>
</tr>
<tr>
<td>Hx of blood transfusion</td>
<td>4 (6.9)</td>
<td>12 (6.3)</td>
<td>0.54</td>
<td>1.1</td>
<td>0.34 – 3.53</td>
</tr>
<tr>
<td>Hx of family cancer</td>
<td>12 (20.7)</td>
<td>36 (19)</td>
<td>1.0</td>
<td>1.1</td>
<td>0.45 – 2.61</td>
</tr>
<tr>
<td>Hx of family breast cancer</td>
<td>6 (9.6)</td>
<td>3 (1.6)</td>
<td>0.23</td>
<td>4.3</td>
<td>0.41 – 46.00</td>
</tr>
<tr>
<td>Hx of high-risk sexual behavior</td>
<td>4 (6.9)</td>
<td>6 (3.2)</td>
<td>0.59</td>
<td>2.2</td>
<td>0.32 – 14.67</td>
</tr>
<tr>
<td>Hx of prison</td>
<td>12 (20.7)</td>
<td>3 (1.6)</td>
<td>0.004</td>
<td>13.0</td>
<td>1.64 – 103.38</td>
</tr>
<tr>
<td>HIV-positive partner</td>
<td>6 (10.3)</td>
<td>–</td>
<td>0.029</td>
<td>0.9</td>
<td>0.79 – 1.02</td>
</tr>
<tr>
<td>Hx of STD</td>
<td>12 (20.7)</td>
<td>12 (6.3)</td>
<td>0.003</td>
<td>3.8</td>
<td>1.6 – 9.1</td>
</tr>
<tr>
<td>IV drug user</td>
<td>4 (6.9)</td>
<td>24 (12.7)</td>
<td>0.34</td>
<td>0.5</td>
<td>0.2 – 1.5</td>
</tr>
<tr>
<td>Cigarette smoking</td>
<td>12 (20.7)</td>
<td>9 (4.8)</td>
<td>0.026</td>
<td>4.3</td>
<td>1.17 – 16.17</td>
</tr>
<tr>
<td>Contraception</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Condom</td>
<td>12 (20.7)</td>
<td>57 (30.2)</td>
<td>0.28</td>
<td>0.5</td>
<td>0.20 – 1.48</td>
</tr>
<tr>
<td>OCP</td>
<td>2 (3.4)</td>
<td>15 (7.9)</td>
<td>0.66</td>
<td>0.4</td>
<td>0.05 – 3.5</td>
</tr>
<tr>
<td>IUD</td>
<td>–</td>
<td>45 (23.8)</td>
<td>0.002</td>
<td>1.3</td>
<td>1.14 – 1.5</td>
</tr>
<tr>
<td>TL</td>
<td>–</td>
<td>9 (4.8)</td>
<td>0.55</td>
<td>1.0</td>
<td>0.99 – 1.11</td>
</tr>
<tr>
<td>Non</td>
<td>40 (69)</td>
<td>51 (27.0)</td>
<td>0.001</td>
<td>2.6</td>
<td>1.59 – 4.10</td>
</tr>
<tr>
<td>Pap smear result</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inflammation in smear</td>
<td>46 (80)</td>
<td>90 (47.6)</td>
<td>0.006</td>
<td>1.7</td>
<td>1.2 – 2.3</td>
</tr>
<tr>
<td>Abnormal smear</td>
<td>12 (20.7)</td>
<td>6 (3.2)</td>
<td>&lt; 0.001</td>
<td>2.4</td>
<td>1.2 – 4.6</td>
</tr>
<tr>
<td>HSIL</td>
<td>6 (10.3)</td>
<td>–</td>
<td>&lt; 0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD4 cut-point</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CD4 ≤ 400 cells/µl</td>
<td>22 (37.9)</td>
<td>15 (7.9)</td>
<td>&lt; 0.001</td>
<td>7.1</td>
<td>3.4 – 14.9</td>
</tr>
</tbody>
</table>

AUB = abnormal uterine bleeding, BV = bacterial vaginosis, HSIL = high grade cervical squamous intraepithelial lesion, Hx = History, IUD = intrauterine device, OCP = oral contraceptive pill, PCB = postcoital bleeding, TL = tubal ligation, TV = trichomonal vaginitis, UTI = urinary tract infections, OR = odds ratio, CI = confidence intervals

for variables displaying normality behavior tested, using the Shapiro-Wilk statistics. To assess the effect of categorical demographic factors on HIV disease and cervical smear abnormality, the number of cases and controls with and without each risk factor was compared using Fishers Exact tests and odds ratios were determined. Group testing of categorical data is presented as n (%), and groups were compared with chi square test or Fisher exact test. Significance level was set at p < 0.05.

RESULTS

Between July 2007 and July 2010, 58 out of 60 HIV-positive women registered in North and East Tehran Health Centers, were included in the study group. Out of 200 eligible women registered in the same centers, 189 participated in the study as controls.

Cases compared with controls

All cases and controls were married and had the education at the level of undergraduate. The mean age was matched in cases and controls (35.7 ± 7.6 Vs 36.2 ± 7.4 years, p = 0.63). The mean of BMI values was not significantly different between cases and controls (24.5 ± 4.6 Vs 25.7 ± 4.4, p = 0.07). Among case group 40 (69%) participants compared with 51 (27%) controls had not used contraception (p = 0.001). None of cases and 45 (23.8%) out of the control group had used an intrauterine device for contraception (p = 0.002).

As shown in Table 1, there were higher rates in cases than controls about situations such as a history of STD, bacterial vaginosis, herpes, weight loss, chronic cough, fever, chronic diarrhea, hospitalization, prisoner, and smoking behaviors as well as having HIV-positive partners. In contrast, the mean of hematocrit (p = 0.001)
and platelet count ($p < 0.001$) were significantly lower in women involved with HIV infection compared with controls (Table 2). A low rate of candidiasis was observed among cases compared with controls ($34.5$ % vs $69.8$ %, $p < 0.001$).

As expected, the mean of CD4+ count was significantly lower in cases ($541.8 ± 289.1$ vs $894.1 ± 393.0$, $p < 0.001$) and $22 (37.9$%) cases ($573.0 ± 306.9$ vs $383.7 ± 123.6$, $p = 0.042$), although not significant, incidence of previous smear cases ($26.6 ± 2.8$ vs $24.0 ± 4.9$ kg/m$^2$, $p = 0.005$) was significantly different in these two subgroups.

The prevalence of abnormal smear was significantly higher in cases $20.7$% (15 LSIL + 6 HSIL) compared with controls $3.2$% (6 ASCUS) ($OR = 2.4$, $95% CI 1.2$ to $4.6$, $p < 0.001$). Inflammation seen on cervical smear, was significantly more common in cases compared with controls ($80$ Vs $47.6$%, $OR = 1.67$, $CI 1.2$ to $2.3$, $p = 0.006$).

### Case group

In cases all risk factors were compared between women with normal and abnormal smear subgroup. The mean age of cases with and without normal smear was ($32.6 ± 7.2$ Vs $36.4 ± 7.6$ years) and their BMI was ($26.6 ± 2.8$ Vs $24.0 ± 4.9$ kg/m$^2$). They were not significantly different in these two subgroups.

The mean of CD4 count was significantly higher in cases with normal smear compared with abnormal smear cases ($573.0 ± 306.9$ vs $383.7 ± 123.6$, $p = 0.042$), (Table 3). Although not significant, incidence of previous STD, bacterial vaginosis, postcoital bleeding, abnormal uterine bleeding, smoking, previous hospitalization, and weight loss was higher in cases with the presence of SIL, while the mean of platelet count among these cases was significantly lower.

### DISCUSSION

In a population in Tehran, Iran, we studied associations between SIL and HIV infection and CD4 count. Several studies indicated that HIV infected persons are at excess risk for HPV-related cancers[15-19]. Our data suggested that nearly one in three ($36.2$%) Iranian women with HIV infection might be at risk of developing cervical cytology abnormality on smear. Similar result was demonstrated by Sahasrabuddhe et al in India[20], where over a quarter of their HIV infected participants had CIN1 or more severe lesions. They revealed independent predictors of increasing severity of CIN which included receiving antiretroviral therapy currently and presence of cervical high-risk HPV-DNA.

Although LSIL had a high rate among cervical abnormalities in HIV positive women which mostly regress over time, the reasons for existence of high-prevalence of abnormal cervical smear in HIV infected women compared with normal population could be partially attributed to the fact that the cases were recruited after establishment of the disease, registered to receive HAART, having a CD4+ significantly lower compared with controls showing their immunity suppression having enough time for HPV infection to be persistent and stimulate the progression to intraepithelial lesion. Another possible explanation for the high rate of cervical abnormalities detected in our study cases is the taking and reading of the samples

### Table 2: Peripheral blood parameters in case and control patients

<table>
<thead>
<tr>
<th>Variables</th>
<th>Cases (N = 58) Mean ± SD</th>
<th>Controls (N = 189) Mean ± SD</th>
<th>p-value</th>
<th>Mean Diff.</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC ($10^3$/μl)</td>
<td>5.1 ± 1.3</td>
<td>7.3 ± 1.5</td>
<td>&lt; 0.001</td>
<td>-2.2</td>
<td>-2.3 - -1.8</td>
</tr>
<tr>
<td>Hb (g/dl)</td>
<td>12.8 ± 1.0</td>
<td>13.4 ± 1.5</td>
<td>0.005</td>
<td>-0.6</td>
<td>-0.0 - -0.2</td>
</tr>
<tr>
<td>Hct (%)</td>
<td>38.7 ± 2.8</td>
<td>40.5 ± 3.6</td>
<td>&lt; 0.001</td>
<td>-1.8</td>
<td>-2.8 - -0.7</td>
</tr>
<tr>
<td>MCV (fL)</td>
<td>92.1 ± 13.1</td>
<td>84.4 ± 9.3</td>
<td>&lt; 0.001</td>
<td>7.6</td>
<td>4.6 - 10.7</td>
</tr>
<tr>
<td>PLT ($10^3$/μl)</td>
<td>234.9 ± 57.6</td>
<td>280.4 ± 85.1</td>
<td>&lt; 0.001</td>
<td>-45.5</td>
<td>-69.1 - -22.0</td>
</tr>
<tr>
<td>CD4 (cells/μl)</td>
<td>541.8 ± 289.1</td>
<td>894.1 ± 393.0</td>
<td>&lt; 0.001</td>
<td>-352.3</td>
<td>-462.1 - -242.5</td>
</tr>
</tbody>
</table>

CI = confidence intervals, WBC = white blood cells, Hb = hemoglobin, Hct = hematocrit, MCV = mean corpuscular volume, PLT = platelets

### Table 3: Peripheral blood parameters in cases with and without normal smear

<table>
<thead>
<tr>
<th>Variable</th>
<th>Normal smear (N = 46) Mean ± SD</th>
<th>Abnormal smear (N = 12) Mean ± SD</th>
<th>p - value</th>
<th>Mean Diff.</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC ($10^3$/μl)</td>
<td>5.0 ± 1.2</td>
<td>5.0 ± 1.9</td>
<td>0.9</td>
<td>-0.273</td>
<td>-0.935 - -0.880</td>
</tr>
<tr>
<td>Hb (g/dl)</td>
<td>12.86 ± 1.1</td>
<td>12.4 ± 1.02</td>
<td>0.2</td>
<td>0.5</td>
<td>-1.3 - -2.4</td>
</tr>
<tr>
<td>Hct (%)</td>
<td>38.8 ± 3.1</td>
<td>38.2 ± 1.9</td>
<td>0.6</td>
<td>0.9</td>
<td>-3.9 - -4.2</td>
</tr>
<tr>
<td>MCV (fL)</td>
<td>91.7 ± 12.9</td>
<td>94.4 ± 15.2</td>
<td>0.5</td>
<td>-2.7</td>
<td>-12.9 - -7.5</td>
</tr>
<tr>
<td>PLT ($10^3$/μl)</td>
<td>240.8 ± 59.1</td>
<td>199.6 ± 55.1</td>
<td>0.03</td>
<td>41.2</td>
<td>3.3 - 79</td>
</tr>
<tr>
<td>CD4 (cells/μl)</td>
<td>573.0 ± 306.9</td>
<td>383.7 ± 123.6</td>
<td>0.042</td>
<td>189.3</td>
<td>47.1 - 371.9</td>
</tr>
</tbody>
</table>

CI = confidence intervals, Hb = hemoglobin, Hct = hematocrit, MCV = mean corpuscular volume, WBC = white blood cells, PLT = platelets
by highly qualified people. Similarly, in a case-control study between 1998 and 2001 in South Africa Moodley et al.[21] found increased risk associated with HIV for LSIL and HSIL.

As expected, most cases compared with controls had significantly less CD4, more chronic illnesses like diarrhea and cough or lower hemoglobin, hematocrit, and platelets. Also CD4 count was lower in abnormal smear HIV infected women which indicates the significant higher rate of immunosuppression in this group than normal smear HIV positive cases. Firnhaber et al had comparable findings which indicated HIV seropositive women with CD4 count less than 200 cells/μl had a higher risk for cervical lesions than CD4 level more than 500/μl[21].

The high risk behavior and conditions such as being prisoner, cigarette smoking, previous STD, bacterial vaginosis reported in smear, HIV infection in partners, and sex without contraception, were significantly higher in cases. These results might represent immunosuppressive state of women with HIV, their ignorance about safe sexual relationships, their vulnerability to contract STD including HPV and their inability in accessing preventive and therapeutic clinical care.

Limitations of the study
As the prevalence of HIV infection and cervical cancer is very low in Iran, a major limitation of this study was our sample size. Thus said, 58 women were all HIV positive women who came from the metropolitan area of Iran. Therefore, it might be worth confirming these results by larger studies.

The other limitation of our study was that we had no access to HPV-DNA typing due to financial difficulties.

CONCLUSION
Although HPV testing in HIV positive women may lead to improved results, the use of HPV test for this high-risk population needs inexpensive and simple tests for early detection of HPV. Based on this study, an effort towards the provision of gynecological care at the same health center as HIV care, in HIV infected Iranian women as well as providing a cervical cancer screening and treatment program that benefits the average woman accessing these centers is highly recommended.

ACKNOWLEDGEMENTS
The research was funded by Infertility and Reproductive Health Research Center, Beheshti Medical University. The funding source had no involvement in any aspect of this research. We acknowledge the help of the North and East Health Centers of Tehran in providing us with their census data, as well as the women who participated in the study. There was no conflict of interests in this research.

REFERENCES


Original Article

Papillary Microcarcinomas of the Thyroid Gland: Do We Need to be Aggressive in the Management?

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Kuwait University Hospital Medical School, Sana’a University, Yemen

Kuwait Medical Journal 2011; 43 (4): 297 - 300

ABSTRACT

Objectives: To identify patients with papillary microcarcinomas of the thyroid gland (PMCT) and adopt a policy for their management
Design: Retrospective
Setting: Kuwait University Hospital, Sana’a, Yemen
Subjects: Five hundred and fifty consecutive patients who underwent thyroidectomy
Intervention: Ultrasound (US) and fine needle aspiration (FNA)
Main Outcome Measures: Clinical course of subjects with PMCT
Result: The overall PMCT rate was 9.5% (44 / 465) and female to male ratio was 10:1. Fine needle aspiration (FNA), performed pre-operatively showed a benign lesion in about 50% of the patient. Subtotal thyroidectomy was performed in 50% patients, while the rest were managed by lobectomy or near total thyroidectomy.
Conclusion: PMCT is not uncommon among patients with benign thyroid diseases. The sensitivity of neck ultrasound and FNA in detecting PMCT is rising. The lack of guidelines created a wide range of management policies. We recommend a less aggressive procedure for PMCT of 5 mm and less. A sound policy and guideline in preoperative investigation will assist this approach.

KEY WORDS: fine needle aspiration (FNA), papillary microcarcinomas of thyroid (PMCT), ultrasound (US)

INTRODUCTION

Papillary microcarcinomas of the thyroid gland (PMCT), also called “occult papillary carcinomas”, are defined as tumors of size of 10 mm or less in diameter, that are too small to be palpated and are diagnosed by ultrasound (US) and other neck imaging modalities, or are identified incidentally at surgery for benign thyroid disorders[1-3].

In the majority of cases their behavior is benign. It has been reported that occult papillary carcinomas may be found at an autopsy in upto 24% of the cases. They are considered to be a subgroup of well-differentiated carcinomas of the thyroid and it was believed that they could rarely cause cervical or distant metastases. Nevertheless, papillary microcarcinomas may occasionally present in a more aggressive manner with lymph nodes or even distant metastases.

The extensive use of US and fine-needle aspiration (FNA) biopsy for thyroid lesions has recently increased incidence of its diagnosis. The “ideal” therapeutic approach for such patients remains a subject of debate among endocrinologists and surgeons.

In a recent observational trial, Ilto et al[4] showed that only 10.2% of low-risk PMCT enlarged by more than 10 mm during five years of follow-up and only 1.2% of patients developed lymph node metastases in the lateral compartments; more than 70% of tumors either did not change or decreased in size compared to the initial size at diagnosis, suggesting that PMCT may be observed as long as the tumor shows no progression. Moreover, Ilto et al further suggested that “if surgical treatment is performed for low-risk PMCT, prophylactic modified radical neck dissection is not necessary, and lobectomy (with isthmusectomy) and central node dissection is adequate if the tumor is located only in one lobe”.

The diagnosis of PMCT in patients operated on for a benign disease is frequent[5], in spite of the wide availability of ultrasonography and fine-needle aspiration biopsy. These incidental thyroid carcinomas go undetected by preoperative imaging studies and are identified by pathological examination of surgical specimens.

The majority is less than one cm in diameter and is exclusively papillary and according to the World Health Organization are termed papillary thyroid microcarcinomas.

The clinical importance of these microcarcinomas is debatable. Some authors have observed that they have a benign behavior and do not progress over
a mean follow-up period of 3.8 years. In contrast, other authors have reported cases with local lymph node and distant metastases at the time of diagnosis and during follow-up evaluation. Occasionally, these tumors cause cancer-related death.[6]

**Table 1: Presentation (clinical examination)**

<table>
<thead>
<tr>
<th>Clinical presentation</th>
<th>n</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multinodular goitre</td>
<td>26</td>
<td>59.1</td>
</tr>
<tr>
<td>Diffuse goitre</td>
<td>12</td>
<td>27.3</td>
</tr>
<tr>
<td>Solitary thyroid nodule</td>
<td>6</td>
<td>13.6</td>
</tr>
</tbody>
</table>

The majority of these tumors is indolent and slow growing. However, approximately 10% of PMCT exhibit aggressive clinical course, while less than 1% result in mortality. Age, sex, and postoperative thyroglobulin level were found to be the main prognostic factors in the high-risk group of patients with these tumors.

In this study, we reviewed the incidental discovery of these tumors upon histological examination of thyroidectomy specimens performed for benign thyroid disease in Yemeni patients, given the difficulty of patient follow-up after surgery.

**PATIENTS AND METHODS**

This is a retrospective study conducted in Al-Kuwait University Hospital in Sana’ Yemen during the period from January 2004 to December 2009. The medical records of 550 patients who were operated for benign goiter were reviewed to select those patients in whom the final diagnosis of PMCT was made. The study was approved by the local ethical committee.

Data on age, sex, clinical presentation and thyroid function test, US of the thyroid and pathological assessment by fine needle aspiration (FNA) and the mode of surgery were collected. The exclusion criteria included all cases who were diagnosed preoperatively as papillary carcinoma or whose postoperative histopathology showed a macropapillary thyroid carcinoma.

Subtotal thyroidectomy was the most frequent surgical procedure performed for the patients (45.5%) followed by hemithyroidectomy in (36.6%). The rest of the patients had total and near total thyroidectomy (18.2%).

**Table 2: Patient distribution according to the results of FNA and neck US**

<table>
<thead>
<tr>
<th>Groups</th>
<th>Frequency (n)</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>FNA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benign</td>
<td>24</td>
<td>54.5</td>
</tr>
<tr>
<td>Malignant</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Indefinite</td>
<td>12</td>
<td>27.3</td>
</tr>
<tr>
<td>Inadequate</td>
<td>8</td>
<td>18.2</td>
</tr>
<tr>
<td>Neck US</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diffuse</td>
<td>13</td>
<td>29.5</td>
</tr>
<tr>
<td>Nodular cystic</td>
<td>27</td>
<td>61.4</td>
</tr>
<tr>
<td>Solid nodule</td>
<td>4</td>
<td>9.1</td>
</tr>
</tbody>
</table>

Intra-operative assessments of the gross pathological state of the thyroid revealed a benign looking thyroid in 70.5% of the patients. Suspicious looking thyroids were noted in 25% of the patients. Only two cases (4.5%) were highly suspicious of being malignant. Intra-operative finding of lymph nodes were noted in only five patients (11.4%).

**RESULT**

A total of 465 patients were eligible for this study. Forty-four patients had a final histopathological diagnosis of PMCT. The majority were females (F: 90.9% M: 9.1%). Over 38% were aged 31 to 40 years (Fig. 1). More than 60% of the patient presented with neck swelling, while the rest presented with mild palpitation (27%), dyspnea (15%) and feeling of heaviness (2.2%). Family history of thyroid cancer was present in nine patients (20.5%). Clinically, 26 patients (59.1%) had multinodular goiter, 12 patients (27.3%) had diffuse goiter and six patients (13.6 %) had solitary thyroid nodule (Table 1). Preoperative thyroid function test was within normal range except in four patients who had hyperthyroid results correlating with their clinical presentation. FNA was not helpful in preoperative diagnosis (Table 2).

Intra-operative examination of the tissue by the operating surgeon documented four patients as highly suggestive of malignancy (Table 3).

Intra-operative assessments of the gross pathological state of the thyroid revealed a benign looking thyroid in 70.5% of the patients. Suspicious looking thyroids were noted in 25% of the patients. Only two cases (4.5%) were highly suggestive of malignancy.

**Table 3: Patients distribution according to the intra-operative findings**

<table>
<thead>
<tr>
<th>Intra-operative Groups and findings</th>
<th>Frequency (n)</th>
<th>(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thyroid gland intra-operative clinical diagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Benign</td>
<td>31</td>
<td>70.5</td>
</tr>
<tr>
<td>Suspicious</td>
<td>11</td>
<td>25.0</td>
</tr>
<tr>
<td>Highly suggestive</td>
<td>2</td>
<td>4.5</td>
</tr>
<tr>
<td>Intra-operative LN finding</td>
<td></td>
<td></td>
</tr>
<tr>
<td>+ve</td>
<td>5</td>
<td>11.4</td>
</tr>
<tr>
<td>-ve</td>
<td>39</td>
<td>88.6</td>
</tr>
</tbody>
</table>
looking thyroid in 70.5% of patients. Suspicious looking thyroids were noted in 25% patients. Only two cases (4.5%) were highly suspicious of being malignant. Intra-operative finding of lymph nodes were noted in only five patients (11.4%).

The type of surgery in the majority of patients was decided on the operation table. In suspicious cases total thyroidectomy was the method of choice (Table 4).

