Original Article

Is Brucellosis a Common Infectious Cause of Pyrexia of Unknown Origin in Kuwait?

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ABSTRACT

Objectives: To investigate the prevalence of brucellosis and to compare it with other causes of pyrexia of unknown origin (PUO) in Kuwait
Design: Retrospective study
Setting: Infectious Disease Hospital, Kuwait
Subjects: All patients admitted to Infectious Disease Hospital with a diagnosis of PUO between January 2001 and December 2004 were included in this study.
Main Outcome Measures: Age, gender, nationality, occupation, residence and laboratory investigations
Results: One hundred thirty six patients were admitted with PUO to the hospital. Their mean age was 36.7 ± 11.69 years (range: 14-80 years). The mean duration of hospitalization was 8.7 ± 7.8 days. Infectious diseases were the most common causes of PUO. Brucellosis was diagnosed in 80 (58.8%) patients, respiratory tract infection in 10 (7.4%), gastrointestinal diseases in 14 (10.3%) and HIV was diagnosed in three patients. Other diseases such as thyroiditis and glaucomatous hepatitis were diagnosed in 15 (11%) patients. Brucellosis patients had high alanine amino transferase (ALT) level and lower white blood cell (WBC) count than other PUO patients (56.9 ± 40.6 Vs. 38 ± 31.4, $p < 0.003$ and 7.1 ± 3.9 Vs. 8.5 ± 4.04, $p < 0.01$ respectively). Brucellosis was common among Asian population (58.8% compared to Gulf residents 31.3% and other nationals 10%, $p = 0.022$). Brucellosis is common among patients in high-risk occupations (62.5% compared to non-high risk occupations 37.5%, $p < 0.0001$).
Conclusion: Brucellosis is the common infectious cause of PUO among Asian and patients in high-risk occupations in Kuwait.

KEY WORDS: KEY WORDS: brucellosis, Kuwait, pyrexia of unknown origin

INTRODUCTION

Brucellosis remains a major public health problem in many developing countries[1-3]. Transmission of *Brucella* can be the result of oral ingestion, direct contact *via* skin abrasion and mucous membranes (including the conjunctiva), and inhalations. Risk factors for infection include handling of infected animals, ingestion of contaminated animal products such as unpasteurized milk and milk products (including cow, goat, and camel milk), meat, and handling of specimen cultures. Diagnosis of human brucellosis relies on blood culture and serological tests, including the standard tube agglutination test (STAT), Coombs test, and enzyme-linked immuno-sorbent assay (ELISA)[4,5]. Data from developing countries in the Mediterranean basin, particularly the Middle East, report seroprevalence rates ranging from 8% in Jordan to 12% in Lebanon and Kuwait[6,7].

Back pain, headache, fever, chills, night sweats, weakness, myalgia, arthralgia, bone pain are common presenting features. Brucellosis as a cause of pyrexia of unknown origin was not intensively highlighted[8]. The objective of this study was to investigate prevalence of brucellosis and to compare it with other causes in patients with pyrexia of unknown origin (PUO) in Kuwait.

SUBJECTS AND METHODS

Between January 2001 and December 2004 all patients who were admitted to Infectious Disease Hospital (IDH) with PUO were included in this study. Patient's records were reviewed for age, gender, nationality, occupation and residence. Laboratory investigations such as IgA, IgG, IgM for brucella and blood culture were recorded. Blood cultures were done automatically.

PUO is defined as body temperature higher than 38.3 °C on several occasions and lasting longer than three weeks, with the etiology remaining uncertain after one week of investigation.

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Table 1: Demographic characteristic of the patients

	Brucellosis n (%)	Other PUO n (%)	Total n (%)	p-value
Age (in years)	36.7	31.4	34.5	0.035
Gender				
M	71 (88.8)	46 (82.1)	117 (86.0)	0.274
F	9 (11.3)	10 (17.9)	19 (14.0)	
Nationality				
GCC	25 (31.3)	30 (53.6)	55 (40.4)	
Asian	47 (58.8)	20 (35.7)	67 (49.3)	0.022
Others	8 (10.0)	6 (10.7)	14 (10.3)	
Occupation				
Population at exposure risk	50 (62.5)	6 (10.7)	56 (41.2)	0.001
Population not at risk	30 (37.5)	50 (89.3)	80 (58.8)	
Area				
Hawalli	10 (12.5)	18 (32.1)	28 (20.6)	
Capital	4 (5.0)	10 (17.9)	14 (10.3)	
Jahra	21 (26.3)	3 (5.4)	24 (17.6)	> 0.05
Farwania	32 (40.0)	19 (33.9)	51 (37.5)	
Ahmadi	6 (7.5)	6 (10.7)	12 (8.8)	
Mubarak	7 (8.8)	0 (0)	7 (5.1)	
Total	80 (100.0)	56 (100.0)	136 (100.0)	