<table>
<thead>
<tr>
<th>Operation</th>
<th>Frequency (n)</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subtotal thyroidectomy</td>
<td>20</td>
<td>45.5</td>
</tr>
<tr>
<td>Lobectomy + isthmectomy</td>
<td>16</td>
<td>36.4</td>
</tr>
<tr>
<td>Near total thyroidectomy</td>
<td>5</td>
<td>11.4</td>
</tr>
<tr>
<td>Total thyroidectomy</td>
<td>3</td>
<td>6.8</td>
</tr>
</tbody>
</table>

**DISCUSSION**

The 44 patients with PMCT in our study represented 9.5% of the total thyroidectomy patients operated upon for benign thyroid disease; (44 / 465 patients). This percentage is slightly higher than what is reported in other studies. Elio Roti et al[2] found 52 patients with incidental PMCT in a series of 1265 patients operated for Grave’s disease and nodular goiter, giving an incidence of 4.1% of finding an incidental PMCT in their study. Sakorafas et al[8] found an incidence of 7.1% of incidental PMCT in patients operated for benign thyroid diseases, i.e., 27 out of 380 patients. In the work done by Miccoli et al[8] on 998 thyroid patients 10.4% had incidental thyroid carcinoma out of which 99% were incidental PMCT.

In this study the majority of patients presented with multinodular goiter (59.1%) followed by diffuse goiter (27.3%). Only six patients (27.3%) presented with solitary thyroid nodule. No differences were found in relation to the type of goiter presentation. The prevalence of thyroid cancer was similar between patients with a solitary nodule (4.8%) and patients with multiple nodules (4.9%). However, a solitary nodule had a higher likelihood of malignancy than a non-solitary nodule (p < 0.01).

More than half of the patients (56.8%) were symptom free; nonetheless, some presented with symptom which did not indicate the possibility of a malignancy. Therefore, our finding suggests that symptomatology is a poor predictor of malignancy[9]. In our study, US also was not helpful in detecting malignant or suspicious nodules or lymph nodes virtually giving a near nil sensitivity for suspected malignancy.

In our study, we excluded preoperative FNA positive patients. However, all our patients who were diagnosed postoperatively had negative FNA result.

In our patients, the aspiration was not done under US guidance, which could have raised the preoperative diagnosis of malignancy and changed the line of management[10,11]. US-guided FNA has become the gold-standard for assessment of thyroid nodules. US-guided FNA has a higher rate of adequate cytological material and it is effective in sampling thyroid nodules less than one cm in diameter. In a series of 267 patients with non-palpable thyroid nodules examined by Nam-Goong et al, the specimen was adequate in 32% patients. Dong Wook et al, demonstrated a 55% true positive for microcarcinoma of less than 5 mm diameter when using US guided aspiration. They concluded that small size alone does not guarantee low risk in incidentally found thyroid cancers and recommend US-guided FNA as the diagnostic method in these patients[12,13]. Roti et al[14] reported that two patients (2 of 68) with thyroid cancer less than five mm had regional lymph node metastases.

In our series, the most common surgical procedures were subtotal thyroidectomy and lobectomy. The size of the tumour was not found to be indicative of a low risk for malignancy since even small PMCT were found to be associated with multifocality, extrathyroidal growth as well as lymph node metastases[15]. Accordingly, many authors advocate completion of total or near total thyroidectomy with radioactive iodine for these tumors.

This is obviously much higher than what has been found in other studies. It has been stated that approximately 5% of non-medullary thyroid carcinomas (NMTC) are of familial origin and that when two or more family members are diagnosed with non-medullary thyroid cancer in the absence of other known associated syndromes, it is termed familial non-medullary thyroid cancer (FNMC)[16]. The prevalence of familial cases among all NMTCs ranges between 3.5 - 6.2%[17]. Tuya Pal et al found that 17 of 339 (5.0%) patients with NMTC had at least one first degree relative affected with thyroid cancer[18].

Moreover, Ilto et al further suggested that “if surgical treatment is performed for low-risk PMCT, prophylactic modified radical neck dissection is not necessary, and lobectomy (with isthmusectomy) and central node dissection is adequate if the tumor is located only in one lobe[19].

Since our primary aim was surgery for a benign pathology, the approach was either lobectomy, subtotal or near total thyroidectomy and if lymph nodes were palpable or the multinodularity was extensive we would proceed to total thyroidectomy.

Twenty percent of our patients had a family history of thyroid cancer. In our opinion, our patients needed a more aggressive surgical approach. Despite the limited surgical resection in some patients we have no recurrence on the follow up. Nevertheless, we have adopted a different approach in managing benign thyroid lesions. Postoperatively, we do
not use radioactive iodine. The only postoperative management is to observe the patient once a year with ultrasonography and, if necessary, fine-needle aspiration cytology as well as checking serum thyroglobulin levels.

Despite the controversy at present in the management of PMCT and the lack of prediction of the prognosis, we have adopted our own protocol; biopsy is done under US guidance for almost all cases in the hope that it will reduce the postoperative incidental discovery of PMCT. Those with family history are considered high risk and are given the choice of surgery. Additionally, we have recommended a shift towards near total or total thyroidectomy.

Bilimoria et al[23] in a review demonstrate that total thyroidectomy resulted in lower recurrence rates and improved survival rates for tumors of one cm or more size. This represents the first published report of a survival benefit for total thyroidectomy.

CONCLUSIONS

PMCT are not uncommon among patients with benign thyroid diseases. The sensitivity of neck US and FNA in detecting PMCT is rising. The lack of guidelines has created a wide range of management strategies. We have since adopted near total thyroidectomy for all our cases where there is an indication. US is more often utilized during aspiration to aid in the proper diagnosis. All tumors above 0.5 cm size were managed more aggressively (near total thyroidectomy).

REFERENCES

Related factors for Rectosigmoid Hyperplastic Polyps: A Hospital-Based Study

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4School of Medicine, Tzu Chi University, Hualien, Taiwan

ABSTRACT

Objectives: Little evidence is available about the related factors for colorectal hyperplastic polyps in Taiwan. The aim of this study was to explore the prevalence of rectosigmoid hyperplastic polyps and to determine the related factors.

Setting: Medical center in Taichung city, Taiwan

Design: Retrospective hospital-based, cross-sectional study.

Subjects: We analyzed the medical records of all subjects receiving periodic health examination at one medical center in Taichung city in Taiwan from 2001 to 2004. A total of 4413 subjects were enrolled in this study.

Intervention Main Outcome Measure: All subjects underwent a 60-cm flexible sigmoidoscopic examination and laboratory survey.

Main Outcome Measure: Prevalence of hyperplastic Polyps and related factors

Results: There were 2444 men (55.4%) and 1969 women (44.6%). The mean age was 49.3 years (standard deviation 12.3, range from 20 to 87). The overall prevalence of hyperplastic polyps was 5.5%, with higher prevalence in men than in women (6.9% Vs 3.7%, p < 0.001). After controlling for the other co-variates, multivariate logistic regression model showed that the related factors for hyperplastic polyps were increasing age (OR = 1.03, 95% CI = 1.02 - 1.05, p < 0.001), male gender (OR = 1.79, 95% CI = 1.31 - 2.46, p < 0.001), generalized obesity (OR = 1.59, 95% CI = 1.10 - 2.28, p = 0.012), and smoking (OR = 1.40, 95% CI = 1.02 - 1.93, p = 0.038).

Conclusions: These findings reveal that increasing age, male gender, generalized obesity and smoking are the related factors for rectosigmoid hyperplastic polyps.

INTRODUCTION

In 2006, cancer was the first leading cause of death in Taiwan[1]. However, colorectal cancer ranked as the third leading cause of cancer death for people in Taiwan and accounted for approximately 4284 deaths in 2006. Most colorectal cancers are currently thought to arise from pre-existing polyps conventionally called adenomas[2]. The hypothesis of colorectal adenoma-carcinoma sequence is now widely established[3,4].

On the other hand, another type of colorectal polyp known as hyperplastic polyp has a type of cellular proliferation different from that of an adenoma[5,6]. Unlike adenoma, It has been traditionally believed as a benign non-neoplastic lesion[7,8]. That is, hyperplastic polyps are generally thought to lack malignant potential. Therefore, patients with hyperplastic polyps are not at increased risk of colorectal cancer[9]. It is not necessary to perform surveillance colonoscopy in patients with hyperplastic polyps. Recently, several studies and case reports have identified that some hyperplastic polyps are not always harmless, and even have neoplastic evolution[2,7-11]. Now, there is marked evidence that hyperplastic polyps may play a role as the precursor of colorectal cancers with DNA methylation and deficient DNA mismatch repair[12]. As the literature shows, the risk factors for neoplastic evolution of hyperplastic polyps include multiplicity, large size, right-sided polyps, and found in association with a family history of carcinoma[8,10,12]. Although little is known about the etiology of the hyperplastic polyps, numerous epidemiological studies have demonstrated that several factors including serum insulin levels, dietary factors, alcohol consumption, cigarette smoking, use of aspirin and other non-steroidal anti-inflammatory drugs were related to colorectal hyperplastic polyps[10,13,14].

According to the above reviews, colorectal hyperplastic polyps should be clinically thought of as a unique entity. Thus, it may not be correct to
do nothing about hyperplastic polyps. Therefore, we hypothesize a link between the neoplastic evolution of hyperplastic polyps and the risk factors. That is, interplayed by the detrimental effect of the risk factors, patients with colorectal hyperplastic polyps may have a more complex neoplastic evolution under certain circumstances.

To the best of our knowledge, there is little prospective evidence of colorectal hyperplastic polyps in Taiwan. As it concerns public health, it will be necessary to identify the risk factors for hyperplastic polyps that are especially prone to initiate tumor genesis. If more epidemiological studies can be undertaken, effective screening of individuals at increased risk for neoplastic evolution of hyperplastic polyps can be advocated. Therefore, the purpose of this present study is to address the following objectives: (a) what is the prevalence of rectosigmoid hyperplastic polyps in Taiwan? and (b) what are the related factors for rectosigmoid hyperplastic polyps?

MATERIALS AND METHODS

Study population

This was a retrospective hospital-based, cross-sectional study. We analyzed the medical records of all subjects undergoing self-referred health examination at one medical center located at Taichung city in Taiwan from 2001 to 2004. The institutional review board of this medical center approved this study. Subjects with previous malignant diseases were excluded from the study. All subjects underwent a 60-cm flexible sigmoidoscopic examination and laboratory survey. A total of 4413 subjects were included for analysis.

Data collection

Subjects who currently smoked were classified as smokers. The others were defined as non-smokers. Subjects who never drank alcohol were classified as non-drinkers. Subjects who reported drinking alcohol often were classified as habitual drinkers. Blood pressure was measured by a mercury sphygmomanometer while the subject was in a sitting position. Height and weight were measured. Body mass index (BMI) was calculated as follows: weight (kg) ÷ height (m)². Waist circumference (WC) was measured as the minimum circumference with the tape positioned between xyphoid process and the umbilicus at the end of a normal expiration. Venous blood samples were obtained in the morning after a 12-hour overnight fasting. A number of biochemical markers, such as total cholesterol, triglyceride, low density lipoprotein cholesterol (LDL), high density lipoprotein cholesterol (HDL), fasting glucose and uric acid were measured by a biochemical autoanalysser (Hitachi 736-15, Tokyo, Japan) at the Department of Clinical Laboratory of this medical center. Hepatitis B surface antigen was detected by ELISA test (Enzygnost, Dade Behring Marburg GmbH, Marburg, Germany). Antibody to hepatitis C virus was detected by EIA test (Abbott HCV EIA, third generation, Abbott Laboratories, Abbott Park, IL).

Diagnostic criteria

Generalized obesity was defined as BMI ≥ 27(kg/m²)[20-22]. Abdominal obesity was defined as WC ≥ 90 cm for men and ≥ 80 cm for women, respectively with adoption of the Asian criteria[20-22]. Hypercholesterolemia was defined as fasting total cholesterol level ≥ 5.2 mmol/l[23]. Hypertriglyceridemia was defined as fasting triglyceride level ≥ 1.7 mmol/l[24]. High level of LDL was defined as fasting LDL ≥ 3.4 mmol/l[23]. Low level of HDL was defined as fasting HDL < 1.03 mmol/l for men and < 1.3 mmol/l for women, respectively[24]. Diabetes mellitus was defined as fasting plasma glucose level ≥ 6.9 mmol/l or people on drug treatment of elevated glucose[25]. Subjects were considered to have hypertension if the average of both arm readings exceeded 140 mmHg systolic and/or 90 mmHg diastolic or people on antihypertensive drug treatment[26]. Hyperuricemia was defined as serum uric acid level ≥ 420 μmol/l for men and ≥ 390 μmol/l for women, respectively[27]. Metabolic syndrome was defined as involving three or more of the following conditions proposed by American Heart Association / National Heart, Lung, and Blood Institute in 2005[24]. High blood pressure was defined as blood pressure ≥ 130/85 mmHg or people on antihypertensive drug treatment. Hyperglycemia was defined as fasting plasma glucose level ≥ 5.6 mmol/l or people on drug treatment of elevated glucose. Hypertriglyceridemia was defined as fasting triglyceride level ≥ 1.7 mmol/l. Low level of HDL was defined as fasting HDL < 1.03 mmol/l for men and < 1.3 mmol/l for women, respectively. Abdominal obesity was defined as WC ≥ 90 cm for men or ≥ 80 cm for women, with adoption of the Asian criteria for abdominal obesity.

Statistical analysis

We used a SPSS package (Taiwan Version 10.0, Sinter Information Corp, Taipei, Taiwan). The t test was performed for continuous variables and the chi-squared test was performed for qualitative variables. The relative risks were estimated by adjusted odds ratio (OR) and 95% confidence interval (CI) using a multivariate logistic regression model. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Characteristics of the study population

There were 2444 men (55.4%) and 1969 women (44.6%). The mean age was 49.3 ± 12.3 years (age range from 20 to 87). Among 4413 subjects undergoing 60-cm flexible sigmoidoscopy, 3759 subjects (85.2%)
had normal finding, and the remaining 654 subjects (14.8%) had at least one rectosigmoid polyp. Among 654 subjects with polyps, 505 subjects underwent a polypectomy or biopsy. The histological findings revealed that 225 subjects had adenomas only, 214 subjects had hyperplastic polyps only, 29 subjects with mixed adenomas and hyperplastic polyps, six subjects with adenocarcinomas, and 31 subjects with inflammatory polyps or other lesions. There were 149 subjects with polyps found on examination but no polypectomy or biopsy was taken (Table 1). We compared the clinical and the demographic features between people with isolated hyperplastic polyps only and those with mixed adenomas and hyperplastic polyps. There were no related factors that distinguished the two groups. Finally, 243 subjects with hyperplastic polyps (including 214 subjects with hyperplastic polyps only, and 29 subjects with mixed adenomas and hyperplastic polyps) and 3759 normal subjects were included for further analysis.

Fig. 1, shows the prevalence of hyperplastic polyps in both gender and three age groups. The overall prevalence of hyperplastic polyps was 5.5% (243 / 4413). The prevalence was significantly higher in men than in women (6.9% Vs 3.7%, p < 0.001). Men also had higher prevalence than women did among the same age groups (p = 0.016, p < 0.001 and p = 0.011, respectively). The prevalence also increased with age in men and in women (p < 0.001 and p < 0.001, respectively).

Comparison of related factors between subjects with normal findings and with hyperplastic polyps was done using univariate analysis.
Using the chi-square test, subjects with hyperplastic polyps were compared with those with normal findings. The statistically related factors for hyperplastic polyps were gender (p < 0.001), generalized obesity (p < 0.001), abdominal obesity (p = 0.015), diabetes mellitus (p = 0.003), hypertension (p < 0.001), hypertriglyceridemia (p = 0.049), low level of HDL (p = 0.042), metabolic syndrome (p < 0.001), smoking (p < 0.001), and alcohol consumption (p = 0.001). There was also statistical difference in the mean age by the t test (p < 0.001) (Table 2).

Related factors for hyperplastic polyps by multivariate logistic regression

Only the statistically related factors identified in univariate analysis were further analyzed. After controlling for the other co-variates, the multivariate logistic regression model exhibited that the related factors for hyperplastic polyps were increasing age (OR = 1.03, 95% CI = 1.02 - 1.05, p < 0.001), male gender (OR = 1.79, 95% CI = 1.31 - 2.46, p < 0.001), generalized obesity (OR = 1.59, 95% CI = 1.10 - 2.28, p = 0.012), and smoking (OR= 1.40, 95% CI = 1.02 - 1.93, p = 0.038) (Table 3).

**DISCUSSION**

Table 3: Odds ratio of related factors for hyperplastic polyps

<table>
<thead>
<tr>
<th>Variables</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (every one year)</td>
<td>1.03</td>
<td>1.02 - 1.05**</td>
</tr>
<tr>
<td>Gender (men Vs women)</td>
<td>1.79</td>
<td>1.31 - 2.46**</td>
</tr>
<tr>
<td>Generalized obesity (yes Vs no)</td>
<td>1.59</td>
<td>1.10 - 2.28*</td>
</tr>
<tr>
<td>Abdominal obesity (yes Vs no)</td>
<td>0.92</td>
<td>0.64 - 1.32</td>
</tr>
<tr>
<td>Diabetes mellitus (yes Vs no)</td>
<td>1.05</td>
<td>0.71 - 1.55</td>
</tr>
<tr>
<td>Hypertension (yes Vs no)</td>
<td>1.23</td>
<td>0.90 - 1.69</td>
</tr>
<tr>
<td>Hypertriglyceridemia (yes Vs no)</td>
<td>0.89</td>
<td>0.63 - 1.26</td>
</tr>
<tr>
<td>Low level of HDL (yes Vs no)</td>
<td>1.20</td>
<td>0.89 - 1.62</td>
</tr>
<tr>
<td>Metabolic syndrome (yes Vs no)</td>
<td>1.10</td>
<td>0.71 - 1.68</td>
</tr>
<tr>
<td>Smoke use (yes Vs no)</td>
<td>1.40</td>
<td>1.02 - 1.93*</td>
</tr>
<tr>
<td>Alcohol use (yes Vs no)</td>
<td>1.43</td>
<td>0.97 - 2.11</td>
</tr>
</tbody>
</table>

*p < 0.05, ** p < 0.001, OR = odds ratio, CI = confidence intervals

To date, there is little evidence about the information of colorectal hyperplastic polyps in Taiwan. That is why we performed this study. In autopsy studies, the prevalence of colorectal hyperplastic polyps is 4.9 - 13%.[28,29] The prevalence is 5.5% in our study. The prevalence might be underestimated because there were 149 subjects with polyps found on examination where no biopsy was taken. As commented by the gastroenterologists at this medical center, these polyps were usually too small and so it was not necessary to perform a biopsy. However, more frequent colonoscopic surveillance was suggested. We did not enroll these subjects, so as to avoid the effect of confounding factors on the analysis. However, as suggested by the literature[30,31], all polyps should be removed or biopsied to determine their type during sigmoidoscopy or colonoscopy because the high prevalence of adenomas among small polyps is noted.

A retrospective case-control study in Japan and a necropsy study in New Zealand[10,32], showed that age is a related factor for hyperplastic polyps. In Vatn's study[33], the prevalence of hyperplastic polyps increases with age in men, but not in women. In our study, the prevalence increases with age in both genders. Multivariate logistic regression model also showed that increasing age is one of the related factors for hyperplastic polyps. We think that after a long duration of exposure to numerous environmental factors and potential genetic factors, the likelihood of hyperplastic polyp formation increases. That is, the older the people, the higher the risk for hyperplastic polyps.

After controlling the other co-variates, our study showed that BMI ≥ 27 is also related to hyperplastic polyps. To the best of our knowledge, only two studies have revealed that body mass index is positively associated with hyperplastic polyps[14,32]. Prior studies have disclosed that increased BMI is associated with the risk for colorectal adenomas and cancers[33-35]. The above results strongly support the hypothesis that generalized obesity is a risk factor for colorectal hyperplastic polyps, adenomas, and cancers. As suggested by Yamaji[34], body weight reduction can be used to decrease this risk.

In our study, smoking is one of the related factors for hyperplastic polyps, and this finding is compatible with previous studies[6,13-18]. Prior studies have disclosed that cigarette smoking is associated with increased risk for colorectal adenomas and cancers[15,36,37]. These findings strongly support the concept that the adverse effect of smoking may play an important role in the formation of colorectal hyperplastic polyps, adenomas and cancers. As suggested by Shrubsole[35], quitting smoking may substantially reduce this risk.

In Kim study[30], metabolic syndrome was an important risk factor for colorectal adenoma. In our study, although metabolic syndrome was related to hyperplastic polyps in the chi-square test, we could not find this result in the multivariate logistic regression model. Similarly, several other factors were not informative. We also could not find an association between abdominal obesity, diabetes mellitus, hypertriglyceridemia or alcohol consumption and hyperplastic polyps. In contrast, these factors were found to be related to colorectal adenomas and cancers in prior studies[30,42]. Thus, we think that colorectal hyperplastic polyps, adenomas and cancers do not completely share common risk factors.

Growing evidence of neoplastic evolution of hyperplastic polyps is elicited by morphological and molecular studies. Recent new morphological data have recognized the model of hyperplastic polyp-
serrated adenoma-adenocarcinoma pathway[43,44], that is apparently different from the classic adenoma-to-carcinoma sequence[3,4,3].

Recent strong molecular evidence has also shown that extensive DNA methylation, deficient DNA mismatch repair, and microsatellite instability may characterize hyperplastic polyps in the pathogenesis of neoplastic evolution[45,46]. Under the molecular level, the progression through sequential steps of the pathway is driven. At first, neoplastic changes may begin in a hyperplastic polyp, then progressing to atypical hyperplastic polyp (known as sessile serrated adenoma), further to dysplastic serrated adenoma, and ultimately to serrated carcinom[46,47]. In the interest of public health, early detection of morphological and molecular changes of hyperplastic polyps which are more likely to have the potential of neoplastic evolution is needed. Thus, colorectal cancer can be prevented.

LIMITATION

There are several limitations in this study. The first, using flexible sigmoidoscopy rather than a full colonoscopy precluded identification of hyperplastic, adenomatous polyps, and serrated adenomas in the right colon, which are also more likely to be detected in the right colon. The prevalence of hyperplastic polyps may be underestimated. The second, although the literature now recognizes that some previously termed hyperplastic polyps do carry malignant potential, we cannot recheck the pathologic slides to determine whether any of the hyperplastic polyps removed during the examination had histologic features of serrated adenomas. The third, because this study was retrospective (review of medical records), history of first-degree relatives with colorectal neoplasia and polyps, dietary factors, use of aspirin and other non-steroidal anti-inflammatory drugs, could not be included in details due to incomplete documentation. The fourth, there is a bias of sampling population. Since the study participants were all from one hospital in Taiwan, there is limited generalizability of the results. The fifth, because of inherent limitations to a cross-sectional design, a causal-effect relationship between an exposure of interest and an outcome cannot be established. The sixth, because no pathology reports were available in 149 subjects with polyps, they could not be categorized and had to be excluded. Finally, only 243 subjects with hyperplastic polyps (including 214 subjects with hyperplastic polyps only, and 29 subjects with mixed adenomas and hyperplastic polyps) and 3759 normal subjects were included for further analysis.

CONCLUSION

Based on these preliminary data, we find that increasing age, male gender, generalized obesity and smoking are risk factors for rectosigmoid hyperplastic polyps in Taiwan. Whereas the clinical significance of hyperplastic polyps remains inconclusive and a consensus for regular colonoscopic surveillance is not available, lifestyle modification including smoking cessation and body weight reduction can still be suggested by clinicians to reduce the risk of hyperplastic polyps. Further detailed studies are needed to confirm these conclusions.

Conflict of interest: The authors report no conflicts of interest.

REFERENCES

Case Report

Colo-Colic Intussusception in Amoebic Colitis: A Case Report

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ABSTRACT

Intussusception is a common cause of acute abdomen in the pediatric population. However, the condition is quite rare among adults. Intussusception among adults differs from the pediatric counterpart in having an underlying pathology, commonly neoplastic on most occasions. Pre-operative diagnosis is rarely established. Most cases require surgical treatment. We present a case of colo-colic intussusception in an adult involving the transverse colon, which was precipitated by amebic colitis. The diagnosis was made by abdominal CT scan and the condition was effectively treated non-surgically by colonoscopic reduction.

KEY WORDS: adult intussusception, colonoscopic reduction

INTRODUCTION

Intussusception is defined as telescoping of one segment of gastro-intestinal tract into the adjacent one[1]. While intussusception is a common cause of intestinal obstruction in pediatric population, it is a rare phenomenon among adults. Such intussusception involving colon is rarer. Colonic amebiasis is quite common in this part of the world. However such amebiasis serving as a lead point for colo-colic intussusception is rarest of the events. While most cases of adult intussusception require surgical intervention, colonoscopic reduction may prove to be of benefit in a select few. Colonoscopic reduction may buy precious time for planning definitive surgical treatment if needed, or may totally avoid the need for surgical intervention in select few[1].

CASE REPORT

A 30-year-old male agriculturist presented to us with history of colicky abdominal pain and bilious vomiting of one day duration. The pain was predominantly experienced in the central portion of the abdomen and was associated with mild abdominal distension. There was no history of passage of blood in the stools. Fifteen days ago, there was an episode of diarrhea which lasted for four days and resolved spontaneously. On examination, patient was hemodynamically stable. Abdomen was distended. There was no palpable mass, organomegaly or free fluid in the abdomen. There were no features of peritonitis. His biochemical and hematological investigations were normal. Abdominal X-ray studies revealed dilated small bowel loops with multiple air-fluid levels. Computed tomography (CT) scan of the abdomen showed ‘bowel in bowel’ appearance involving the region of hepatic flexure and transverse colon up to the splenic flexure with transposition of transverse colon suggestive of colo-colic intussusception. There were multiple enhancing nodular lesions in the pericolic area representing lymph nodes. There were no signs of bowel gangrene. Subsequent colonoscopic study revealed intraluminal bowel mass in the region of transverse colon which got reduced with air insufflation. Multiple ulcers were seen in the cecum, ascending colon and transverse colon. Biopsy taken from the ulcers suggested amebic colitis. Amebiasis was further confirmed by positive amebic serological tests. Patient was treated for amebic colitis and has been followed up regularly for about a year now. The symptoms have not recurred as yet. A follow up colonoscopy has confirmed complete healing of the ulcers in colon.

DISCUSSION

Intussusception is defined as telescoping of a segment of the gastrointestinal tract into an adjacent one. About 5% of all intussusceptions occur among adults and about 1% of bowel obstructions in adults result from intussusception[1]. Approximately 80 to 90% of intussusceptions in adults are secondary to an underlying pathology. Neoplasms account for
65% of these cases. Non-neoplastic causes account for 15 to 25% of cases and idiopathic or primary intussusception accounts for 10%.[2] Intussusception can occur anywhere in the gastro-intestinal tract. Most adult intussusceptions involve small intestine. Only about 8-19% of adult intussusceptions involve colon[3]. Involvement of transverse colon as in our patient is the rarest of events. In a review of 48 cases, only two cases involved transverse colon[3]. The exact mechanism that precipitates intussusception is not known, but it is generally believed that any lesion in the bowel wall or irritant within the bowel lumen may alter the normal peristaltic pattern, initiate intestinal invagination thereby precipitating intussusception[4]. The most common causes of intussusception in adults are neoplasms. Other common causes are post-operative adhesions and Meckel’s diverticulum. In our patient, colonic amebiasis precipitated colo-colic intussusception, which we believe is the rarest etiology. The clinical presentation of adult intussusception varies considerably from their pediatric counterpart. The acute form may present with abdominal pain, nausea, and vomiting while intermittent abdominal pain or vomiting are common symptoms in subacute or chronic intussusception. CT scan is the investigation of choice in suspected cases of intussusception[3]. The appearance of bowel within bowel configuration with or without fat is pathognomonic of intussusception.

The role of colonoscopy in adult intussusception is controversial. It has been suggested that non-operative reduction should not be attempted in colonic intussusception and surgical intervention is necessary in almost all adult patients with intussusception[5]. However, more recent reports[1] suggest feasibility of endoscopic reduction in selected cases. We believe that endoscopic reduction by air insufflation may be tried in select group of cases of adult intussusception where there is no evidence of compromised vascularity of involved bowel. While surgical intervention may be required in most cases of adult intussusception, in rare cases where the benign etiology of intussusception is proved, non-operative reduction using contrast enema or colonoscopy may be tried.

CONCLUSIONS
We believe that this case report is of a rarest kind and delivers the following messages:
• Intussusception can be a cause of intestinal obstruction among adults, although very rare
• An underlying cause should be always sought for in cases of adult intussusception
• Colonoscopy can be a useful tool of both diagnostic and therapeutic value particularly when there is no evidence to suggest compromised vascularity of the bowel.

REFERENCES

Case Report

Unusual Presentation of Organic Foreign Body in Upper Aerodigestive Tract: Report of Two Cases

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ABSTRACT

Foreign body ingestion is one of the leading causes of pediatric accidents. Delayed presentations of organic foreign bodies are usually surprising due to their ability to stick, swell and obstruct the lumen. Obstruction of upper aerodigestive tract due to seeds after one week of aspiration resembling esophageal stricture or lobar pneumonia is a very rare presentation. We report on two such cases of organic foreign body that presented late with obstructive symptoms. Both the cases were successfully dealt with simple endoscopic removal without adverse sequelae. We recommend endoscopic management even for an organized organic foreign body in the aerodigestive tract.

KEY WORDS: bronchoscopy, esophagoscopy, seed

INTRODUCTION

Foreign body ingestion is quite common in pediatric surgery practice. Eighty percent of aspirated bodies comprise of household objects like coins, pins, needles, hair, denture, seeds, battery cells and fish bone. Problems usually arise in proportion to the duration of impaction of the foreign body. Delayed presentation is always a challenge for the endoscopist, because organic foreign bodies get organized and swell with time. We report on two cases of foreign body aspiration; one in the esophagus and the other in the bronchus. They presented late with poor health and symptoms of obstruction. Both cases were managed endoscopically. The objective of our study is to re-emphasize the use of endoscope even in cases of organized organic foreign body.

CASE HISTORY

Case 1: A six-year-old female patient presented in the Cardio-thoracic-vascular surgery (CTVS) outpatient department (OPD) with complaints of dysphagia since last 12 days especially with solids. There was no history of corrosive ingestion, hematemesis or any breathing difficulty. She was accepting liquids normally. Barium swallow showed a stricture in the midesophagus with food particles in the proximal dilated esophagus (Fig. 1a & b). Distal esophageal segment was normal. Esophagoscopy showed an inspissated ingested blackberry seed adherent to the mucosa with a circumferential mucosal ulcer at the site of obstruction. The seed was removed, the whole esophagus was inspected and found to be normal. The child was allowed oral intake from the evening. She was discharged on sucralfate for one week. Patient was found asymptomatic after one month during follow-up.

Case 2: An 11-year-old mentally retarded female patient was referred to us with history of inhalation of peanut 10 days ago. The patient was having high grade fever, cough, and dyspnea at the time of admission. Her pulse rate was 110/min, blood pressure 108/68 mmHg and respiratory rate was 36/min and laboured. On auscultation; there was no air entry on the right side of the chest. Previous chest X-ray (Fig. 2a) showed right-sided collapsed lung with mediastinal shift. A computed tomography (CT) scan (Fig. 2b) revealed non-radio-opaque foreign body in the right main bronchus with collapsed right lobe.

She underwent rigid bronchoscopy under general anesthesia revealing degraded peanut with mucoid debris blocking the right main bronchus. The entire debris was removed piecemeal. She was kept on intravenous antibiotic, bronchodilators and high flow oxygen in the Intensive care unit (ICU). After 48 hours her vitals settled down, right sided breath sound were normal with few crepts and repeat chest X-ray showed hyperinflated lung (Fig. 2c). She was discharged on the 6th day after admission.

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DISCUSSION

Foreign body aspiration is known since human intellect let him explore himself. No age group is spared from this accident, although it is more common among children between one to three years of age and mentally retarded individuals. Inability to adequately perceive danger, control their impulses and understand the consequences of their actions explain their susceptibility. Most common mode is accidental.

Almost every household objects has been described in world literature. The most common organic items aspirated are small or smooth food objects, such as nuts, raisins, sunflower seeds, improperly chewed pieces of meat, grapes, and sausages. An estimated 80% of aspirated foreign bodies are radiolucent.

Presentation of foreign body aspiration is varied and ranges from asymptomatic cases to asphyxia and death, depending upon two factors. Factor related to offending object includes its nature; whether degradable or not, size, shape, migration, and its reaction in the host body. Among host factors affecting the presentation are patient’s intellect, percentage of blockade, presence of narrowed segment, and existing co-morbidity of the individual. Organic foreign body has natural hygroscopic property and causes mucosal edema and ulceration due to local tissue reaction leading to luminal obstruction. Overall, 80% of ingested foreign bodies will enter the gastrointestinal tract, whereas 20% will find their way into the upper respiratory tract.

Esophageal foreign bodies: Esophageal foreign body usually presents with dysphagia, choking and drooling. Most ingested foreign bodies that have gone beyond the esophagus will pass uneventfully, through the digestive tract without causing any major disturbances. Sharp and large foreign bodies usually presents with complications such as perforation or obstruction in 15 to 35% patients. Possible complications due to ingested foreign bodies include ulceration, hemorrhage, stricture formation, tracheoesophageal fistula, erosion through the wall of the esophagus with mediastinal abscess or penetration into major blood vessels. Diagnosis is mainly based on history and clinical presentation. Simple X-ray is enough in locating radio opaque objects. Barium esophagogram may be required for radiologically non-visualizing esophageal foreign bodies.

Many techniques to dislodge the esophageal foreign body have been described including flexible esophagoscopy, esophageal bougienage, and balloon extraction with fluoroscopy. Still, rigid esophagoscopy has been the procedure of choice for removal of a foreign body. Advantages include the ability to perform the procedure, with a high degree of success, in a controlled environment.

Bronchial foreign bodies: Inhalation of a foreign body is followed by choking, gagging and subsequently there may be a symptom free interval. Later cough, signs of pulmonary collapse and suppuration may
The commonest radiological finding in foreign body bronchus is obstructive emphysema. However, the chest radiograph may be normal in 20% cases, less than 5% have atelectasis and pneumonia. However, for more detailed condition of surrounding structures, a CT scan is more helpful.

Rigid bronchoscopy under general anesthesia is the gold standard for investigation as well as for therapy for metallic as well as organic foreign bodies in the airway.

**CONCLUSION**

Organic foreign body aspiration in pediatric patients is not very common. They usually present early but delayed presentation is more devastating and difficult to manage. However, endoscopic removal using a rigid instrument is still the management of choice.
Case Report

Small Cell Carcinoma Metastatic to the Appendix, with Acute Suppurative Appendicitis

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ABSTRACT

Malignancy of the appendix is uncommon. A small subset of these lesions is actually metastatic cancers. Metastasis to the appendix is very rare and infrequently symptomatic. Metastatic lesions can cause obstruction, appendicitis and perforation. We report a case of small cell carcinoma of the lung with metastasis to the appendix, accompanied by perforation induced by acute suppurative appendicitis.

KEY WORDS: appendix, acute suppurative appendicitis, metastasis

INTRODUCTION

Lung cancer, the most common cause of cancer-related death in men and women, is responsible for 1.3 million deaths worldwide annually[1]. The main types of lung cancer are small cell lung carcinoma and non-small cell lung carcinoma. Small cell lung cancer (SCLC) is an aggressive malignancy characterized by rapid growth and early metastasis, approximately comprising 14 percent of all new lung cancer[2]. The main causes of cancer include carcinogens (such as those in tobacco smoke), ionizing radiation, and viral infection. This exposure causes cumulative changes to the DNA in the tissue lining the bronchi of the lungs (the bronchial epithelium). As more tissue becomes damaged, eventually a cancer develops[3]. Metastasis mostly occurs through extrathoracic lymph nodes[4]. It commonly metastasizes to the adrenal glands, liver, brain, and bone[3]. A tumor metastasizing to the gastrointestinal tract infrequently misleads the clinical manifestations. One such site is the appendix, where metastasis is very rare. Wolf[3] found only one patient with hematogenous metastasis to the appendix in a review of 22,000 cases with histologic examination of the appendix over a period of eight years. A thorough review of literature revealed three documented cases of histologically diagnosed small cell carcinoma metastatic to the appendix[6-8].

To the best of our knowledge, this is the only documented case of surgically treated acute suppurative appendicitis complicated by perforation, which was histologically confirmed to be associated with small cell carcinoma metastatic to the appendix.

CASE REPORT

A 42-year-old woman, smoker, was admitted to our hospital with a history of cough for four months and dyspnea for one week. Thoracic computed tomography (CT) showed a 7 x 8 cm mass in the left lower lobe of the lung, and revealed mediastinal hilar lymphadenopathy with blockage of the lower left bronchus (Fig. 1). On admission, physical examination revealed an elevated temperature (> 38 ºC), heart rate (129 / min), and respiratory rate (22 / min). Leukocyte count was 9.76 x 10^9/l with 73.9% polymorphonuclear leukocytes. Laboratory investigations on admission revealed elevation of CA-125 at 99.68 U/ml (0 - 35), and marked elevation of neuron specific enolase at 41.62 ng/ml (0 - 15). Alpha fetoprotein and carcinoembryonic antigen levels were within normal limits.

There was no abdominal tenderness. The patient was treated with antibiotics and expectorant. Three days after admission, the patient felt pain in the hypogastrium. A mass was palpated at McBurney’s point of the right lower quadrant, with obvious tenderness. Abdominal ultrasonography revealed a sausage-shaped hypoechoic mass of size 4 cm in the ileocecal region. Cecal wall were also thickened. In
the core of the hypoechoic mass, an inhomogeneous hyperechoic solid mass was observed (Fig. 2A). Purulent ascites and inflammation was seen around the mass (Fig. 2B).

Sonography was performed using C5-2 convex and L12-5 linear array probes (Philips Medical Systems, HD11). An emergency axial CT showed a low-density mass; however, it was difficult to distinguish the boundary of the mass from the upper intestinal wall (Fig. 3). Fatty tissues of greater density were seen surrounding the mass. The peritoneum was thicker on the ipsilateral than on the contralateral side. Appendectomy was performed, with a gross impression of acute suppurative appendicitis. However, the histology of the appendiceal specimen was more compatible with SCLC. Immunohistochemical examination revealed positivity for CGA, CD56, and TTF-1. Histopathologic diagnosis was SCLC metastatic to the appendix (Fig. 4A, B).

**DISCUSSION**

Appendiceal carcinoma is very rare, accounting for 1% of all colorectal malignancies and 1% of all appendectomy specimens. The most common type of appendiceal neoplasm is a carcinoid tumor, with mucinous cystadenocarcinomas and adenocarcinomas next in frequency. Tumors metastatic to the gastrointestinal tract are rare, with approximately 55 cases described in the international literature. There is no age difference between genders for malignant neoplasms of the appendix (mean age in women: 58, range 14 – 83 years Vs mean age in men: 55, range 16 – 78 years). Our patient was within this range. A variety of conditions affect the detection of appendiceal carcinoma. Incidental finding of carcinoma often mimicking appendicitis was also reported in the literature.

Undoubtedly, ultrasound plays an important role in the diagnosis of right lower quadrant pain and suspected acute appendicitis. In our case, sonography revealed an acutely distended, incompressible appendix with a thickened wall and echogenic inflammatory changes in the surrounding adipose tissue. Inside the appendix, there was an inhomogeneous, relatively hypoechoic mass, similar to findings reported by Wolf and Puylaert.

In addition, in our case, purulent ascitic fluid was detected by ultrasonographic examination. It
may be difficult to distinguish tumors metastatic to the appendix from primary tumors of the appendix because of the rarity of appendiceal masses. Rare case reports have described solid masses of the appendix on sonographic examination. An appendiceal adenocarcinoma was described in a study by Skaane\cite{15} as a round, hypoechoic mass with an echogenic core. Powell described a leiomyoma of the appendix as a hypoechoic mass\cite{16}. The sonographic appearance of appendiceal mucocele is variable because of the content. Parietal calcification of an appendiceal mucocele as a valuable finding was described in case reports by Karakaya et al\cite{17}. Occasionally, appendiceal mucocele displays the peculiar internal echogenicity of onion skin morphology\cite{18}. Cystoadenoma and carcinoid may be seen as a large hypoechoic cystic mass without inflammatory signs in the right lower quadrant\cite{19}.

On CT scan, the initial appearance of appendiceal metastasis is an isolated solitary nodular mass abutting the appendix\cite{20}. In our case, the metastatic tumor had penetrated the lumen completely, eventually leading to perforation and its complications. CT scan showed a well-defined soft tissue mass in the appendix.

Tumors metastatic to the appendix involve primarily the serosa, muscular wall, and mucosa. The mucosal epithelium is usually unremarkable, provided it has not been completely replaced by tumor and does not show any evidence of dysplasia or in situ carcinoma. As the tumor grows and encroaches on the appendiceal wall, the lumen becomes obstructed, and eventually signs and symptoms of acute appendicitis develop\cite{21}. In our patient, the lumen was completely obstructed. This process can progress to inflammation and eventually to perforation of the appendix.

CONCLUSION

We report a case of SCLC metastatic to the appendix, accompanied by acute appendicitis. The tumor obstructed the orifice of the appendix, and this appears to have caused the perforation. Our patient had a history of pulmonary masses, as well as increased levels of serum neuron specific enolase. Imaging examination showed a solid mass accompanied by inflammatory changes, as is documented in rare case reports. Prior to appendectomy for acute appendicitis, it would be useful to know if the appendiceal pathology is related to a malignancy, either primary or metastatic. The rarity of appendiceal carcinoma, primary or metastatic, has made its diagnosis preoperatively difficult for clinicians. However, correlating the patient’s history, other abnormalities or findings can help both the clinician and radiologist in making a preoperative diagnosis so that proper surgical management can be carried out.

REFERENCES


Case Report

Cecal Carcinoma Presenting with Adult Intussusception

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ABSTRACT

Adult intussusception is an uncommon cause of bowel obstruction. It usually presents with longstanding, intermittent and non-specific symptoms with subsequent delay in diagnosis and management. Diagnosis is often made at emergency laparotomy and an underlying lesion is found in most cases. With more frequent use of computed tomography in the evaluation of patients with abdominal pain, the condition can now be diagnosed more reliably at an earlier stage and this is of importance as 50% of adult intussusceptions are due to malignancy. We report a case of a 55-year-old lady who presented to the emergency department with ileocolic intussusception which was diagnosed on CT scan and necessitated an emergency right hemicolectomy. The leading point was a small cecal cancer reflecting the importance of early intervention and resection in cases of adult intussusception. This case also highlights the fact that early cecal cancer may first present and declare itself as intussusception.

KEY WORDS: adult intussusception, cecal cancer, laparotomy

INTRODUCTION

Intussusception is the telescoping of one segment of the gastrointestinal tract into an adjacent one. This condition is uncommon in adults, with only 2-3 cases occurring in a population of 1,000,000 per annum and accounts for less than 0.1% of all adult hospital admissions[1]. It goes unsuspected clinically, as patients present with long history of vague, non-specific abdominal pain with unremarkable abdominal signs. However, computerized tomography (CT) scan findings are characteristic and awareness of these findings allows the radiologist to make the correct diagnosis[2]. As intussusception is frequently associated with a lead point which might be malignant lesion in more than 50% of cases in adults, it should always be resected[3]. Cecal carcinoma commonly presents with iron deficiency anemia, diarrhea or right iliac fossa mass, but very rarely with intussusception. We present a case of adult ileo-colic intussusception secondary to a small cecal cancer as a lead point which presented as an emergency, diagnosed early on CT scan of the abdomen and dealt with promptly by emergency right hemicolecotomy.

CASE REPORT

A 55-year-old hypertensive and dyslipidemic lady presented to emergency room with epigastric pain of 5-day duration radiating to the back and aggravated by heavy meals. It was also associated with abdominal distension and frequent vomiting. She had lumbar and cervical spine surgeries 12 and 14 years ago, respectively. On examination, her abdomen was pendulous with epigastric fullness and generalized deep mild abdominal tenderness. All routine laboratory tests were within normal values and abdominal X-ray was unremarkable. CT abdomen revealed ileo-colic intussusception (Fig. 1 & 2). She underwent diagnostic laparoscopy which revealed free fluid in the peritoneal cavity which was aspirated for culture and sensitivity and cytology. The intussusception had already reduced spontaneously and it was difficult to determine the underlying pathology laparoscopically. Hence, it was converted to an exploratory laparotomy which revealed a small lesion (1 x 2 cm) at the ileocecal valve region which was the presumed lead point. A right hemicolecotomy was performed. The histopathology revealed a well differentiated adenocarcinoma of the cecum with four out of 17 lymph nodes involved (T2 N1 M0). Postoperative recovery was uneventful and she was discharged home five days later. She received adjuvant chemotherapy and remained well at six-month follow up.

DISCUSSION

Intussusception in adults differs from that in children in various aspects. Unlike the childhood
variety, idiopathic etiology is rare, and a cause is often identified in 70 - 90% of the adult intussusceptions[1]. Moreover, the classical symptoms of vomiting, abdominal pain, palpable sausage-shaped mass and passage of red current jelly stools seen in all children are rarely observed in adults. They may be seen only in 15 - 20% of cases[1,4]. In adult patients pain is the commonest symptom, being present in 70 - 90% of patients, with vomiting and bleeding per rectum as the next most common symptoms[3]. The pain is often periodic and intermittent in nature, which makes the diagnosis elusive and accounts for the delay in making the diagnosis, with only half the cases being diagnosed before operation[5,6]. Abdominal mass is noted in 24 - 42% cases[6,7].

The lead points for the intussusceptions are attributable to benign, malignant, or idiopathic causes[8-11] and surgical resection is almost always required[1]. Moreover, a definable structural lesion is found mainly in the colon[12,13].

An etiological pathology is present in 70 - 90% of adults with intussusception, but present in less than 10% of pediatric cases. Benign lesions account for almost 25% of cases of intussusceptions in adults and the commonest is a lipoma in the colon[10] while in more than two thirds of cases, the etiological pathology is a malignant tumor resulting in intussusceptions[3,14].

Intussusception has also been noted in patients with AIDS-related gut disease, tropical sprue, celiac disease, abdominal trauma, and during the postoperative period[15].

For the diagnosis, CT scan has proved to be the most useful diagnostic radiological method and with its liberal use to investigate abdominal pain, adult intussusception is now increasingly diagnosed early. The appearance is characteristic on CT scan with presence of a target or sausage-shaped mass lesion which has been described as a “target mass” associated with obstruction[1,6,16].

Flexible endoscopy of the lower GI tract can be considered in evaluating cases of intussusception presenting with subacute or chronic large bowel obstruction[17]. Its main benefit is confirmation and localization of the underlying organic lesion serving as a lead point. However, any endoscopic intervention such as snare polypectomy is not advisable due to the high risk of perforation occurring in a background of chronic tissue ischemia and possible necrosis of the intussuscepted bowel wall[18,19].

Nevertheless, in patients with a risk of a short bowel syndrome due to multiple small intestinal polyps causing intussusception, such as Peutz-Jeghers syndrome, a combined approach with limited intestinal resections (open or laparoscopic) and multiple endoscopic snare polypectomies is beneficial[20,21]. This is also useful in patients complicated with postoperative bowel obstruction due to intussusceptions since endoscopic reduction may be carried out provided that the bowel appears non-ischemic and viable during laparoscopy.

However, the standard teaching is that adult intussusception warrants laparotomy rather than attempts at hydrostatic reduction in view of the high incidence of underlying abnormality[6,17]. Controversy remains as to whether reduction of the intussuscepting lesion should be attempted at operation or not. Early reports advocated reducing the intussusception before
resection as this may preserve considerable lengths of bowel and thereby prevent development of short bowel syndrome. However, the disadvantage of this is the theoretical risk of malignant cell dissemination during the process of resection. Begos et al suggested resection without attempting reduction when the bowel is inflamed, ischemic, or friable and in cases of obvious colo-colic intussusception due to the high likelihood of malignancy. In all other cases, reduction should always be attempted initially. However, Azar and Berger suggested that routine surgical resection without attempted reduction as the preferred treatment in adults, as almost 50% of both colonic and enteric intussusceptions are associated with malignancy. Simple reduction is however acceptable in post-traumatic and idiopathic intussusceptions where no pathological cause is usually present in the bowel. The dilemma of ‘to reduce or not to reduce’ was not encountered in our case as the intussusception had reduced by the time surgical intervention was undertaken.

The role of laparoscopy in management of intussusceptions due to benign and malignant lesions has been increasingly advocated. In our case laparoscopic approach was started first. However, the intussusception has already reduced and it was difficult to ascertain laparoscopically the exact site or nature of the lead point (the pathology) due to lack of tactile sensation. A blind right hemicolectomy was felt unjustifiable and hence, the procedure was converted to open and this helped to locate and identify the tumor and perform the correct procedure.

This unusual initial presentation of intussusception by early cecal carcinoma has been reported. Review of the world literature revealed three similar cases; one in a 29-year-old female presenting with cecocolic intussusceptions, another in a 79-year-old female with ileo-cecal intussusceptions and a third case of colo-colic intussusception in a 62-year old male with a large ileo-cecal cancer. To the best of our knowledge, this could be the 4th case of cecal cancer presenting with adult intussusception in the world literature. It is therefore, recommended that cecal cancer is suspected in any case of adult ileo-colic or colo-colic intussusception.

CONCLUSION

Adult intussusception is a rare condition with non-specific clinical presentation that warrants a low index of clinical suspicion. It can be confirmed by CT scan of the abdomen which is characteristically diagnostic and early laparoscopy or laparotomy is advocated as the standard treatment so as not to miss the underlying triggering malignant lead point which can be curable if discovered early and excised, but potentially lethal if missed and left untreated. Moreover, in any case of adult ileocolic intussusception, an underlying cecal cancer should be thought of.

ACKNOWLEDGMENT

Conflict of Interests: Nothing to declare

REFERENCES


Case Report

Acute Bilateral Cataract in a Non-Complicated Type 1 Diabetic Youngster: A Case Report

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ABSTRACT

It is rare for young type 1 diabetics to develop cataract within the first five years of their disease. The overall prevalence of cataract in young diabetics is < 1%. We describe a case of a 13-year-old type 1 diabetic female, known to be diabetic for last three years, who presented with severe diabetic ketoacidosis and decreased vision over the past three weeks. Initial examination revealed absent red reflex and bilateral cataracts, confirmed by an ophthalmological assessment to be bilateral mature cortical cataracts. The vision was totally restored after successful bilateral cataract extractions and intra-ocular lens implantation.

Development of cataract in early stage of diabetes is very exceptional. This raises the possibility of the presence of unusual genetic susceptibility and perhaps, some environmental elements. We emphasize the need for vigilant examination for ocular complication in type 1 diabetic patients, even in the first few years of their disease.

KEY WORDS: acute cataract, diabetic ketoacidosis (DKA)

INTRODUCTION

Diabetic patients have a high incidence of developing cataract, especially those with longstanding type 2 diabetes. It is rare for young type 1 diabetics to develop cataract within the first five years of their disease. The overall prevalence of cataract in young diabetics is < 1%[1] with only a few cases reported in literature. We report the case of a 13-year-old type 1 non-complicated diabetic girl with acute bilateral mature cataract.

CASE PRESENTATION

A 13-year-old Kuwaiti girl was a known case of type 1 diabetes for the last three years on twice daily insulin injections. She was not compliant to diet and insulin treatment and had been admitted to the hospital in the past with recurrent diabetic ketoacidosis. The current admission was for severe diabetic ketoacidosis and decreased vision that initially was thought to be due to her severe glycemcic decompensation and ketoacidosis. Blood glucose was 31.2 mmol/l, HCO\textsubscript{3} was 9.3 mmol and heavy ketonuria was detected. Her HbA1c level was 14.3% on admission and 16.3 % seven months earlier, indicating prolonged poor control. IV fluid and Insulin therapy was started and the patient was rendered euvglycemic.

The patient was underweight, with a body weight of 36 kilogram and a body mass index of 19.2 kg/m\textsuperscript{2}. On further questioning and assessment the patient had bilateral, progressive loss of vision over the past three weeks to the extent that she stopped going to school as she could not see her class blackboard. Surprisingly enough, her initial examination revealed absent red reflex and bilateral cataracts.

Physical examination was otherwise unremarkable. She had no evidence of other diabetic complications such as proteinuria or neuropathy. Fundus could not be visualized due to presence of bilateral cataracts.

Ophthalmological referral and assessment revealed reduced visual acuity to finger counting at three meters and bilateral sub-capsular snowflake cataracts. The cataracts expectedly did not resolve, nor did the vision improve, despite a reduction in glycemic levels with blood glucose profiles in the range of 6.2 - 11.3 mmol/l. The patient had base line ophthalmic examination and fundus photography as a part of her routine initial screening and documentation of diabetic complications at the onset of her diabetes. This had revealed normal vision at ophthalmic evaluation. Also, the patient had normal vision and eye examination during routine follow up.

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visits. The rapid deterioration of her vision had only started within the last two weeks at about the same time of her recent severe glycemic decompensation and Diabetic ketoacidosis (DKA) presentation.

Other causes of cataract had been ruled out by extensive biochemical investigations (e.g., serum calcium and parathyroid levels, serum and urinary cortisol). She had no history of antecedent trauma, life-threatening diarrhea, or renal failure, and no exposure to chemicals, radiation or drugs known to be associated with cataracts, such as steroids, barbiturates, phenothiazines and diuretics. There were no features to suggest chronic hypocalcemia, no dysmorphic features of cataract associated genetic syndromes and no family history of cataracts.

One month after presentation, she had successful bilateral cataract extractions and intra-ocular lens implantation at different sessions with subsequent complete restoration of vision. At the time of surgery the patient had bilateral anterior and posterior sub-capsular snowflake cataract which was operated upon as a two-step surgery two days apart under local anesthesia. Fundus examination was again surprisingly normal with no evidence of retinopathy. She was discharged on multiple daily injections regimen (4 insulin analogue injections). Further follow-up was done in our diabetes unit under a multi-disciplinary team approach for better glycemic control with repeated dietitian visits and education sessions from diabetes specialist nurse leading to a gradual improvement in her HBA1c.

DISCUSSION

The lens is a unique physical structure that cannot be repaired, but it accumulates damage if it occurs over a period of times. Cataracts account for half of the causes of blindness in underdeveloped countries[3].

It comes in a variety of types such as senile cataract and non-senile cataract. The former occurs in those above the age of 60 years, although the process begins a decade earlier[3]. The non-senile type is usually congenital or secondary to trauma, infection, ultraviolet radiation, exposure to chemicals or systemic disease like diabetes[3]. Diabetic or metabolic cataracts are characterized by diffuse posterior and / or anterior, subcapsular or cortical ‘snowflake’ opacities[2]. This is followed by appearance of more diffuse cloudiness and opacification. Cataract formation is linked to calcium and sodium leakage through the damaged membrane and loss of antioxidant defense of the lens, which is caused by poor diet and aging[4].

In diabetes, cataract is a well-known complication in longstanding disease. It is hastened by hyperglycemia. Perhaps there are other contributing factors like genetics, nutrition and use of other drugs like steroids[5].

Our case had developed cataract three years after the diagnosis of her type 1 diabetes. Development of cataract in early stage of diabetes is very exceptional. This raises the possibility of the presence of unusual genetic susceptibility in this patient and perhaps, some environmental elements. The strong relationship between cataract, retinopathy and neuropathy in diabetic patient with long duration of the disease has been described in literature[5]. However, our patient did not have any form of diabetic complication, which makes her early cataract unusual.

Congenital cataract presents at birth or shortly after. Even the category of infantile cataract is unlikely as it presents before the age of six months. Depending on the age of cataract presentation and in view of her completely normal vision and ophthalmic examination just prior to the last presentation at age of 13 years, the diagnosis of congenital cataract is unlikely. Usually, a patient with diabetic cataract has the following criteria and these were present in our diabetic patient, namely,

a) History of prolonged poor diabetic control with high HbA1C (our patient had HbA1C in the range of 14 – 16%), b) recent severe glycemic decompensation (DKA presentation) that parallels her acute diminution of vision (this shows the causal link between acute cataract and severe hyperglycemia) and c) usually bilateral (as was seen in our case).

The explanation for the dramatic changes in the lens and acute cataractogenesis with lack of it at other places such as the retina is still controversial. The lens is a unique transparent osmotic structure that can be specifically sensitive to hectic glycemic control (hyperglycemia and hypoglycemia). It can accumulate damage when it occurs over a period of time. The proposed mechanisms are a) genetic susceptibility (as some rare cases of bilateral cataract in identical twins with type 1 diabetes mellitus were described), b) sorbitol damage via polyol pathway, c) osmotic damage, d) oxidative stress damage and e) non-enzymatic glycation damage[6].

Despite reported higher incidence of diabetes in males, acute diabetic cataract is higher in females for unknown reasons. In the cohort of Dutta et al[6], three out of five patients with type 1 diabetes who developed cataracts close to the date of diagnosis of diabetes were female. All had prolonged duration of symptoms and high HbA1c. Wilson Jr et al[9] reviewed the medical records of 14 patients with diabetes and cataracts from seven institutions. Eleven of their patients were female. In another series, eight out of nine patients of diabetes with
cataract were female[7]. An exception is the series of Costagliola et al[8].

Although the appearance of acute diabetic cataract after three years from diagnosis of type 1 diabetes in our patient was somewhat surprising, other authors report more acute cases at onset or shortly after diagnosis of type 1 diabetes, some of them reversible after glycemic control. Cornwell et al[9] reported a case of a 19-year-old newly diagnosed patient of diabetes with normal ophthalmic examination at presentation, developing bilateral cataracts requiring surgery within six weeks. Seven out of fourteen patients in the series of Wilson Jr et al[10] developed cataracts shortly after being diagnosed to have diabetes. Santiago et al[11], reported a nine-year-old girl who presented with sudden onset of progressive diminution of vision over 11 days. A diagnosis of diabetes was established and history of osmotic symptoms elicited in retrospect. Scarpitta et al[12] reported a 14-year-old girl with no antecedent illness or family history of diabetes, who was hospitalized for cataract removal and subsequently diagnosed to have diabetes. In the cohort of Wilson Jr et al[10] bilateral cataracts were present in some, while others had sequential involvement of the other eye.

Glycemic control may not be the treatment modality for diabetic cataract[13], but it helps significantly in reducing the formation of cataract. Some rare cases are reversible after glycemic control[14]. Surgery is the treatment of choice.

CONCLUSION

We emphasize the need for vigilant examination for ocular complications in type 1 diabetic patients, even in the first few years of their disease. In particular, those young diabetic patients with visual complaints must be evaluated carefully for treatable eye conditions. Conversely, the appearance of lens opacities in young patients should alert the ophthalmologist to the existence of diabetes.

REFERENCES

Case Report

Atypical Presentation of Vibrio Cholera

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ABSTRACT

Cholera is known to be one of the most infectious diseases and is characterized by profuse watery diarrhea, vomiting and muscular cramps leading to dehydration, collapse and high mortality. Cholera is not endemic in Kuwait. We report a case of a Kuwaiti patient with atypical presentation of cholera that was diagnosed accidently by detection of Vibrio cholera in constipated stool. The patient was given treatment and discharged after clinical and laboratory cure. This patient is considered the first Kuwaiti cholera carrier over last ten years (documented by prevention control department in Kuwait).

KEY WORDS: constipation, dehydration, Vibrio cholera

INTRODUCTION

Cholera is an infectious disease characterized by profuse watery diarrhea, vomiting and muscular cramps leading to dehydration, collapse and high mortality. Cholera is caused by toxicogenic Vibrio cholera, which colonizes the small intestine and produces an enterotoxin.

Vibrio cholera is gram negative curved bacilli and is classified according to somatic O- antigen into O- group and non O- group. There are more than 200 O-serogroups of Vibrio but only O-group 1 is important and is further divided into Classical type and EL-Tor type (including Inaba, Hikojima and Ogawa)[1].

Cholera is endemic in Southern Asia, parts of Africa and Latin America, where seasonal outbreaks occur widely and are particularly associated with poverty and poor sanitation. The source of the infection is humans only[2]. Cholera is transmitted by drinking water or eating food contaminated with the cholera bacterium. The source of the contamination is usually the feces of an infected person. So, the disease can spread rapidly in an area with inadequate treatment of sewage and drinking water[3,4].

In epidemic situations a clinical diagnosis is made by taking history of symptoms from the patient and by a brief clinical examination only. Treatment is usually started without or before confirmation by laboratory analysis of specimens. Stool and swab samples collected in the acute stage of the disease, before antibiotics have been administered, are the most useful specimens for laboratory diagnosis[5-7]. In most cases, cholera can be successfully treated with rehydration therapy which remains the principal treatment of cholera, as dehydration and electrolyte depletion occurs rapidly. Antibiotics shorten the course of the disease, reduce the severity of the symptoms and play secondary role in management of cholera[8-10].

CASE REPORT

Our patient was a 31-years-old Kuwaiti lady, housewife and mother of four children who was four months pregnant. This lady was transferred to the Infectious Diseases Hospital complaining of diarrhea of three days duration (about 3 - 5 motions per day, watery with mucus, no blood and odorless). This diarrhea was associated with dry tongue and abdominal pain but there was no history of fever, vomiting, muscle cramp, cough, and dysuria. After a while, the diarrhea improved and the patient started complaining of constipation.

On examination, the patient appeared well, was of average built, fully conscious, oriented and well-hydrated. The vital signs were: temperature 37°C, blood pressure 110/70 mmHg, respiratory rate 20 bpm, pulse 80 beats per minute, regular with average volume, and no special character with intact peripheral pulsation. No abnormalities were detected on the

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DISCUSSION

As cholera is not endemic in Kuwait, it is unusual to detect a Kuwaiti patient who carried *Vibrio cholera*, although the patient did not travel abroad since a long time. This patient is interesting because of her atypical presentation, where the patient initially presented with diarrhea for three days that recovered without any treatment. Then she complained of constipation. Secondly, the analysis of constipated stool revealed *Vibrio cholera* in three successive specimens. Thirdly, there was no significant difference between CBC, liver function test, kidney profile and serum electrolytes over different periods of time. This patient was diagnosed accidentally by stool culture although clinical presentation was not typical of cholera.

Carrier is a person who shows no symptoms of a disease but harbors the infectious agent of that disease and is capable of transmitting it to others[11-13]. According to the definition, we can consider this lady as a carrier and a source of infection to others because she can shed the organism of cholera in her stool without apparent symptoms of the disease. The presence of such a carrier without detection is very dangerous to the community. The question now is how did this patient get infection? We cannot find an explanation for this patient getting this infection, especially, since she did not travel to an endemic area.

However, there are many factors which could explain why the patient got an infection. Firstly, this patient is highly susceptible to infection because of a) weakened immune system due to pregnancy, b) decreased gastric acidity (from the use of antacids) and c) malnutrition[11]. Secondly, after taking careful history from the patient, we found that the patient had a servant from Nepal in the community. The question now is how did this patient get infection? We cannot find an explanation for this patient getting this infection, especially, since she did not travel to an endemic area. However, there are many factors which could explain why the patient got an infection. Firstly, this patient is highly susceptible to infection because of a) weakened immune system due to pregnancy, b) decreased gastric acidity (from the use of antacids) and c) malnutrition[11]. Secondly, after taking careful history from the patient, we found that the patient had a servant from Nepal which is an endemic country for cholera[12].

CONCLUSION

In conclusion, this patient was a carrier who was detected accidentally. Detection and management of this patient prevented the spread of the infection in the community.

REFERENCES


*Table 1: Laboratory investigation results on admission and after one week

<table>
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<th>Investigations</th>
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<td>Urea</td>
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*Table shows no significant differences in laboratory investigation results at admission and one week later

CBC: complete blood count, WBC: white blood cell, HGB: hemoglobin, PLT: platelets, ESR: erythrocyte sedimentation rate

head, neck, upper limbs, lower limbs, chest and heart examination but abdominal examination showed mild abdominal enlargement, mainly supra pubic due to pregnancy. The laboratory investigations revealed normal CBC, liver function tests, kidney profile and serum electrolytes (Table 1). The stool analysis showed formed stool and was negative for intestinal parasites. No salmonella or shigella were isolated from stool but stool culture for *Vibrio cholera* (ogawa) was positive for three successive stool samples and was sensitive to ampicillin, tetracycline and sulfa. Widal test was done to rule out typhoid type of cholera but the result was negative. The abdominal ultrasound showed a viable fetus with average volume of amniotic fluid.

The patient started treatment three days after her admission in Infectious Diseases Hospital in the form of ampicillin 500 mg every 8 hours, intravenous, for five days. Although the main treatment of cholera is rehydration therapy, this patient did not need rehydration because she was constipated and well-hydrated. The patient was discharged after three successive stool samples were negative.


Case Report

Short-lasting Unilateral Neuralgiform Headache Attacks with Conjunctival Injection and Tearing (SUNCT) Syndrome Secondary to Pituitary Apoplexy

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Kuwait Medical Journal 2011; 43 (4): 327 - 329

ABSTRACT

Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) syndrome is a rare form of pituitary headache disorder, although secondary causes, particularly due to posterior fossa abnormalities, are well-known.

We report a case of SUNCT syndrome secondary to prolactinoma, with complete resolution of the SUNCT attack after trans-sphenoidal resection of the pituitary macroadenoma.

KEY WORDS: headache, pituitary macroadenoma, prolactinoma

INTRODUCTION

Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) syndrome is a rare form of strictly unilateral headache that occurs in association with cranial autonomic features. The pain is abrupt in onset, of short duration, stabbing or burring in quality and is accompanied by prominent ipsilateral cranial autonomic features, particularly lacrimation and conjunctival injection, nasal stuffiness and rhinorrhoea. The headaches are characterized by moderate to severe pain and are usually located in the ocular, periocular region and frontal region in their severe form. In addition, there is forehead sweating.

During the attack, there is increased intraocular pressure on the symptomatic side and swelling of the eyelids. The attacks can be triggered mostly from trigeminally innervated areas, but also from the extra-trigeminal territory. They could as well be spontaneous. The duration of the attack is around 40 seconds, with a frequency ranging from two episodes per day up to 10 to 30 episodes, predominantly during the daytime.

The SUNCT syndrome is predominant in males, with a mean age of onset around 50 years. Primary and secondary forms exist. The secondary form is most commonly associated with lesions of the posterior fossa or pituitary adenoma.

The SUNCT syndrome is refractory to most commonly employed therapies. Lamotrigine has recently been reported as an effective first line therapy. We report a case of SUNCT syndrome secondary to prolactinoma.

CASE REPORT

A 32-year-old gentleman, with no previous medical history, had semen analysis done in August 2008. As this report was abnormal, he was advised to do hormone analysis which was as follows; prolactin 5241 miu/l (56.5 - 281), testosterone 0.8 nmol/l (6.1 - 27.1), LH of 1.8 iu/l (1.24 - 8.62) and FSH low (1.27 - 19.26). Based on these reports he was advised to start dustinex once weekly for six weeks.

In November 2008, his prolactin was 4237 miu/l, and a magnetic resonance imaging (MRI) scan of the posterior fossa, mainly examining the pituitary region was arranged.

On 18 December 2008, prior to the (MRI), the patient developed severe headache, vomiting, decrease in visual acuity and was evaluated by the on call medical staff at that time revealing the following findings: blood pressure 100/60 mmHg on presentation, pulse rate of 80 beats per min, and fever. Chest, heart, abdomen, central nervous system were all normal except for decrease in visual acuity.

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An urgent MRI (Fig. 1) was obtained which showed a 3.2 by 2.5 cm pituitary mass with extension to the right internal carotid artery and sphenoidal sinus with clear areas of hemorrhage and infarction. His laboratory tests showed: T4 = 10.4 pmol/l (7.8 - 16.0), TSH = 1.5 iu/l (0.27 - 4.2), LH = 0.64 iu/l, FSH = 0.63 iu/l, testosterone = 2.38 nmo/l, prolactin more than 4237 miu/l and IGF1 = 31 nmo/l (18 - 53). A low-dose short synacthen test showed cortisol at T0 = 13.86, at T30 minute = 253 and at T60 minute = 174 nmol/l.

The patient was started on dustinex 0.5 mg twice weekly and hydrocortisone 10 mg in the morning, and 20 mg in the evening. Since then patient was having frequent attacks of right sided short lasting headache, with an electrical sensation in the face, associated with vomiting, photophobia, and conjunctival injection. The patient was evaluated by a neurologist who made a provisional diagnosis of cluster headache. The patient was started on amitryptiline and non-steroidal anti-inflammatory drugs (NSAIDs).

On 29th December 2008, the patient yet again developed acute proptosis of the right eye, gross eyelid swelling and conjunctival edema, with no lateralizing neurological signs, as well as no visual field defects, and a low grade fever. The fundus examination showed right papilledema.

A repeat MRI (Fig. 2) showed obliteration of the right cavernous sinus due to tumor expansion. A neurosurgeon was consulted who then advised an urgent transphenoidal resection of the tumor. This was done on 31st December 2008. Postoperatively patient symptoms improved.

On 29th January 2009, a follow-up MRI showed macroadenoma encasing the right cavernous sinus but of a smaller volume. The patient received Gamma Knife Radiosurgery on 11 March 2009. Currently, the patient is taking dustinex 0.5 mg twice weekly and hydrocortisone 10 mg in the morning and 20 mg in the evening.

**DISCUSSION**

SUNCT syndrome, a short-lasting, unilateral, neuralgiform headache attacks with conjunctival injection and tearing, is a rare form of headache that is most common in men after the age of 50. The disorder is marked by bursts of moderate to severe, stabbing, or throbbing pain, usually on one side of the head and around the eye or temple. Attacks typically occur during daytime hours and last from five seconds to four minutes per episode. Patients generally have five to six attacks per hour. Autonomic nervous system responses include watery eyes, reddish or bloodshot eyes caused by dilation of blood vessels (conjunctival injection), nasal congestion, runny nose, sweaty forehead, swelling of the eyelids, and increased pressure within the eye on the affected side of head. Systolic blood pressure may rise during the attacks. Most cases of SUNCT syndrome described in the medical literature are primary but several cases of secondary SUNCT syndrome have been reported. The secondary SUNCT cases can be divided into two groups: posterior fossa and pituitary abnormalities. There are seven case reports of SUNCT syndrome...
secondary to a posterior fossa abnormality that include: homolateral cerebello-pontine angle arteriovenous malformation in two patient\(^{4,5}\), a brainstem cavernous hemangioma\(^{6}\), a posterior fossa lesion in a HIV/AIDS patient\(^{7}\), severe basilar impression causing ponto-medullary compression in a patient with osteogenesis imperfect\(^{8}\), craniosynostosis resulting in a foreshortened posterior fossa\(^{9}\), and ischemic brainstem infarction\(^{10}\), and dopamine agonist induced SUNCT\(^{1}\). There are four case reports of SUNCT syndrome secondary to pituitary adenoma in medical literature. The pathophysiology of pituitary-associated headache is poorly understood, although dural stretch, cavernous sinus invasion, and local pressure effects have been proposed as possible mechanisms\(^{11-13}\). The attacks on SUNCT syndrome occurred on the side ipsilateral to side of the tumor, suggesting a role for a mechanical mode of action. In SUNCT syndrome, there is a lack of persistent, convincingly beneficial effect of drugs or anesthetics blockades that are generally effective in other types of headache\(^{2}\). Corticosteroids and the anti-epileptic drugs gabapentin, lamotrigine, and carbamazepine may help relieve some symptoms in some patient. Neurosurgical intervention should be considered in cases of secondary SUNCT, as in our case the trans-sphenoidal resection of the tumor helped in relieving SUNCT syndrome with immediate results.

**CONCLUSION**

This case emphasized the relationship between pituitary macroadenoma and SUNCT, and although it is difficult to treat, neurosurgical intervention might prove helpful to relieve the symptoms.

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Thrombosis Risk in Carriers of the Factor V Leiden Mutation: Is It Associated with a Defined Skin Color?

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Factor V Leiden (FVL; G1691A) is an autosomal dominant mutation with a high risk for thrombosis. Speculation that founders of FVL lived in the Middle East is supported by a prevalence of FVL that is higher in Arabs residing in Israel, Jordan, Lebanon, and Syria (12-14%) than in other white populations like Europeans (4-5%, up to 15% in the South of Sweden). We sought to verify the appropriate use of skin color as a clinical sign by which Arab individuals in Kuwait are included or excluded from testing for FVL. After institutional approval, 200 healthy Arabs residing in Kuwait consented to participate. Skin type was distinguished for the participants by Fitzpatrick natural skin color classification: 76 (38%) skin type II (white), 96 (48%) Mediterranean skin type IV (brown), and 28 (14%) skin type VI (black). FVL was tested by real-time PCR, and the percentage of carriers was calculated in each group. FVL was positive in 17 (8.5%) of the total subjects: 8 (10.5%) skin type II, 7 (7.3%) skin type IV, and 2 (7.1%) skin type VI. Therefore, FVL shows an even distribution in Arabs, and all Arabs residing in Kuwait should be tested for FVL irrespective of skin color.

Clinical Epidemiology of Crohn’s Disease in Arabs based on the Montreal Classification

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Inflamm Bowel Dis 2011 Oct 10 doi: 10.1002/ibd.21890

Background: There has been a remarkable increase in the incidence of Crohn’s disease (CD) among Arabs in recent years. We conducted this study to determine the clinical epidemiology of CD in Kuwait.

Methods: Sociodemographic and clinical information was collected for a continuous series of 206 Arab patients with CD and age at diagnosis and location and behavior of disease was determined according to the Montreal Classification.

Results: Among the 206 patients, 100 (48.5%) were males and 106 (51.5%) females. The mean age at diagnosis (±SD) was 21.9 ± 10 years. Family history of CD was reported by 39 (18.9%) patients. The disease was limited to the ileum in 115 (55.8%) patients, whereas in 28 (13.6%) it involved the colon and in 63 (30.6%) it involved both the ileum and colon. The behavior of the disease was nonstricturing, nonpenetrating in 146 (70.9%) patients, whereas 49 (23.8%) had stricturing and 11 (5.3%) penetrating disease. Perianal disease was present in 41 (19.9%) patients. In the multivariate analysis, the use of biologic therapy and duration of the disease for ≥6 years were significantly associated with the presence of perianal disease, and the need for surgery was significantly associated with stricturing and penetrating disease behavior.

Conclusions: CD among Arabs is equally common in males and females, presents at a relatively younger age, and in about half of the patients is limited to the small bowel. These features may indicate an underlying genetic predisposition for the disease in this population, which needs further investigation.
Distribution of Human Papillomavirus among Women with Abnormal Cervical Cytology in Kuwait

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This study investigates the distribution of human papillomavirus (HPV) in women with abnormal cervical cytology in Kuwait. Two hundred and ninety-eight (298) abnormal ThinPreps were taken from women seeking routine gynecological care and screened for HPV DNA by real-time PCR. HPV genotyping was determined by PCR-based sequencing. HPV DNA was detected in 152 women (51%), and 29 different HPV genotypes were detected, comprising 16 high-risk (HR) (16, 18, 31, 33, 35, 39, 45, 51, 53, 56, 58, 59, 66, 68, 73, 97), nine low-risk (LR) (6, 11, 54, 61, 74, 81, 90, 102, 106), and four intermediate-risk (IR) (62, 67, 84, 87). HPV16 had the highest prevalence (24.3%), followed by HPV11 (13.8%), HPV66 (11.2%), HPV33 (9.9%), HPV53 (9.2%), HPV81 (9.2%), HPV56 (7.9%) and HPV18 (6.6%). HPV prevalence was 86, 67, and 89% in women with invasive cervical carcinoma (ICC), high-grade squamous intraepithelial lesion (HSIL) and low-grade squamous intraepithelial lesion (LSIL), respectively. As for age distribution, 69% of all HPVs were found in women aged 20-29 years, and the HPV incidence rate deceased with increasing age. The proportion of single infections decreased as the severity of the cytological diagnosis increased, while the proportion of multiple infections increased. This study is the first of its type in Kuwait and one of few in the Middle East. The findings are consistent with the hypothesis that HPV infection is the primary cause of cervical neoplasia. They support HPV vaccine research to prevent cervical cancer and efforts to develop HPV DNA diagnostic tests.

Kikuchi-Fujimoto Disease in Fine-Needle Aspiration Smears: A Clinico-Cytologic Study of 76 Cases of KFD and 684 Cases of Reactive Hyperplasia of the Lymph Node

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Kikuchi-Fujimoto disease (KFD) is cytologically characterized by a polymorphous lymphoid cell population, abundant karyorrhectic debris and histiocytes, many of which are crescentic (Kikuchi histiocytes). As per reviewed literature, KFD may be confused with tuberculosis, lymphoma, and reactive hyperplasia of lymph nodes (RHLN). Since RHLN was found to be a major challenging factor during routine cytodiagnostics of KFD in our material, we tried to find out the differentiating clinico-cytologic features between 76 KFD and 684 RHLN cases seen in Kuwait. 63.2% of KFD were in 3rd and 4th decades of life as compared to 40.2% of RHLN (P = 0.0002). Male to female ratio was 1:2.45 for KFD and 1:1.09 for RHLN (P = 0.0022). Kuwaiti:non-Kuwaiti ratio was 1:2.04 for KFD and 1:1.31 for RHLN (P < 0.0001). Capillary networks was present in 71.1% of KFD smears and 52.6% of RHLN (P = 0.0023). Tingible body macrophages and dendritic reticulum cells were detected in 17.1% and 22.4%, respectively, in KFD as opposed to 50.1% and 58.8%, respectively, in RHLN (P < 0.0001). Kikuchi histiocyte count ranged from 2 to 36% in KFD and was ≥10% in 31 (40.8%). Rare Kikuchi histiocytes were detected in 16 (2.3%) of RHLN cases but in none of them the count exceeded 1%, whereas their count was >1% in all KFD cases (P < 0.0001). Thus, KFD cases differed significantly from RHLN in respect of age and sex distribution, Kuwaiti:non-Kuwaiti ratio, and cytomorphologic features such as capillary networks, Kikuchi histiocyte count, dendritic reticulum cells, and tingible body macrophages.
Factors Influencing Patient Satisfaction in Primary Healthcare Clinics in Kuwait

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Int J Health Care Qual Assur 2011; 24:249-262

Purpose: To measure the quality of health care services patient satisfaction is used as one of the most important indicators. The study aims to identify factors affecting patient’s satisfaction at primary health care clinics.

Design/Methodology/Approach: The data was collected during January 2007 and May 2007 through a randomly-distributed questionnaire. The questionnaires were distributed in primary healthcare clinics that represent all health care regions in Kuwait. A total of 426 completed questionnaires, out of 500, were returned resulting in a response rate of 85.2 percent.

Findings: The majority (87 percent) of the patients responded that the time for communication between physician and patient was not enough. Seventy-nine-percent of the surveyed patients said they would go to the emergency room of the hospital in future if needed instead of going to the primary care clinic. Regarding the quality of the communication relationship between physician and patients most of the patients responded negatively. Exploratory factor analysis identified six factors and reliability of overall scale was found to be 0.61.

Research Limitations/Implications: One limitation to this study was the exclusion of the private sector.

Originality/Value: The authors hope that this study identifies areas of dissatisfaction that can be quickly remedied and ensures enhancement in the areas of satisfaction with ongoing attention and emphasis.

Low Carbohydrate Ketogenic Diet Prevents the Induction of Diabetes Using Streptozotocin in Rats

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Exp Toxicol Pathol 2011; 63:663-669

Diabetes continues to be an overwhelmingly prevalent endocrine disorder that leads to several micro- and macrocomplications. It has been widely accepted that changes in dietary habits could induce or prevent the onset of diabetes. It is shown that low carbohydrate ketogenic diet (LCKD) is effective in the amelioration of many of the deleterious consequences of diabetes. However, its role in preventing the onset of diabetes is not understood. Therefore, this study is focused on the effect of LCKD in preventing the induction of diabetes using streptozotocin (STZ) in rats by biochemical and histological methods. Forty-two Wistar rats weighing 150-250g were used in this study. The animals were divided into three groups: normal diet (ND), low carbohydrate ketogenic diet (LCKD), and high carbohydrate diet (HCD). Specific diets ad libitum were given to each group of animals for a period of 8 weeks. Each group was further subdivided into normal control, sham control and diabetic groups. Animals in the diabetic group were given a single intraperitoneal injection of STZ (55mg/kg). All the animals were sacrificed 4 weeks after the injection of STZ. Daily measurements of food and water intake as well as weekly measurement of body weight were taken during the whole 12 weeks of the experiment. After injecting with STZ, the blood glucose level of all the groups increased significantly except for the group fed on LCKD (p value<0.01). Also, food intake, water intake and urine output were significantly increased in all groups except for the LCKD group (p value<0.01). There was also a significant decrease in the weight gain of the animals that were fed on a LCKD as compared to other groups (p value<0.05). Although, substantial decrease in the number of β cells was noticed in diabetic rats, there were no change in the number of β cells in the LCKD treated diabetic animals as compared to LCKD control group. The results presented in this study, therefore, suggests that LCKD prevents the development of diabetes using streptozotocin in rats.
Revision of Failed Bariatric Procedures to Roux-en-Y Gastric Bypass (RYGB)

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Obes Surg 2011; 21:1157-1160

Bariatric surgery for morbid obesity has been established as an effective treatment method and has been shown to be associated with resolution of co-morbidities. Despite its success, some patients may require revision because of weight regain or mechanical complications. From September 2005 to December 2009, 42 patients underwent revisional Roux-en-Y gastric bypass (RYGB). All procedures were performed by one surgeon. Demographics, indications for revision, complications, and weight loss were reviewed. Thirty-seven patients were treated with laparoscopic (n = 36) or open (n = 1) RYGB after failed laparoscopic adjustable gastric banding. Four patient were treated with laparoscopic (n = 3) or open (n=1) RYGB after failed vertical banded gastroplasty, and one patient underwent open redo RYGB due to large gastric pouch. Conversion rate from laparoscopy to open surgery was 2.5% (one patient). Mean operative time was 145.83 ± 35.19 min, and hospital stay was 3.36 ± 1.20 days. There was no mortality. Early and late complications occurred in six patients (14.2%). The mean follow-up was 15.83 ± 13.43 months. Mean preoperative body mass index was 45.15 ± 7.95 that decreased to 35.23 ± 6.7, and mean percentage excess weight loss was 41.19 ± 20.22 after RYGB within our follow-up period. RYGB as a revisional bariatric procedure is effective to treat complications of restrictive procedures and to further reduce weight in morbidly obese patients.

Inflammatory Bowel Disease in Children, an Evolving Problem in Kuwait

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Saudi J Gastroenterol 2011; 17:323-327

Background/Aims: Inflammatory bowel disease (IBD) was previously thought a rare disease among children in Kuwait since most diarrhea cases were attributed to infections. In the past few years we observed an increase in the number of patients presenting with IBD. In this study we aimed to determine the epidemiology of IBD among children in the State of Kuwait.

Patients and Methods: The charts of all children with IBD who were referred to the pediatric gastroenterology unit during the period February 1998 to January 2008 were retrospectively reviewed. Results: Out of a total of 130 children with IBD, 92 (71%) had Crohn’s disease, 36 (28%) had ulcerative colitis and two (1%) had indeterminate colitis. The estimated annual incidence for IBD was 2.16/10 5 /year. The age range was nine months-15 years (median: 11 years). Fifty-three percent of all patients were females and 77% were Kuwaiti nationals. Positive family history was found in 23%. The most common presenting symptoms were abdominal pain (87%) and diarrhea (82%). Failure to thrive was detected in 35% and short stature in 20% at presentation. The ileocolonic region was the most common presentation site affected in Crohn’s patients and pancolitis was the commonest in ulcerative colitis.

Conclusion: Inflammatory bowel disease is not uncommon in our children. We found no differences regarding disease presentation and clinical features compared to the Western world.
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Dec 26 - Jan 2, 2012
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Email: mail@ams4cme.com

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Contact: CCM, 11440 N Kendall Drive Miami, FL 33176
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Email: bmjd@congressmed.com

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Email: imli@easl.eu

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Contact: American Meetings, Inc., 111 SW 6th Street, Fort Lauderdale, Florida 33316
Tel: 855-353-8731; Fax: 954-337-2476
Email: GYN@americanmeetings.com

AGA Clinical Congress of **Gastroenterology and Hepatology:** Practice, Evidence and Quality in 2012
Jan 20 - 21, 2012
Loews Miami Beach Hotel, Miami, FL, *United States*
Contact: AGA, 4930 Del Ray Avenue Bethesda, MD 20814
Tel: 301-654-2055; Fax: 301-654-5920
Email: member@gastro.org

**Preventive Cardiology and Lipidology**
Jan 22 - 29, 2012
MSC Cruises’ Splendida, Barcelona, Spain
Contact: Reservations, 5700 4th Street N. St Petersburg, Florida 33703
Tel: 1 800 422 0711; Fax: 1 727 522 8304
Email: contactus@continuingeducation.net

Dealing with **Disability**
Royal Caribbean’s Allure of the Seas, Ft. Lauderdale, FL, *United States*
Jan 22 - 29, 2012
Contact: Reservations, 5700 4th Street N. St Petersburg, Florida 33703
Tel: 1 800 422 0711; Fax: 1 727 522 8304
Email: contactus@continuingeducation.net

**Primary Care:** Addressing Issues of Aging Patients
Jan 22 - 29, 2012
Holland America’s ms Ryndam, Tampa, FL, *United States*
Contact: Reservations, 5700 4th Street N. St Petersburg, Florida 33703
Tel: 1 800 422 0711; Fax: 1 727 522 8304
Email: contactus@continuingeducation.net

**Preventive Cardiology and Lipidology**
Jan 22 - 29, 2012
MSC Cruises’ Splendida, Barcelona, Spain
Contact: Reservations, 5700 4th Street N. St Petersburg, Florida 33703
Tel: 1 800 422 0711; Fax: 1 727 522 8304
Email: contactus@continuingeducation.net

**Internal Medicine:** A Clinical Update
Jan 23 - 27, 2012
Hyatt Regency, Sarasota, FL, *United States*
Contact: D. Reece Pierce, PA-C, P.O. Box 49947
Tel: 866-267-4263; Fax: 941-365-7073
Email: mail@ams4cme.com

**T-cell Lymphoma** Forum 2012
Jan 26 - 28, 2012
Hotel Nikko, San Francisco, CA, *United States*
Contact: Damaris Cruz, 220 Kinderkamack Road
Tel: 201-594-0400; Fax: 201-594-0409
Email: dcruz@jwoodassoc.com
Multidisciplinary Head and Neck Symposium
Jan 26 - 28, 2012
Arizona Biltmore, Phoenix, United States
Contact: Yen Dinh, 8280 Willow Oaks Corporate Drive, Suite 500, Fairfax, VA 22031
Tel: 703-502-1550
Email: astrottemp3@astro.org

3rd National Conference: Renal and Bladder Cancer 2012
Jan 26 - 27, 2012
Hallam Conference Centre, London, United Kingdom
Contact: Florence Doel, St Judes Church, Dulwich Road, London, SE24 0PB
Tel: +44 (0)207 501 6762; Fax: +44 (0)207 978 8319
Email: flo.doel@markallengroup.com

Hematology Review
Jan 28, 2012
graves | 601 hotel, Minneapolis, Minnesota, MN, United States
Contact: MSCPID, 200 1st Street SW/Rochester, MN 55905
Tel: 800-323-2688; Fax: 507-284-0532
Email: cme@mayo.edu

Internal Medicine
Jan 28 - Feb 4, 2012
Celebrity Cruises’ Eclipse, Miami, FL, United States
Contact: Reservations, 5700 4th Street N. St Petersburg, Florida 33703
Tel: 1 800 422 0711; Fax: 1 727 522 8304
Email: contactus@continuingeducation.net

32nd Annual Occupational Safety and Health Winter Institute
Jan 29 - Feb 3, 2012
Orlando, FL, United States
Contact: NC ERC, PO Box 16248 Chapel Hill, NC 27516
Tel: 919-962-2101; Fax: 919-966-7579
Email: osherc@unc.edu

Geriatrics: A Primary Care Approach to the Aging Population
Jan 30 - Feb 3, 2012
Hyatt Regency, Sarasota, FL, United States
Contact: D. Reece Pierce, PA-C, P.O. Box 49947
Tel: 866-267-4263; Fax: 941-365-7073
Email: mail@ams4cme.com

4th Health and Environment Conference
Jan 30 - Feb 2, 2012
Hamdan Bin Mohammed e-University, Dubai, United Arab Emirates
Contact: Amrita, P.O. Box 71400 Dubai UAE
Tel: 00971480033000; Fax: 009744393959
Email: congress@hbmeu.ac.ae

Frequently Encountered Ethical Dilemmas Ethics in Critical Care Practice
Feb 1 - 3, 2012
Siebens Building / Mayo Clinic, Rochester, MN, United States
Contact: Kammi Englund, 200 1st Street SW/Rochester, MN 55905
Tel: 800-323-2688; Fax: 507-284-0532
Email: englund.kammi@mayo.edu

Course in Advanced Endocrinology
Feb 3 - 5, 2012
Pan Pacific Hotel, Singapore, Singapore
Contact: Kelly Chan, 695E East Coast Road, Singapore 459059
Tel: 6346 4402 Fax: 6346 4403
Email: kellychan@themeetinglab.com

The 6th World Congress World Institute of Pain
Feb 4 - 6, 2012
Miami Beach, FL, United States
Contact: Kenes International, 1-3 Rue de Chantepoulet PO Box 1726, CH-1211, Geneva 1 Switzerland
Telephone: +41 22 908 0488; Fax: +41 22 906 9140
Email: wip@kenes.com

Mayo Clinic Interactive Surgery Symposium
Feb 5 - 10, 2012
Grand Hyatt Kauai Resort and Spa, Kauai, HI, United States
Contact: CME Staff, 13400 E. Shea Boulevard, Scottsdale, AZ 85259
Tel: (480) 301-4580; Fax: (480) 301-8323
Email: mca.cme@mayo.edu

Preventive Medicine
Feb 5 - 12, 2012
Celebrity Cruises’ Solstice, Ft. Lauderdale, FL, United States
Contact: Reservations, 5700 4th Street N. St Petersburg, Florida 33703
Tel: 1 800 422 0711; Fax: 1 727 522 8304
Email: contactus@continuingeducation.net

Rheumatology: Improving Primary Care Outcomes through Diagnosis and Treatment
Feb 6 - 10, 2012
Hyatt Regency, Sarasota, FL, United States
Contact: D. Reece Pierce, PA-C, P.O. Box 49947
Tel: 866-267-4263; Fax: 941-365-7073
Email: mail@ams4cme.com
Advanced Technologies & Treatments for Diabetes
Geneva, Switzerland
Feb 8 - 11, 2012
Contact: Kenes, 1-3, Rue de Chantepoulet
Tel: 4122908048; Fax: 4122906914
Email: attd@kenes.com

31st Annual Squaw Valley Retinal Symposium
Feb 9 - 12, 2012
Resort at Squaw Creek, Olympic Valley, CA, United States
Contact: Laura Wendell1, 3939 J Street, Suite 106, Sacramento, CA 95819
Tel: 916 483-6299; Fax: 916 483-6297
Email: laurawendel@comcast.net

New Orleans Academy of Ophthalmology 61st Annual Symposium
Feb 10 - 12, 2012
Sheraton New Orleans Hotel, New Orleans, LA, United States
Contact: Amber Howell, 7733 Maple Street New Orleans, LA 70118
Tel: 504-861-2550; Fax: 504-861-2549
Email: amber@noao.org

Family Medicine: An Evidence-Based Approach to Patient Care
Feb 13 - 17, 2012
Hyatt Regency, Sarasota, FL, United States
Contact: D. Reece Pierce, PA-C, P.O. Box 49947
Tel: 866-267-4263; Fax: 941-365-7073
Email: mail@ams4cme.com

Orthopaedics & Sports Injuries
Feb 14 - 15, 2012
London, United Kingdom
Contact: Heather Ikwuemesi, St Jude’s Church, Dulwich Road, London, SE24 0PB
Tel: 02075016760
Email: Heather.ikwuemesi@markallengroup.com

ACDS 2012 (23RD Annual International Colorectal Disease Symposium combined with 32nd Annual Turnbull Symposium)
Feb 15 - 18, 2012
Marriott Harbor Beach Resort and Spa, Fort Lauderdale, United States
Contact: Cleveland Clinic Florida Registration, 2950 Cleveland Clinic Blvd.
Tel: (855) 353-8731; Fax: (954) 337-2476
Email: ACDS@americanmeetings.com

Teaching Course with International Faculty on: Retinal and Vitreous Surgery. Minimal Extraocular Surgery for Retinal Detachment and Prophylaxis of the Fellow Eye
Feb 16 - 20, 2012
Abu Dhabi, United Arab Emirates
Contact: Prof. Dr. Ingrid Kreissig, Dept. of Ophthalmology, Univ. of Mannheim - Heidelberg, 69167 Mannheim, Germany
Tel: +49 - (0) 621 - 383 25 97
Email: Ingrid.kreissig@medma.uni-heidelberg.de

Gastroenterology and Hepatology Symposium (in conjunction with the ACDS 2012 Symposium)
Feb 17 - 18, 2012
Marriott Harbor Beach, Ft Lauderdale, United States
Contact: Cleveland Clinic Florida Registration, 2950 Cleveland Clinic Blvd., Cleveland, OH
Tel: (855) 353-8731; Fax: (954) 337-2476
Email: GI@americanmeetings.com

Infectious Disease Review
Feb 18 - 25, 2012
Norwegian Cruise Line Jewel, New York, NY, United States
Contact: Reservations, 5700 4th Street N. St Petersburg, Florida 33703
Tel: 1 800 422 0711; Fax: 1 727 522 8304
Email: contactus@continuingeducation.net

Sports Medicine
Feb 18 - 25, 2012
Holland America’s ms Eurodam, Ft. Lauderdale, FL, United States
Contact: Reservations, 5700 4th Street N. St Petersburg, Florida 33703
Tel: 1 800 422 0711; Fax: 1 727 522 8304
Email: contactus@continuingeducation.net

Oral Dermatology and Oral Pathology
Feb 18 - 25, 2012
Holland America’s ms Oosterdam, San Diego, CA, United States
Contact: Reservations, 5700 4th Street N. St Petersburg, Florida 33703
Tel: 1 800 422 0711; Fax: 1 727 522 8304
Email: contactus@continuingeducation.net

11th Annual Surgery of the Foregut Symposium
Feb 19 - 21, 2012
The Biltmore Hotel Miami, Coral Gables, United States
Contact: Cleveland Clinic Florida Registration, 2950 Cleveland Clinic Blvd.
Tel: (855) 353-8731; Fax: (954) 337-2476
Email: Foregut@americanmeetings.com
Emergency Medicine: Practicing According to the Evidence
Feb 20 - 24, 2012
Hyatt Regency, Sarasota, FL, United States
Contact: D. Reece Pierce, PA-C, P.O. Box 49947
Tel: 866-267-4263; Fax: 941-365-7073
Email: mail@ams4cme.com

Cardiovascular Disease Prevention 2012: Tenth Annual Comprehensive Symposium
Feb 23 - 26, 2012
Fontainebleau Hotel, Miami Beach, FL, United States
Contact: Julie Zimmett, 8900 N. Kendall Drive, Miami, Florida 33176
Tel: 786-596-8612
Email: juliez@baptisthealth.net

Palliative Medicine & Supportive Oncology 2012: The 15th International Symposium
Feb 23 - 25, 2012
The Marriott Key Largo Bay Beach Resort, Key Largo, FL, United States
Contact: Jennifer Wasner, 3050 Science Park Dr., Beachwood, Ohio 44122
Tel: 216-448-0812; Fax: 216-448-0782
Email: wasnerj@ccf.org

Medical Ethics & Legal Medicine
Feb 25 - Mar 3, 2012
Royal Caribbean’s Oasis of the Seas, Ft. Lauderdale, FL, United States
Contact: Reservations, 5700 4th Street N. St Petersburg, Florida 33703
Tel: 1 800 422 0711; Fax: 1 727 522 8304
Email: contactus@continuingeducation.net

Radiology for the Non-Radiologist
Feb 27 - Mar 2, 2012
Hyatt Regency, Sarasota, FL, United States
Contact: D. Reece Pierce, PA-C, P.O. Box 49947
Tel: 866-267-4263; Fax: 941-365-7073
Email: mail@ams4cme.com

Gastroenterology & Hepatology
Mar 1 - 4, 2012
Hotel Del Coronado, Coronado, CA, United States
Contact: MSCPD, 200 1st Street SW/Rochester, MN
Tel: 800-323-2688; Fax: 507-284-0532
Email: cme@mayo.edu

1st International Conference on Heart and Brain - ICHB 2012
Hotel Pullman Paris Montparnasse, Paris, France
Mar 1 - 3, 2012
Contact: Kenes International, 1-3 Rue de Chantepoulet, CH-1211 Geneva 1 Switzerland
Tel: +41 22 908 0488
Email: heart-brain@kenes.com

International Conference on Nutrition & Growth
Paris Marriott Rive Gauche Hotel & Conference Center, Paris, France
Mar 1 - 3, 2012
Contact: Kenes International, 1-3 Rue de Chantepoulet, CH-1211 Geneva 1 Switzerland
Tel: +41 22 908 0488
Email: nutrition-growth@kenes.com

Sleep Health & Safety 2012
Mar 2 - 3, 2012
JW Marriott, Washington, DC, United States
Contact: Inne Barber, 1010 N. Glebe Road, Suite 310, Arlington, VA 22201
Tel: (703) 243-1697
Email: ibarber@sleepfoundation.org

The 30th Annual Emergencies in Medicine Conference
Mar 4 - 8, 2012
Hyatt Escala, Park City, UT, United States
Contact: Karina Rey, 2033 San Elijo Ave., #351, Cardiff, CA
Tel: 760-942-7859
Email: krey@checourse.com

XIII Pan American Congress of Neurology
Mar 4 - 8, 2012
Radisson Plaza Hotel La Paz, La Paz, Bolivia
Contact: Kenes International, La Concepcion 266 Of. 501, Santiago, Chile
Tel: +56-2-946 2633
Email: pcn2012@kenes.com

Pediatric Infectious Diseases: An Evidence-Based Approach
Mar 5 - 9, 2012
Hyatt Regency, Sarasota, FL, United States
Contact: D. Reece Pierce, PA-C, P.O. Box 49947
Tel: 866-267-4253; Fax: 941-365-7073
Email: mail@ams4cme.com

Imperial Spine 2012
Mar 7 - 9, 2012
The Royal College of Surgeons of England, London, United Kingdom
Contact: Kenes UK, 1st Floor, Chesterfield House 385 Euston Road London, NW1 3AU United Kingdom
Tel: +44 (0) 20 7383 8030
Email: eci@kenes.com
Contraceptive Technology
Mar 7 - 10, 2012
Hyatt Regency, San Francisco, CA, United States
Contact: Registration Dept at Contemporary Forums, 6377 Clark Ave., Suite 200, Dublin, CA 94568
Tel: 800-377-7707; Fax: 800-329-9923
Email: in@cforums.com

Infectious Diseases: Adult Issues in the Outpatient and Inpatient Settings
Mar 7 - 11, 2012
Hyatt Regency, Sarasota, FL, United States
Contact: D. Reece Pierce, PA-C, P.O. Box 49947
Tel: 866-267-4263 Fax: 941-365-7073
Email: mail@ams4cme.com

Pain Medicine for the Non-Pain Specialist
Mar 8 - 10, 2012
Marriott Marco Island, Marco Island, FL, United States
Contact: MSCPD, 200 1st St./Rochester, MN 55905
Tel: 800-323-2688; Fax: 507-284-0532
Email: cme@mayo.edu

ICJR 2nd Annual Advances in Orthopaedic Trauma and Arthroplasty Course
Mar 8 - 10, 2012
Biltmore Hotel, Miami, FL, United States
Contact: Sylke Anderson, 2033 San Elijo Ave., #351, Miami, FL
Tel: 760-942-7859
Email: sanderson@icjr.net

8th International Congress of Autoimmunity
Mar 9 - 13, 2012
Palacio de Exposiciones y Congresos de Granada, Granada, Spain
Contact: Kenes International, 1-3 Rue de Chantepoulet
Tel: +41 22 908 0488; Email: isppd@kenes.com

Infectious Disease Review
Mar 11 - 26, 2012
Celebrity Cruises’ Infinity, Valparaiso, Chile
Contact: Reservations, 5700 4th Street N. St Petersburg, Florida 33703
Tel: 1 800 422 0711; Fax: 1 727 522 8304
Email: contactus@continuingeducation.net

Pulmonary Medicine
Mar 11 - 18, 2012
Holland America’s ms Nieuw Amsterdam, Ft. Lauderdale, FL, United States
Contact: Reservations, 5700 4th Street N. St Petersburg, Florida 33703
Tel: 1 800 422 0711; Fax: 1 727 522 8304
Email: contactus@continuingeducation.net

Thoracic Imaging 2012
Mar 11 - 14, 2012
Hyatt Regency Huntington Beach Resort & Spa, Huntington Beach, CA, United States
Contact: Tracy Parks, P O Box 7169 Rochester, MN 55903
Tel: 507-288-5620; Fax: 507-288-0014
Email: tracy@matrixmeetings.com

Neurology and Pain Management
Mar 13 - 16, 2012
Hyatt Regency, Sarasota, FL, United States
Contact: D. Reece Pierce, PA-C, P.O. Box 49947
Tel: 866-267-4263; Fax: 941-365-7073
Email: mail@ams4cme.com

Pediatric Emergency Medicine: Detection, Diagnosis and Developing Treatment Plans
Mar 12 - 16, 2012
Holland America’s ms Volendam, Sydney, Australia
Contact: Reservations, 5700 4th Street N. St Petersburg, Florida 33703
Tel: 1 800 422 0711; Fax: 1 727 522 8304
Email: contactus@continuingeducation.net

9th Mediterranean Meeting on Hypertension and Atherosclerosis
Mar 14 - 18, 2012
Maxx Royal Hotel, Antalya, Turkey
Contact: Yesim Tanriverdi, Istanbul, Turkey
Tel: +90 212 3476500; Fax: +90 212 3476505
Email: yesim@stlsurizm.com.tr

Emergency Medicine: An Evidence-Based Approach to Adult Care
Mar 19 - 23, 2012
Hyatt Regency, Sarasota, FL, United States
Contact: D. Reece Pierce, PA-C, P.O. Box 49947
Tel: 866-267-4263; Fax: 941-365-7073
Email: mail@ams4cme.com
15th World Conference on Tobacco or Health
Mar 21 - 24, 2012
Singapore, Singapore
Contact: Su-Ying Low, Department of Respiratory and Critical Care Medicine
Telephone: +65 63214700; Fax: +65 62271736
Email: low.su.ying@sgh.com.sg

ICJR 2nd Annual Cleveland Arthroplasty Course
Mar 22 - 23, 2012
Castele Learning Center at Lutheran Hospital, Cleveland, OH, United States
Contact: Barbie Mitros, 2033 San Elijo Ave., #351, Cleveland, OH
Tel: 760-942-7859
Email: bmitros@icjr.net

2012 Abdominal Radiology Course
Mar 25 - 30, 2012
Fairmont Scottsdale Princess, Scottsdale, AZ, United States
Contact: ARC Meetings Dept, 4550 Post Oak Place, Suite 342
Tel: 713-965-0566; Fax: 713-960-0488
Email: arc@meetingmanagers.com

15th World Congress of Anesthesiologists (WCA) 2012
Mar 25 - 30, 2012
Buenos Aires, Argentina
Contact: Janet McCready
Telephone: 44-0-1462-438-409; Fax: 44-0-1462-452-562
E-Mail: janet.mccready@choicelive.com

Contraceptive Technology - Boston
Mar 28 - 31, 2012
Sheraton Boston, Boston, MA, United States
Contact: Registration Dept. @ Contemporary Forums, 6377 Clark Ave., Suite 200, Dublin, CA 94568
Tel: 800-377-7707; Fax: 800-329-9923
Email: info@cforums.com

9th European Congress on Menopause and Andropause
Mar 28 - 31, 2012
Megaron Athens International Conference Center - M.A.I.C.C., Athens, Greece
Contact: Kenes International, 1-3 Rue de Chantepoulet, CH-1211 Geneva 1 Switzerland
Tel: +41 22 908 0488
Email: emas@kenes.com

Female Pelvic Floor Disorders
Mar 29 - Apr 2, 2012
The Ritz-Carlton, Fort Lauderdale, FL, United States
Contact: Cleveland Clinic Florida Registration, 2950 Cleveland Clinic Blvd.
Tel: (855) 353-8731; Fax: (954) 337-2476
Email: Pelvic@americanmeetings.com

Aseptic Surgery Forum 2012
Mar 29 - 30, 2012
Cité des Sciences, PARIS, France
Sponsoring Organization: Oriex Communication
Contact: sylviane ROBINET, 25 Rue André Joineau - 93310 Le Pré Saint Gervais
Telephone: +33 1 48 91 89 89; Fax: 0033148434994
Email: s.robinet@simpleway.fr

Pediatric Emergency Medicine: An Evidence-Based Approach
Apr 2 - 6, 2012
Hyatt Regency, Sarasota, FL, United States
Contact: D. Reece Pierce, PA-C, P.O. Box 49947
Tel: 866-267-4263; Fax: 941-365-7073
Email: mail@ams4cme.com

Aseptic Surgery Forum 2012
Apr 3 - 4, 2012
Espace Champerret, Paris, France
Contact: sylviane ROBINET, 25 Rue André Joineau - 93310 Le Pré Saint Gervais
Tel: +33 1 48 91 89 89; Fax: 0033148434994
Email: s.robinet@simpleway.fr

Neurology Updates for Primary Care
Apr 9 - 13, 2012
Hyatt Regency, Sarasota, FL, United States
Contact: D. Reece Pierce, PA-C, P.O. Box 49947
Tel: 866-267-4263; Fax: 941-365-7073
Email: mail@ams4cme.com

World Congress of Cardiology Scientific Sessions 2012
Apr 18 - 21, 2012
Dubai International Convention and Exhibition Centre, Dubai, United Arab Emirates
Contact: Registration, MCI Suisse SA, Rue de Lyon 75, 1211 Geneva 13, Switzerland
Tel: +41 22 33 99 585
Email: congress@worldheart.org

Internal Medicine 2012
Apr 19 - 21, 2012
Ernest N. Morial Convention Center, New Orleans, LA, United States
Contact: American College of Physicians, 190 Independence Mall West, Philadelphia, PA, 19106
Tel: 800-523-1546, ext 2600; Fax: 215-351-2799
Email: custserv@acponline.org

Primary Care Update: Cardiac Health, Metabolic Syndrome, Obesity and Related Disorders
Apr 22 - 29, 2012
Royal Caribbean’s Allure of the Seas, Ft. Lauderdale, FL, United States
Contact: Reservations, 5700 4th Street N. St Petersburg, Florida 33703
Tel: 1 800 422 0711; Fax: 1 727 522 8304
Email: contactus@continuingeducation.net
Forthcoming Conferences and Meetings

December 2011

NWAC World Anesthesia Convention 2012
Apr 24 - 28, 2012
Hilton Hotel Istanbul, Istanbul, Turkey
Contact: Kenes International, 1-3 Rue de Chantepoulet
PO Box 1726 CH-1211, Geneva 1 Switzerland
Tel: +41 22 908 0488; Fax: +41 22 906 9140
Email: nwac@kenes.com

Pediatrics Review
Apr 27 - May 4, 2012
Holland America’s ms Eurodam, Civitavecchia, Italy
Contact: Reservations, 5700 4th Street N. St Petersburg, Florida 33703
Tel: 1 800 422 0711; Fax: 1 727 522 8304
Email: contactus@continuingeducation.net

American Association for Thoracic Surgery (AATS) 92nd Annual Meeting 2012
Apr 28 - May 02, 2012
San Francisco, CA, United States
Contact: Meeting Organiser: American Association for Thoracic Surgery (AATS)
Tel: 978-927-8330; Fax: 978-524-8890

Family Medicine: Improving Your Outcomes through Diagnosis and Treatment
Apr 30 - May 4, 2012
Hyatt Regency, Sarasota, FL, United States
Contact: D. Reece Pierce, PA-C, P.O. Box 49947
Tel: 866-267-4263; Fax: 941-365-7073
Email: mail@ams4cme.com

8th International Congress on Mental Dysfunction & Other Non-Motor Features in Parkinson's Disease and Related Disorders
May 3 - 6, 2012
Intercontinental Berlin Hotel, Berlin, Germany
Contact: The Seventh International Congress on Vascular Dementia, 1-3 Rue de Chantepoulet, CH-1211 Geneva 1 Switzerland
Tel: +41 22 908 0488
Email: mdpd@kenes.com

12th International Conference on Cochlear Implants and other Implantable Auditory Technologies
May 3 - 5, 2012
Baltimore, MD, United States
Sponsoring Organization: Johns Hopkins University (JHU)
Contact: Corinne Aderhold, 1101 North Delaware, Suite 200, Indianapolis, IN 46202
Tel: 1-317-635-4755; Fax: 1-317-635-4757
Email: corinnea@cmcglobal.com

Immunology 2012: 99th Annual Meeting of the American Association of Immunologists
May 04 - 08, 2012
Boston, MA, United States
Contact: Meeting Organiser: The American Association of Immunologists
Tel: 301-634-7178; Fax: 301-634-7887
E-mail: meetings@aai.org

30th Annual Meeting of the European Society for Paediatric Infectious Diseases
May 8 - 11, 2012
HELEXPO, Thessaloniki, Greece
Contact: Kenes International, 1-3 Rue de Chantepoulet
Tel: 41 22 908 0488; Fax: 41 22 732 2850
Email: espid@kenes.com

12th International Stockholm/Springfield Symposium on Advances in Alzheimer Therapy
May 9 - 12, 2012
City Conference Centre, Stockholm, Sweden
Contact: Ann Hamilton, SIU, Office of CME, PO Box 19602, Springfield, IL 62794-9602, USA
Tel: +1-217-545-7711; Fax: +1-217-545-4413
Email: ahamilton@siumed.edu

HIV Management 2012: The New York Course
May 10 - 11, 2012
The Hudson Theater, New York, NY, United States
Contact: Julie Krantz, 1000 Franklin Village Dr # 103
Franklin, MA 02038
Tel: 888-391-3996; Fax: (508) 528-7880
Email: info@newyorkcourse.com

State of the Art Techniques: IMRT, IGRT, and SBRT
May 11 - 13, 2012
Encore at Wynn Las Vegas, Las Vegas, NV, United States
Type of Event: Conference
Contact: Sara Mansoor, 8280 Willow Oaks Corporate Drive, Suite 500, Fairfax, VA 22031
Tel: 703-502-1550
Email: education@astro.org

Rheumatology and Orthopaedics
May 11 - 21, 2012
Holland America’s ms Eurodam, Civitavecchia, Italy
Contact: Reservations, 5700 4th Street N. St Petersburg, Florida 33703
Tel: 1 800 422 0711; Fax: 1 727 522 8304
Email: contactus@continuingeducation.net

Pain Management/Neurology/Compliance
May 12 - 21, 2012
Royal Caribbean’s Vision of the Seas, Oslo, Norway
Contact: Reservations, 5700 4th Street N. St Petersburg, Florida 33703
Tel: 1 800 422 0711; Fax: 1 727 522 8304
Email: contactus@continuingeducation.net
Women’s Health
May 13 - 20, 2012
Holland America’s ms Veendam, New York, NY, United States
Contact: Reservations, 5700 4th Street N. St Petersburg, Florida 33703
Tel: 1 800 422 0711; Fax: 1 727 522 8304
Email: contactus@continuingeducation.net

International Research Congress for Integrative Medicine & Health
May 15 - 18, 2012
Mariott Hotel Downtown Waterfront, Portland, OR, United States
Contact: Karly Kopra, 2545 SW Spring Garden Street, Suite 150, Portland, OR 97219
Tel: 503-244-4294; Fax: 503-244-2401
Email: ircimh@conferencesolutionsinc.com

6th International Congress of the World Federation of Skull Base Societies
May 16 - 19, 2012
Hilton Brighton Metropole, Brighton, United Kingdom
Contact: Kenes UK, 1st Floor, Chesterfield House, Brighton, UK
Tel: +44 (0) 20 7383 8030
Email: skullbase@kenes.com

The 2nd Global Congress for Consensus in Pediatrics & Child Health
May 17 - 20, 2012
Radisson SAS Slavyanskaya, Moscow, Russia
Contact: Meital Fridenzon, 18 Avenue Louis-Casai, 1209 Geneva, Switzerland
Tel: 41 22 5330 948; Fax: 41 22 5330 948
Email: cip@cipediatrics.org

2nd International Meeting on Cardiac Problems in Pregnancy
May 17 - 20, 2012
Leonardo Royal Hotel, Berlin, Germany
Contact: Shirley Dinenson, 18 Avenue Louis-Casai, 1209 Geneva, Switzerland
Tel: +41 22 5330 948; Fax: +41 22 5802 953
Email: secretariat@cppcongress.com

ENT for the Primary Care Physician
May 18, 2012
Siebbs Medical Education Building, Rochester, MN, United States
Contact: MSCPD, 200 1st St. SW / Rochester MN
Tel: 800-323-2688; Fax: 507-284-0532
Email: cme@mayo.edu

Digestive Disease Week® (DDW)
May 19 - 22, 2012
San Diego Convention Center, San Diego, CA, United States
Contact: DDW Administration, 4930 Del Ray Avenue
Bethesda, MD 20814
Tel: 301-272-0022; Fax: 301-654-3978
Email: ddwadmin@gastro.org

11th International Congress of the European Society of Pediatric Otorhinolaryngology
May 20 - 23, 2012
Grand Hotel Krasnapolsky, Dam Square, Amsterdam, Netherlands
Contact: J. van Dulmen, Po Box 18, 5298 ZG Liempde, the Netherlands
Tel: +31 411 611199; Fax: +31 411 633805
Email: info@congresservice.nl

NYU’s Sports Medicine Imaging State of the Art 2012
May 21 - 24, 2012
NYU Langone Medical Center, New York, NY, United States
Contact: Michelle Koplik, 462 First Ave, New York, NY
Tel: 212-263-3936
Email: michelle.koplik@nymc.org

40th Annual Workshops in Clinical Hypnosis - Introductory and Advanced
Radisson Hotel and Conference Center, Minneapolis, MN, United States
Jun 2 - 4, 2011
Contact: Office of Continuing Medical Education, University Park Plaza, Ste 601; 2829 University Ave SE; Minneapolis, MN 55414
Tel: 612-626-7600 or 800-776-8636; Fax: 612-626-7766
Email: cme@umn.edu

2011 Pittsburgh Liver Update Symposium (2011 Plus)
William Pitt Union, Pittsburgh, PA, United States
Jun 3 - 4, 2011
Contact: Jill March, UPMC Montefiore, 3459 Fifth Avenue Room E-736, Pittsburgh, PA 15213
Tel: 412-647-9509; Fax: 412-802-8799
Email: marchjk@upmc.edu

CINP 2012 - Congress of the Internation College Neuropsychopharmacology
Jun 3-7, 2012
Stockholm, Sweden
Contact: Vivien Kitzing, Paulsborner Str. 44, Glasgow G74 3XH, Scotland UK
Tel: +49 30 300 669 0
Email: vkitzing@cpo-hanser.de
The 18th Annual Clinical Reviews and Primary Care Update
The Ritz-Carlton, Amelia Island, FL, United States
Jun 6 - 10, 2011
Contact: Denise Klarich, 4550 San Pablo Rd
Tele: 800-462-9633; Fax: 904-953-2954
Email: cme-jax@mayo.edu

Primary Care: Neurology Update 2012
Jun 9 - 16, 2012
Holland America’s ms Westerdam, Seattle, WA, United States
Contact: Reservations, 5700 4th Street N. St Petersburg, Florida 33703
Tel: 1 800 422 0711; Fax: 1 727 522 8304
Email: contactus@continuingeducation.n

Primary Care Update: Cardiac Health, Metabolic Syndrome, Obesity and Related Disorders
Jun 14 - 24, 2012
Holland America’s ms Eurodam, Copenhagen, Denmark
Contact: Reservations, 5700 4th Street N. St Petersburg, Florida 33703
Tel: 1 800 422 0711; Fax: 1 727 522 8304
Email: contactus@continuingeducation.n

Family Medicine: Dermatology Review
Jun 16 - 23, 2012
Holland America’s ms Westerdam, Seattle, WA, United States
Contact: Reservations, 5700 4th Street N. St Petersburg, Florida 33703
Tel: 1 800 422 0711; Fax: 1 727 522 8304
Email: contactus@continuingeducation.net

Dermatology for Primary Care
Jun 18 - 22, 2012
Hyatt Regency, Sarasota, FL, United States
Contact: D. Reece Pierce, P.O. Box 49947
Tel: 866-267-4263; Fax: 941-365-7073
Email: mail@ams4cme.com

Cardiomyocyte Regeneration and Protection
Hilton Torrey Pines, La Jolla, CA, United States
Jun 20 - 21, 2011
Contact: Katie, Abcam, 1 Kendall Sq., Suite 341, Cambridge, MA 02139
Tel: 6175774263
Email: ks@abcam.com

13th National Conference: Parkinson’s 2011: recent advances in clinical management
CBI Conference Centre, London, United Kingdom
Jun 21, 2011
Contact: Florence Doel, St Judes Church, Dulwich Road, Herne Hill, London SE24 0PB
Tel: +44 (0) 207 501 6762; Fax: +44 (0) 207 978 8319
Email: flo.doel@markallengroup.com

12th Congress of the European Society of Contraception and Reproductive Health
Jun 20 - 23, 2012
Athens, Greece
Contact: Nancy Habils
Tel: 32-2-582-0852; Fax: 32-2-582-5515
E-Mail: congress@contraception-esc.com

1st Gynecological Surgery Conference 2011
Kellogg Conference Hotel at Gallaudet University, Washington D.C, United States
Jun 23 - 25, 2011
Contact: Romy Meuter, 953 National Road, PMB#110, Wheeling, WV, 26003, USA
Tel: 1-800-662-0183; Fax: 1-800-662-0183
Email: romy@medineo.org

15th World Congress of Pain Clinicians
Jun 27 - 30, 2012
Granada Convention Center, Granada, Spain
Contact: Kenes International, 1-3 Rue de Chantepoulet, CH-1211 Geneva 1 Switzerland
Tel: +41 22 908 0488
Email: wspc2012@kenes.com

30th International Congress of Psychology - ICP 2012
Jul 22-27, 2012
Cape Town International Convention Centre, Cape Town, South Africa
Contact: Fatima Seedat, PO Box 989, Houghton 2041, South Africa
Tel: 011 486 3322; Fax: 011 486 3266
Email: info@icp2012.com

Family Medicine: A Review and Update of Common Clinical Problems
Jun 25 - 29, 2012
Hyatt Regency, Sarasota, FL, United States
Contact: D. Reece Pierce, PA-C, P.O. Box 49947
Tel: 866-267-4263; Fax: 941-365-7073
Email: mail@ams4cme.com
WHO-Facts Sheet

1. The Global Tobacco Epidemic
2. Diabetes & The World Diabetes Day
3. Action Needed to Reduce Health Impact of Harmful Alcohol Use
4. Threats from Both Infectious and Chronic Diseases
5. Ageing and the Life Course

Compiled and edited by
Babichan K Chandy

Kuwait Medical Journal 2011, 43 (4): 345 - 352

1. THE GLOBAL TOBACCO EPIDEMIC

Leading cause of death, illness and impoverishment

The tobacco epidemic is one of the biggest public health threats the world has ever faced. It kills nearly six million people a year of whom more than five million are users and ex-users and more than 600,000 are nonsmokers exposed to second-hand smoke. Approximately one person dies every six seconds due to tobacco and this accounts for one in 10 adult deaths. Up to half of current users will eventually die of a tobacco-related disease.

Nearly 80% of the more than one billion smokers worldwide live in low- and middle-income countries, where the burden of tobacco-related illness and death is heaviest. Tobacco users who die prematurely deprive their families of income, raise the cost of health care and hinder economic development.

In some countries, children from poor households are frequently employed in tobacco farming to provide family income. These children are especially vulnerable to “green tobacco sickness”, which is caused by the nicotine that is absorbed through the skin from the handling of wet tobacco leaves.

Key facts

- Tobacco kills up to half of its users.
- Tobacco kills nearly six million people each year, of whom more than five million are users and ex-users and more than 600,000 are nonsmokers exposed to second-hand smoke. Unless urgent action is taken, the annual death toll could rise to more than eight million by 2030.
- Nearly 80% of the world’s one billion smokers live in low- and middle-income countries.
- Consumption of tobacco products is increasing globally, though it is decreasing in some high-income and upper middle-income countries.

Gradual killer

Because there is a lag of several years between when people start using tobacco and when their health suffers, the epidemic of tobacco-related disease and death has just begun.

- Tobacco caused 100 million deaths in the 20th century. If current trends continue, it will cause up to one billion deaths in the 21st century.
- Unchecked, tobacco-related deaths will increase to more than eight million per year by 2030. More than 80% of those deaths will be in low- and middle-income countries.

Surveillance is key

Good monitoring tracks the extent and character of the tobacco epidemic and indicates how best to tailor policies. Fifty-nine countries, representing almost half of the world’s population, have strengthened their monitoring to include recent or representative data for both adults and youths, collecting this data at least every five years. Still, more than 100 countries either lack such data or have no data at all.

Second-hand smoke kills

Second-hand smoke is the smoke that fills restaurants, offices or other enclosed spaces when people burn tobacco products such as cigarettes, bidis and water pipes. There is no safe level of exposure to second-hand tobacco smoke. Every person should be able to breathe smoke-free air.

- Only nearly 11% of people are protected by comprehensive national smoke-free laws.
- The number of people protected from second-hand smoke is up to 11%.

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smoke more than doubled to 739 million in 2010, from 354 million in 2008.
• Of the 100 most populous cities, only 22 are smoke free
• Almost half of children regularly breathe air polluted by tobacco smoke
• Over 40% of children have at least one smoking parent
• Second-hand smoke causes more than 600,000 premature deaths per year
• In 2004, children accounted for 28% of the deaths attributable to second-hand smoke.
• There are more than 4000 chemicals in tobacco smoke, of which at least 250 are known to be harmful and more than 50 are known to cause cancer.
• In adults, second-hand smoke causes serious cardiovascular and respiratory diseases, including coronary heart disease and lung cancer. In infants, it causes sudden death. In pregnant women, it causes low birth weight.

Tobacco users need help to quit

Studies show that few people understand the specific health risks of tobacco use. For example, a 2009 survey in China revealed that only 37% of smokers knew that smoking causes coronary heart disease and only 17% knew that it causes stroke.

Among smokers who are aware of the dangers of tobacco, most want to quit. Counseling and medication can more than double the chance that a smoker who tries to quit will succeed.
• National comprehensive health-care services supporting cessation are available in only 19 countries, representing 14% of the world’s population.
• There is no cessation assistance in 28% of low-income countries and 7% of middle-income countries.

Picture warnings work

Hard-hitting anti-tobacco advertisements and graphic pack warnings – especially those that include pictures – reduce the number of children who begin smoking and increase the number of smokers who quit.

Studies carried out after the implementation of pictorial package warnings in Brazil, Canada, Singapore and Thailand consistently show that pictorial warnings significantly increase people’s awareness of the harms of tobacco use.

Mass media campaigns can also reduce tobacco consumption, by influencing people to protect non-smokers and convincing youths to stop using tobacco.
• Just 19 countries, representing 15% of the world’s population, meet the best practice for pictorial warnings, which includes the warnings in the local language and cover an average of at least half of the front and back of cigarette packs. No low-income country meets this best-practice level.
• Forty-two countries, representing 42% of the world’s population, mandate pictorial warnings.
• Graphic warnings can persuade smokers to protect the health of non-smokers by smoking less inside the home and avoiding smoking near children.
• More than 1.9 billion people, representing 28% of the world’s population, live in the 23 countries that have implemented at least one strong anti-tobacco mass media campaign within the last two years.

Ad bans lower consumption

Bans on tobacco advertising, promotion and sponsorship can reduce tobacco consumption.
• A comprehensive ban on all tobacco advertising, promotion and sponsorship could decrease tobacco consumption by an average of about 7%, with some countries experiencing a decline in consumption of up to 16%.
• Only 19 countries, representing 6% of the world’s population, have comprehensive national bans on tobacco advertising, promotion and sponsorship.
• Forty-six per cent of the world’s population lives in countries that do not ban free distribution of tobacco products.

Taxes discourage tobacco use

Tobacco taxes are the most effective way to reduce tobacco use, especially among young people and poor people. A tax increase that increases tobacco prices by 10% decreases tobacco consumption by about 4% in high-income countries and by up to 8% in low- and middle-income countries.
• Only 27 countries, representing less than 8% of the world’s population, have tobacco tax rates greater than 75% of the retail price.
• In countries with available information, tobacco tax revenues are 154 times higher than spending on tobacco control.

WHO response

WHO is committed to fight the global tobacco epidemic. The WHO Framework Convention on Tobacco Control entered into force in February 2005 and has become one of the most widely embraced treaties in the history of the United Nations with more than 170 Parties covering 87% of the world’s population. In 2008, WHO introduced a package of tobacco control measures to further counter the tobacco epidemic and to help countries to implement the WHO Framework Convention. Known by their acronym MPOWER, the
measures are identified as “best buys” and “good buys” in tobacco control. Each measure corresponds to at least one provision of the WHO Framework Convention on Tobacco Control.

The six MPOWER measures are:
• Monitor tobacco use and prevention policies
• Protect people from tobacco use
• Offer help to quit tobacco use
• Warn about the dangers of tobacco
• Enforce bans on tobacco advertising, promotion and sponsorship
• Raise taxes on tobacco.

For more information contact:
WHO Media centre. Telephone: +41 22 791 2222

2. DIABETES & THE WORLD DIABETES DAY

Started by the International Diabetes Federation (IDF) and WHO, the World Diabetes Day is celebrated on 14 November to mark the birthday of Frederick Banting who, along with Charles Best, was instrumental in the discovery of insulin in 1922, a life-saving treatment for diabetes patients. It is to raise global awareness of diabetes - its escalating rates around the world and how to prevent the illness in most cases.

WHO estimates that more than 220 million people worldwide have diabetes. This number is likely to more than double by 2030 without intervention. Almost 80% of diabetes deaths occur in low- and middle-income countries.

Key facts
• 346 million people worldwide have diabetes.
• In 2004, an estimated 3.4 million people died from consequences of high blood sugar.
• More than 80% of diabetes deaths occur in low- and middle-income countries.
• WHO projects that diabetes deaths will double between 2005 and 2030.
• Healthy diet, regular physical activity, maintaining a normal body weight and avoiding tobacco use can prevent or delay the onset of type 2 diabetes.

What is diabetes?
Diabetes is a chronic disease that occurs either when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin it produces. Insulin is a hormone that regulates blood sugar. Hyperglycemia, or raised blood sugar, is a common effect of uncontrolled diabetes and over time leads to serious damage to many of the body’s systems, especially the nerves and blood vessels.

Type 1 diabetes
Type 1 diabetes (previously known as insulin-dependent, juvenile or childhood-onset) is characterized by deficient insulin production and requires daily administration of insulin. The cause of type 1 diabetes is not known and it is not preventable with current knowledge.

Symptoms include excessive excretion of urine (polyuria), thirst (polydipsia), constant hunger, weight loss, vision changes and fatigue. These symptoms may occur suddenly.

Type 2 diabetes
Type 2 diabetes (formerly called non-insulin-dependent or adult-onset) results from the body’s ineffective use of insulin. Type 2 diabetes comprises 90% of people with diabetes around the world, and is largely the result of excess body weight and physical inactivity.

Symptoms may be similar to those of Type 1 diabetes, but are often less marked. As a result, the disease may be diagnosed several years after onset, once complications have already arisen. Until recently, this type of diabetes was seen only in adults but it is now also occurring in children.

Gestational diabetes
Gestational diabetes is hyperglycemia with onset or first recognition during pregnancy. Symptoms of gestational diabetes are similar to Type 2 diabetes. Gestational diabetes is most often diagnosed through prenatal screening, rather than reported symptoms.

Impaired glucose tolerance (IGT) and impaired fasting glycemia (IFG)
Impaired glucose tolerance (IGT) and impaired fasting glycemia (IFG) are intermediate conditions in the transition between normality and diabetes. People with IGT or IFG are at high risk of progressing to type 2 diabetes, although this is not inevitable.

What are common consequences of diabetes?
Over time, diabetes can damage the heart, blood vessels, eyes, kidneys, and nerves.
• Diabetes increases the risk of heart disease and stroke. 50% of people with diabetes die of cardiovascular disease (primarily heart disease and stroke).
• Combined with reduced blood flow, neuropathy in the feet increases the chance of foot ulcers and eventual limb amputation.
• Diabetic retinopathy is an important cause of
blindness, and occurs as a result of long-term accumulated damage to the small blood vessels in the retina. After 15 years of diabetes, approximately 2% of people become blind, and about 10% develop severe visual impairment.

- Diabetes is among the leading causes of kidney failure. 10-20% of people with diabetes die of kidney failure.
- Diabetic neuropathy is damage to the nerves as a result of diabetes, and affects up to 50% of people with diabetes. Although many different problems can occur as a result of diabetic neuropathy, common symptoms are tingling, pain, numbness, or weakness in the feet and hands.
- The overall risk of dying among people with diabetes is at least double the risk of their peers without diabetes.

**What is the economic impact of diabetes?**

Diabetes and its complications have a significant economic impact on individuals, families, health systems and countries. For example, WHO estimates that in the period 2006-2015, China will lose $558 billion in foregone national income due to heart disease, stroke and diabetes alone.

**How can the burden of diabetes be reduced?**

**Prevention**

Simple lifestyle measures have been shown to be effective in preventing or delaying the onset of type 2 diabetes. To help prevent type 2 diabetes and its complications, people should:

- achieve and maintain healthy body weight;
- be physically active – at least 30 minutes of regular, moderate-intensity activity on most days. More activity is required for weight control;
- eat a healthy diet of between three and five servings of fruit and vegetables a day and reduce sugar and saturated fats intake;
- avoid tobacco use – smoking increases the risk of cardiovascular diseases.

**Diagnosis and treatment**

Early diagnosis can be accomplished through relatively inexpensive blood testing.

Treatment of diabetes involves lowering blood glucose and the levels of other known risk factors that damage blood vessels. Tobacco use cessation is also important to avoid complications.

Interventions that are both cost saving and feasible in developing countries include:

- moderate blood glucose control. People with type 1 diabetes require insulin; people with type 2 diabetes can be treated with oral medication, but may also require insulin;
- blood pressure control;
- foot care.
- Other cost saving interventions include:
  - screening and treatment for retinopathy (which causes blindness);
  - blood pressure control (to regulate cholesterol levels);
  - screening for early signs of diabetes-related kidney disease.

These measures should be supported by a healthy diet, regular physical activity, maintaining a normal body weight and avoiding tobacco use.

The WHO Global strategy on diet, physical activity and health complements WHO’s diabetes work by focusing on population-wide approaches to promote healthy diet and regular physical activity, thereby reducing the growing global problem of overweight and obesity.

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**3. ACTION NEEDED TO REDUCE HEALTH IMPACT OF HARMFUL ALCOHOL USE**

Wider implementation of policies is needed to save lives and reduce the health impact of harmful alcohol drinking, says a new report launched in February 2011, by WHO. Harmful use of alcohol results in the death of 2.5 million people annually, causes illness and injury to many more, and increasingly affects younger generations and drinkers in developing countries. Harmful use of alcohol is defined as excessive use to the point that it causes damage to health and often includes adverse social consequences.

**Global alcohol report**

The Global status report on alcohol and health analyses available evidence on alcohol consumption, consequences and policy interventions at global, regional and national levels.

“Many countries recognize the serious public health problems caused by the harmful use of alcohol and have taken steps to prevent the health and social burdens and treat those in need of care. But clearly much more needs to be done to reduce the loss of life and suffering associated with harmful alcohol use,” says Dr Ala Alwan, WHO Assistant Director-General for Noncommunicable Diseases and Mental Health.

**Health implications**

Harmful use of alcohol has many implications on public health.
- Nearly 4% of all deaths are related to alcohol.
Most alcohol-related deaths are caused by alcohol result from injuries, cancer, cardiovascular diseases and liver cirrhosis.

- Globally, 6.2% of all male deaths are related to alcohol, compared to 1.1% of female deaths. One-in-five men in the Russian Federation and neighboring countries die due to alcohol-related causes.
- Globally, 320 000 young people aged 15-29 years die annually, from alcohol-related causes, resulting in 9% of all deaths in that age group.

Too few countries use effective policy options to prevent death, disease and injury from alcohol use. From 1999, when WHO first began to report on alcohol policies, at least 34 countries have adopted some type of formal policies to reduce harmful use of alcohol. Restrictions on alcohol marketing and on drink-driving have increased, but there are no clear trends on most preventive measures. Many countries have weak alcohol policies and prevention programs.

Effective strategies

The Global Strategy to reduce the harmful use of alcohol, endorsed by WHO’s Member States in May 2010, promotes a range of proven effective measures for reducing alcohol-related harm. These include taxation on alcohol to reduce harmful drinking; reducing availability through allowing fewer outlets to sell alcohol, raising age limits for those buying and using effective drink-driving measures.

The Global Strategy also promotes the screening and brief interventions in healthcare settings to change hazardous patterns of drinking, and treatment of alcohol use disorders; regulating or banning marketing of alcoholic beverages; and conducting information and educational campaigns in support of effective policy measures.

Consumption

Worldwide consumption in 2005 was equal to 6.13 liters of pure alcohol consumed per person aged 15 years or older, according to the report.

Despite widespread consumption, most people do not drink. Almost half of all men and two-thirds of women did not consume alcohol in 2005, according to the latest information made available in the report. Abstention rates are low in high-income, high consumption countries, and higher in North African and South Asian countries. But those who do drink in countries with high abstention rates consume alcohol at high levels.

Harmful alcohol use is one of four common risk factors, along with tobacco use, poor diet and physical inactivity, for the four main groups of noncommunicable diseases (NCDs) – cardiovascular diseases, cancer, chronic lung diseases and diabetes.

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4. THREATS FROM BOTH INFECTIOUS AND CHRONIC DISEASES

New data site makes WHO data and analyses widely available

An increasing number of countries are facing a double burden of disease as the prevalence of risk factors for chronic diseases such as diabetes, heart diseases and cancers increase and many countries still struggle to reduce maternal and child deaths caused by infectious diseases, for the Millennium Development Goals, according to the World Health Statistics 2011 released by the World Health Organization (WHO) in May 2011.

Noncommunicable diseases such as heart diseases, stroke, diabetes and cancer, now make up two-thirds of all deaths globally, due to the population aging and the spread of risk factors associated with globalization and urbanization. The control of risk factors such as tobacco use, sedentary lifestyle, unhealthy diet and excessive use of alcohol becomes more critical. The latest WHO figures showed that about 4 out of 10 men and 1 in 11 women are using tobacco and about 1 in 8 adults is obese.

In addition, many developing countries continue to battle health issues such as pneumonia, diarrhoea and malaria that are most likely to kill children under the age of five. In 2009, 40% of all child deaths were among newborns (aged 28 days or less). Much more needs to be done to achieve the MDGs by the target date of 2015, but progress has accelerated:

- Child mortality declined at 2.7% per year since 2000, twice as fast as during the 1990s (1.3%). Mortality among children under five years fell from 12.4 million in 1990 to 8.1 million in 2009.
- Maternal mortality declined at 3.3% per year since 2000, almost twice as fast in the decade after 2000 than during the 1990s (2%). The number of women dying as a result of complications during pregnancy and childbirth has decreased from 546,000 in 1990 to 358,000 in 2008.

“This evidence really shows that no country in the world can address health from either an infectious disease perspective or a noncommunicable disease one. Everyone must develop a health system that addresses the full range of the health threats in both areas,” says Ties Boerma, Director of WHO’s Department of Health Statistics and Informatics.
The report also shows that more money is being spent on health and people can expect to live longer (life expectancy in 2009 was 68 years, up from 64 years in 1990); but the gap in health spending between low- and high-income countries remains very large.

- In low-income countries, per capita, health expenditure is an estimated USD 32 (or about 5.4% of gross domestic product) and in high-income countries it is US$ 4590 (or about 11% of gross domestic product).
- High-income countries have, per capita, on average 10 times more doctors, 12 times more nurses and midwives and 30 times more dentists than low-income countries.
- Virtually all deliveries of babies in high-income countries are attended by skilled health personnel; but this is the case for only 40% of deliveries in low-income countries.

World Health Statistics 2011 is an annual report based on more than 100 health indicators reported by WHO’s 193 Member States and other reliable sources. These data provide a snapshot of the global health situation and trends. However, timely, accurate health information is hard to obtain in some parts of the world, because the country health information systems are weak.

The release of the report coincides with the launch of WHO’s new Global Health Observatory, a new website that serves as a one-stop shop for data and analyses on health priorities around the world. The Observatory provides easy access to the world’s largest and most comprehensive collection of health data, bringing together WHO’s data from all major health and disease programmes. It includes easy access to over 50 databases and 800 indicators with analyses of the global health situation and trends, covering priority health topics such as child, maternal and reproductive health, infectious diseases, noncommunicable diseases and risk factors, environmental health, mortality and burden of diseases, road safety, health systems and equity. An online version of the World Health Statistics dataset is also available through the Observatory.

The World Health Statistics 2011 can be found at: http://www.who.int/gho/publications/en/

Chronic diseases and health promotion

Chronic diseases, such as heart disease, stroke, cancer, chronic respiratory diseases and diabetes, are by far the leading cause of mortality in the world, representing 60% of all deaths. Out of the 35 million people who died from chronic disease in 2005, half were under 70 and half were women.

This invisible epidemic is an under-appreciated cause of poverty and hinders the economic development of many countries. Contrary to common perception, 80% of chronic disease deaths occur in low and middle income countries.

10 Facts on physical activity

Physical inactivity is the fourth leading risk factor for global mortality. Increasing levels of physical inactivity are seen worldwide, in high-income countries as well as low- and middle-income countries.

However, given a supportive environment, increasing levels of physical activity bring health benefits across age groups. WHO provides recommendations for the optimal amounts of activity, but doing some physical activity is better than doing none. Inactive people should start with small amounts of physical activity and gradually increase duration, frequency and intensity over time.

All sectors and all levels within governments, international partners, civil society, non-governmental organizations and the private sector have vital roles to play in shaping healthy environments and contributing to the promotion of physical activity.

What we do

Promote: Promote healthy living (better diet, more physical activity and tobacco cessation) and healthy societies, especially for the poor and those living in disadvantaged populations.

Prevent: Prevent premature deaths and avoid unnecessary disability due to chronic diseases. The solutions exist now, and many are simple, cheap and cost effective.

Treat: Treat chronic diseases effectively, using latest available knowledge. Make treatment available to all, especially those in the poorest settings.

Care: Help provide appropriate care by facilitating equitable and good quality health care for major chronic diseases.

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5. AGEING AND THE LIFE COURSE

What is “active ageing”?

In almost every country, the proportion of people aged over 60 years is growing faster than any other age group, as a result of both longer life expectancy and declining fertility rates. This population ageing can be seen as a success story for public health policies and for socioeconomic development, but it also challenges society to adapt, in order to maximize the health and functional capacity of older people as well as their social participation and security.

Active ageing is the process of optimizing opportunities for health, participation and security in order to enhance quality of life as people age. It applies to both individuals and population groups.

Active ageing allows people to realize their potential for physical, social, and mental well-being throughout the life course and to participate in society, while providing them with adequate protection, security and care when they need.

The word “active” refers to continuing participation in social, economic, cultural, spiritual and civic affairs, not just the ability to be physically active or to participate in the labor force. Older people who retire from work, ill or live with disabilities can remain active contributors to their families, peers, communities and nations. Active ageing aims to extend healthy life expectancy and quality of life for all people as they age.

“Health” refers to physical, mental and social well being as expressed in the WHO definition of health. Maintaining autonomy and independence for the older people is a key goal in the policy framework for active ageing.

Ageing takes place within the context of friends, work associates, neighbors and family members. This is why interdependence as well as intergenerational solidarity are important tenets of active ageing.

10 FACTS

Ageing and the life course

The ageing of the world’s population - in developing and developed countries - is an indicator of improving global health. The world’s elderly population - people 60 years of age and older - is 650 million. By 2050, the “greying” population is forecast to reach 2 billion.

Special health challenges for the 21st century starts with preparing health providers and societies to meet the needs of older populations such as: training for health professionals on old-age care; preventing and managing age-associated chronic diseases; designing sustainable policies on long-term and palliative care; and developing age-friendly services and settings.

The world’s elderly population - people 60 years of age and older - is the fastest growing age group

Ageing is a global phenomenon. By 2050 about 80% of older people will be living in less developed countries. Population ageing is occurring in parallel with rapid urbanization: in 2007 more than half of the world’s population live in cities. By 2030 that figure is expected to rise to more than 60%.

Population ageing is a triumph of modern society

It reflects improving global health, but also raises special challenges for the 21st century in both developing and developed countries. In 2005, life expectancy in countries like Japan and France was already more than 80 years. Life expectancy is also rising in developing countries. For example, a child born today in Chile, Costa Rica, Jamaica, Lebanon, Sri Lanka or Thailand can expect to live for more than 70 years.

There are vast differences in life expectancy at birth between countries

Vast health inequalities persist, as is clear from differences in life expectancy at birth. For example, while Japan has the highest life expectancy in the world at 82.2 years, in several countries in Africa the figure is 40 years lower.

Within countries, health inequalities are also significant

In the United States of America, for example, higher socioeconomic groups can expect to live up to 20 years longer than people from lower socioeconomic groups.

By 2050, close to 80% of all deaths are expected to occur in people over 60

Health expenditures increase with age but are concentrated in the last two years of life, regardless of how old someone is. As people live longer, it is important to ensure these added years are healthy so that health-care costs can be kept manageable.

Investing in health throughout life produces dividends for societies

Healthy older people represent a resource for their families, communities and economies. It is rarely too late to change risky behaviors to promote health: for example, the risk of premature death decreases by 50% if someone gives up smoking between 60 and 75 years of age.

Effective, community-level primary health care for older people is crucial to promote health, prevent disease and manage chronic illnesses.

In general, training for health professionals includes little if any instruction about specific care for older people. However, they will increasingly
spend time caring for this section of the population. Health providers should be trained on ageing issues, regardless of their profession.

**Disasters and emergencies severely impact older people**

The highest percentage of fatalities caused by the 2004 Indian Ocean tsunami in Indonesia was in people 60 years of age and older, and the majority of the 2003 heat wave victims in Europe were people 70 years of age and older. Policies to protect older persons during emergencies are urgently required.

**In older age, the risk of falls increases and injuries are far more serious**

This leads to significant health, human and economic costs. In Australia, the average health system cost of one fall-related injury for people 65 years of age and older was US$ 3611 in 2001-2002.

**Elder abuse is on the increase as the population ages and social dynamics change**

WHO estimates that between 4% and 6% of older persons worldwide have suffered from a form of elder abuse - either physical, psychological, emotional, financial or due to neglect. Elder abuse is an infringement of human rights.

**Emergencies and Older People**

Emergency situations are increasing worldwide and older people remain one of the most seriously affected groups. Yet, the needs and contributions of older people are generally overlooked by humanitarian organizations in terms of policy and practice.

There are specific health and social factors that can, separately or in combination, affect older persons and impact on them during an emergency situation. These include:

- physical health,
- oral health and dentition,
- mental health,
- functional status and disability,
- lifestyle habits,
- nutrition,
- family and social relations,
- economic situation, and
- gender considerations.

Consideration of these issues within the context of later life can help ensure that older people at risk can be identified before, during and following an emergency situation. For WHO, older people are not simply a vulnerable population group. Rather, very resilient and their knowledge of their community, experience with past emergencies as well as positions of respect within families and communities, makes them valuable resources that should be drawn upon.

Awareness of the needs and contributions of older persons among those developing policies and guidelines and providing care can contribute to more effective interventions, including equitable access to essential health and social services to older people during all phases of an emergency.

**WHO Age-Friendly Environments Program**

The Age-friendly Environments Program is an international effort by WHO to address the environmental and social factors that contribute to active and healthy ageing in societies.

**Rationale**

- In 2000, the global population of people aged 60 and over was 600 million; by 2025 there will be 1.2 billion and, by 2050, almost 2 billion.
- The proportion of the global population aged 60 will double from 11% in 2006 to 22% by 2050.
- Older people play a crucial role in communities - in paid or volunteering work, transmitting experience and knowledge, or helping their families with caring responsibilities. These contributions can only be ensured if older persons enjoy good health and if societies address their needs.
- Making cities age-friendly is one of the most effective policy approaches for responding to demographic ageing.
- In 2008, for the first time in history, the majority of the world’s population lived in cities and by 2030; approximately 3 out of every 5 people will live in an urban area.
Acquired Factor VIII Inhibitor in a Patient with Mixed Connective Tissue Disease: A Case Report. 43(3) 238 - 240

Acute Bilateral Cataract in a Non-Complicated Type 1 Diabetic Youngster: A Case Report. 43(4) 321 - 323

Allergenicity to Allergens like *Prosopis juliflora* and Date Tree Pollens in Saudi Arabia. 43(2) 109 - 112

Appendicitis Caused by Accidentally Ingested Metallic Pin: A Case Report. 43(3) 241 - 243

Atypical Presentation of Vibro Cholera. 43(4) 324 - 326

Autoimmune Adrenal Insufficiency Antedates the Diagnosis of SLE, Does It Really Matter?. 43(2) 136 - 138

Autoimmune Polyendocrinopathy – Candidiasis – Ectodermal Dystrophy Syndrome Presenting as Unexplained Chronic Interstitial Keratitis. 43(1) 44 - 46

Breastfeeding Malnutrition with Hypernatremic Dehydration: Case Report and Literature Review. 43(1) 57 - 59

Buried Bumper Syndrome. 43(2) 150 - 152

Caecal Cancinoma Presenting with Adult Intussusception. 43(4) 317 -320

Characterization of Acrylamide Mediated Testicular Toxicity in Rat: Light and Electron Microscopic Study. 43(2) 196 - 205

Chylous Leakage after Donor Nephrectomy a Rare Complication: Nightmare for Surgeons. 43(4) 277 - 280

Combination of Ballistic Lithotripsy and Transurethral Plasmakinetic Resection for Treating 200 Men with Bladder Calculi and Benign Prostatic Hyperplasia: A Trial with 2-Year Follow-Up. 43 (3) 213 - 215

Colo- Colic Intussusception in Amoebic Colitis: A Case Report. 43(4) 307 -309

Complex Regional Pain Syndrome in a Child; The First Case Report from Kuwait. 43(3) 244 - 246

Complications of Brucellosis in Adults: An Experience from a State Hospital in Southeastern Anatolia Region of Turkey. 43(3) 206 -212

Correlation of Fine Needle Aspiration Cytologic Features of Extrapulmonary Tuberculous Lesions with detection of Acid Fast Bacilli – Mubarak Al-Kabeer Hospital, Kuwait Experience. 43(3) 216 - 219

Duodenal Diverticulum Mimicking Pancreatic Abscess. 43(3) 224 - 226

Ecthyma Gangrenosum with Pseudomonas Sepsis in Previously-Healthy Child. 43(1) 47 - 49

Evaluation of Insulin Resistance by the Homeostasis Model Assessment in Female Patients with Primary Sjögren’s Syndrome. 43(3) 220 - 223

Factors Associated with Patients Bypassing Primary Health Care Facilities in Saudi Arabia: A Cross-Sectional Study. 43(1) 26 - 32

Fenofibrate-Induced Rhabdomyolisis in a Dialysis Patient with Subclinical Hypothyroidism– Case Report. 43(3) 227 - 229

Fine Needle Aspiration Cytology in the Diagnosis of Superficial Lymphadenopathy in Children and Adolescents: An analysis of 869 cases. 43(1) 33 - 36

Gastrointestinal Sarcoidosis: A Case Report. 43(1) 60 - 63

Inducible Clindamycin Resistance in *Staphylococcus Aureus*: A Study from a Tertiary Care Hospital of North India. 43(2) 105 -108

Laparoscopic Removal of a Foreign Body from the Intestine. 43(1) 41- 43

Laparoscopic Treatment of Gallbladder Duplication. 43(1) 50 - 52
Laparoscopic Appendectomy in the Third Trimester of Pregnancy: Report of Two Cases and Description of Technique. 43(2)133 - 135

Late-Onset Chylothorax after a Pneumonectomy for Lung Cancer: a Case Report. 43(2) 143 - 145

Lung Cancer Screening: An insight. 43(4) 267 - 268

Macroinvasive Papillary Thyroid Carcinoma Presenting as Internal Jugular Vein Tumor Thrombus. 43(2) 139 - 142

Magical Mem-Brain- Biology’s Holy Grail. 43(3) 173 - 175

Massive Bleeding in Trauma and Surgery: Role of rFVIIa. 43(4) 269 -276

Multifocal Solitary Subungual Glomus Tumors in a Patient with Neurofibromatosis Type 1. 43(2) 130 -132

Osteoarthritis of the Knee: Review of Risk Factors and Treatment Programs with Special Reference to Evidence-Based Research. 43(3) 176 - 188

Pattern of Chromosomal Abnormalities in Pediatric Acute Lymphoblastic Leukemia (ALL). 43(2) 118 - 124

Papillary Microcarcinomas of the Thyroid Gland: Do We Need to be Aggressive in the Management? 43(4) 297 -300

Pediatric Obstructive Sleep Apnea Syndrome. 43(1) 6 - 15

Persistent Left Superior Vena Cava Draining into the Left Atrium with a Large Primum Atrial Septal Defect - 43(1) 53 - 56

Postgraduate Residency Training Program in Kuwait - Courses to Competencies : A shifting Paradigm. 43(1) 1 – 5

Post- Infantile Presentation of Intestinal Malrotation. 43(4) 281 - 286

Pregnancy-Associated with Brucellosis and Acute Viral Hepatitis: Course and Outcome (Coinfections in Pregnancy). 43(2) 113- 117

Quantitative Postural Sway Assessment by Computerized Dynamic Posturography in Athletes with Chronic Ankle Sprain and Normal Subjects in Kuwait. 43(2) 99 - 104

Re-appraisal of Vaginal Delivery after Previous Two Cesarean Sections. 43(3) 189 – 195

Related Factors for Rectosigmoid Hyperplastic Polyps: A Hospital-Based Study. 43(4) 301 - 306

Short-lasting Unilateral Neuralgiform Headache Attacks with Conjunctival Injection and Tearing (SUNCT) Syndrome Secondary to Pituitary Apoplexy. 43(4) 327 - 329

Small Cell Carcinoma Metastatic to the Appendix, with Acute Suppurative Appendicitis. 43(4) 313 - 316

Splenic Vein Thrombosis: A Rare Complication of Coeliac Disease. 43(3) 230 – 233

Squamous Intraepithelial Lesions Associated with HIV Infection and CD4+ Cell Counts in an Iranian Population. 43(4) 291 - 296

The Diagnostic Value of Sinus-Track Cultures in Secondary Pediatric Chronic Osteomyelitis . 43(2) 125 - 129

The Effect of Oxygenation Technique in General Anesthesia on Postoperative Nausea and Vomiting. 43(1) 37 – 40

The Knowledge of Teratogenicity in the Prevention of Congenital Anomalies. 43(2) 89 – 98

The Role of Trace Elements in Helicobacter Pylori Infected Patients. 43(4) 287 - 290

The Treatment of Chronic Monteggia Lesions and Chronic Traumatic Isolated Radial Head Dislocations. 43(1) 16 - 19

Thyroid Hemi-agenesis: Case Report and Review of Literature. 43(2) 146 - 149

Traumatic Anterior Hip Dislocation (Perineal) with Ipsilateral Avulsion Fracture of the Greater and Lesser Trochanter in an Adolescent. 43(3) 234 – 237

Unusual Presentation of Organic Foreign Body in Upper Aero Digastrics Tract: Report of Two Cases. 43(4) 310 - 312

Value of Abdominal Pressure Measurement in Neonatal Abdominal Surgical Emergencies. 43(1) 20 - 25

What We Need is Not the Will to Believe, but the Will to Find Out. 43(2) 87 - 88
## Yearly Author Index

**Kuwait Medical Journal (KMJ) 2011; Volume 43**


<table>
<thead>
<tr>
<th>Name</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdulla HM</td>
<td>238</td>
</tr>
<tr>
<td>Abdullatif</td>
<td>1</td>
</tr>
<tr>
<td>Abdul-Malik A</td>
<td>244</td>
</tr>
<tr>
<td>Abdulsalam S</td>
<td>324</td>
</tr>
<tr>
<td>Ahmed MM</td>
<td>99</td>
</tr>
<tr>
<td>Al Anbai MM</td>
<td>53</td>
</tr>
<tr>
<td>Al Ansary TA</td>
<td>216</td>
</tr>
<tr>
<td>Al-Ansary TA</td>
<td>33</td>
</tr>
<tr>
<td>Al-Abdoulsalam T</td>
<td>6</td>
</tr>
<tr>
<td>Al-Ajmi AM</td>
<td>60</td>
</tr>
<tr>
<td>Al-Bader</td>
<td>1</td>
</tr>
<tr>
<td>Al-Busairi WA</td>
<td>99</td>
</tr>
<tr>
<td>Al Duajj S</td>
<td>327</td>
</tr>
<tr>
<td>Al enezi I</td>
<td>139</td>
</tr>
<tr>
<td>Al enezi AQKHS</td>
<td>230</td>
</tr>
<tr>
<td>Al-Fadlhi M</td>
<td>324</td>
</tr>
<tr>
<td>Al feeli A</td>
<td>99</td>
</tr>
<tr>
<td>Alghanim SA</td>
<td>26</td>
</tr>
<tr>
<td>Al-Harbash Z</td>
<td>244</td>
</tr>
<tr>
<td>Al-Humoud H</td>
<td>238</td>
</tr>
<tr>
<td>Al humoud E</td>
<td>238</td>
</tr>
<tr>
<td>Al jamaan E</td>
<td>136</td>
</tr>
<tr>
<td>Al Jarallah MA</td>
<td>53</td>
</tr>
<tr>
<td>Al-Jazzaf M</td>
<td>327</td>
</tr>
<tr>
<td>Aljumah A</td>
<td>224</td>
</tr>
<tr>
<td>Al-Muhaiteeb A</td>
<td>150</td>
</tr>
<tr>
<td>Al Mukaimi A</td>
<td>176</td>
</tr>
<tr>
<td>Al mulhim AS</td>
<td>20, 281</td>
</tr>
<tr>
<td>Al mutairi AF</td>
<td>41</td>
</tr>
<tr>
<td>Al mutairi AFM</td>
<td>146</td>
</tr>
<tr>
<td>Al Nassar M</td>
<td>321</td>
</tr>
<tr>
<td>Al Nuaime LA</td>
<td>189</td>
</tr>
<tr>
<td>Al-Othman K</td>
<td>244</td>
</tr>
<tr>
<td>Al Qubati A</td>
<td>297</td>
</tr>
<tr>
<td>Al Saadi A</td>
<td>297</td>
</tr>
<tr>
<td>Al saleh RFS</td>
<td>146</td>
</tr>
<tr>
<td>Al-Sarraf L</td>
<td>241</td>
</tr>
<tr>
<td>Al Senebani J</td>
<td>297</td>
</tr>
<tr>
<td>Al Shammeri AR</td>
<td>321</td>
</tr>
<tr>
<td>Al-sharkawi IA</td>
<td>57</td>
</tr>
<tr>
<td>Al-Sihan M</td>
<td>41</td>
</tr>
<tr>
<td>Ali JI</td>
<td>60</td>
</tr>
<tr>
<td>Ali zadeh K</td>
<td>37</td>
</tr>
<tr>
<td>Al saeed AH</td>
<td>109</td>
</tr>
<tr>
<td>Al Saggaf S</td>
<td>196</td>
</tr>
<tr>
<td>Al wadan A</td>
<td>297</td>
</tr>
<tr>
<td>Amiri Z</td>
<td>291</td>
</tr>
<tr>
<td>Ansari MM</td>
<td>310</td>
</tr>
<tr>
<td>Arumolichelvan A</td>
<td>307</td>
</tr>
<tr>
<td>Aslan S</td>
<td>113</td>
</tr>
<tr>
<td>Ayaz C</td>
<td>125</td>
</tr>
<tr>
<td>Ayed AK</td>
<td>267</td>
</tr>
<tr>
<td>Ayuob N</td>
<td>196</td>
</tr>
<tr>
<td>Aziz HA</td>
<td>44</td>
</tr>
<tr>
<td>Bajaj JS</td>
<td>1</td>
</tr>
<tr>
<td>Bansal N</td>
<td>105</td>
</tr>
<tr>
<td>Baqer AB</td>
<td>99</td>
</tr>
<tr>
<td>Beg MH</td>
<td>310</td>
</tr>
<tr>
<td>Behbehani AM</td>
<td>230</td>
</tr>
<tr>
<td>Belgrami SFH</td>
<td>50</td>
</tr>
<tr>
<td>Barouti E</td>
<td>291</td>
</tr>
<tr>
<td>Bozkurt F</td>
<td>287</td>
</tr>
<tr>
<td>Buhaired W</td>
<td>133</td>
</tr>
<tr>
<td>Can-Ulug N</td>
<td>206</td>
</tr>
<tr>
<td>Celen MK</td>
<td>125</td>
</tr>
<tr>
<td>Cetinkaya R</td>
<td>227</td>
</tr>
<tr>
<td>Chavan VNK</td>
<td>241</td>
</tr>
<tr>
<td>Chaudhary U</td>
<td>105</td>
</tr>
<tr>
<td>Das DK</td>
<td>33</td>
</tr>
<tr>
<td>Dashti K</td>
<td>224</td>
</tr>
<tr>
<td>Ding M</td>
<td>213</td>
</tr>
<tr>
<td>Dorman V</td>
<td>113</td>
</tr>
<tr>
<td>ElAssouli S</td>
<td>196</td>
</tr>
<tr>
<td>Elezeby A</td>
<td>50</td>
</tr>
<tr>
<td>Elezeby AF</td>
<td>139</td>
</tr>
<tr>
<td>El Gebely S</td>
<td>321</td>
</tr>
</tbody>
</table>
El Salawi E ............................................ 176  Owayed SF ............................................. 60
Elsherbiny MMS ................................. 139  Ozturk A ................................................. 143
Elsori H ................................................. 44  Pandittrao M ........................................... 269
Eltair M .................................................. 317  Pandittrao M ........................................... 269
Farzaneh F ........................................... 291  Pathan SK ............................................... 33
George SS ............................................. 33  Poovathumkadavil AJ ............................. 317
George SS ............................................. 216  Pranati M ................................................ 118
Geyik MF ............................................... 287  Prasad S .................................................. 307
Ghosh S .................................................. 130  Qiu L ....................................................... 313
Gopal R ............................................... 130  Raghumani M ........................................... 118
Grover VK ............................................ 50  Rahimi F ................................................... 307
Gulsun S .............................................. 113, 287  Rajeh N ................................................. 196
Gul T ..................................................... 113  RajLaxmi S ............................................. 118
Gulle AA ................................................ 143  Ramachandra L ........................................ 307
Gupta R .................................................. 241  Rashid MA ................................................ 130
Gupta V .................................................. 105  Ray MK .................................................... 277
Gursoy S ............................................... 143  Rifai M ..................................................... 47
Haji BE .................................................. 33, 216  Roach JW .................................................. 16
Harfi H .................................................. 109  Rupa D ..................................................... 118
Hariri AM ............................................. 57  Saltzman HM ........................................... 16
Heberle J ............................................. 234  Samuel AS ................................................ 89
Hegde BM ............................................. 87, 173  Sarac F ................................................... 220
Hosoglu S ............................................. 287  Saraya M ................................................... 324
Hilal JM .................................................. 230  Sari F ....................................................... 227
Hussain YA .......................................... 41  Sarikaya M ................................................ 227
Hussein YAS ........................................ 146  Shahami M .............................................. 291
Jaragh M ............................................... 216  Shamsa M ............................................... 269
Jawad M ............................................... 327  Sharma PK ................................................ 277
Kabasakal Y ....................................... 220  Shyam PS .................................................. 313
Kamal AM ........................................... 20, 281  Sinha K .................................................... 277
Kapila K ................................................ 33  Somanath P ............................................. 118
Kapila K ................................................ 216  Sukumar C ............................................... 118
Karbasi H ............................................. 37  Ulug M ..................................................... 125
Karabulut G ........................................ 220  Ulug M ..................................................... 206
Keyghobadi .......................................... 291  Ustun C .................................................... 287
Kitapcioglu G ..................................... 220  Vijay MK .................................................... 277
Lai S ..................................................... 301  Vijay P ..................................................... 277
Liao K ................................................... 301  Wang J ..................................................... 213
Lindstrand A ........................................ 176  Wang H ..................................................... 213
Meshikhes A ....................................... 317  Wittmans M ............................................... 6
Mishra PK ............................................. 277  Yang D ..................................................... 213
Mokaddas EE ....................................... 216  Yan R ....................................................... 213
Narayanan S ....................................... 150  Yilmaz C ................................................ 220
Naseh G ............................................... 37  Zea MI ..................................................... 310
Necmioglu S ....................................... 125  Zhu M ....................................................... 313
Omar NG ............................................. 57  Zuo Y ....................................................... 213