Table 3: Serological markers and blood cultures

Test	Positive n (%)	Negative n (%)	p-value
IgA	11 (13.8)	69 (86.3)	0.003
IgG	08 (10.0)	72 (90.0)	0.021
IgM	09 (11.3)	71 (88.8)	0.01
Blood culture	67 (83.8)	13 (16.30)	0.0001

One hundred thirty six patients meeting the classic criteria of PUO hospitalized at the IDH were included in the study.

A questionnaire guide was designed specifically for this study to gather information from medical records of all patients with PUO discharged from the IDH during the period under study. Main outcome measure was the final diagnosis established at discharge. The main research variables were age, gender, nationality, occupation, residence and laboratory investigations such as IgA, IgG, IgM for brucella and blood culture.

Statistical analysis: Data were analyzed using SPSS version 12 for Windows. Qualitative variables were expressed as number and percentage while quantitative variables were expressed as mean and standard deviation (SD). Chi-square test was used to compare two qualitative variables. Fisher's exact test was used to compare the difference between two qualitative variables. A p value of < 0.05 was considered as statistically significant.

RESULTS

Demographic characteristic of the patients are shown in Table 1. The mean age of the infected patients was 36.7 ± 11.69 years (range: 14-80 years). Males were more commonly affected than females and out of them 71 (88.8%) were found to have brucellosis. More than 50% of patients who developed brucellosis were at exposure risk. A significantly higher proportion of brucellosis cases were patients from Asian countries as compared to PUO patients from other regions (58.8% Vs 35.7%, p= 0.022).

Table 2: Final diagnosis of PUO

Diagnosis	Frequency	%
Brucellosis	80	58.8
Respiratory Symptom	10	7.4
Gastrointestinal	14	10.3
DAMA or undiagnosed	14	10.3
HIV	3	2.2
Others	15	11
Total	136	100.0

DAMA: discharged against medical advice

Table 4: Abnormal laboratory parameters

Parameters	Brucellosis	Other PUO	p-value
ALT (mean ± SD)	56.9 ± 40.6	38.0 ± 31.4	0.003
AST(mean ± SD)	70.9 ± 50.12	37.5 ± 26.8	0.021
WBC(mean ± SD)	07.1 ± 3.9	08.5 ± 4.0	0.01
ESR(mean ± SD)	30.8 ± 25.19	42.4 ± 33.2	0.0001

The final diagnosis of PUO is shown in Table 2. Infectious diseases were the most common causes of PUO. Brucellosis was diagnosed in 80 (58.8%) patients, respiratory tract infection in 10 (7.4%) patients, gastrointestinal diseases in 14 (10.3%) and HIV was diagnosed in three patients. Other diseases such as thyroiditis and glaucomatous hepatitis were diagnosed in 15 (11%) patients. Serological markers are shown in Table 3.

The overall seroprevalence for brucellosis based on ELISA IgG (OD > 0.6), IgM (OD ≥ 0.6) and IgA (OD ≥ 0.3) was 10, 11.3 and 13.8%, respectively. In 67 (83.8%) patients the blood cultures were positive for brucellosis. Twenty eight patients had positive serological markers as well as positive blood cultures (Table 3). Data related biochemical abnormalities are shown in Table 4. Alanine Amino Transferase (ALT) was significantly higher in brucellosis cases than other PUO patients (p = 0.003). However WBC count was higher in other patients with PUO than brucellosis patients (8.5 ± 4.04 Vs 7.1 ± 3.91, p = 0.01).The most common laboratory abnormality was an elevated erythrocyte sedimentation rate (ESR) (89.6%). The mean duration of hospitalization was 8.7 ± 7.8 days.

DISCUSSION

Clinical finding, isolation from the blood and serological tests are valuable diagnostic tools for brucellosis. Isolation of *Brucella* is diagnostic of brucellosis; however in practice it is difficult due to the early tissue localization and the exacting culture requirements of the organism. In practice, blood cultures are positive in 10-30% of brucellosis cases[9] and the remainder are diagnosed serologically. There is no single test which is confirmatory for brucellosis; our data however, showed more than 80% positive for blood culture. Probably the yield of cultures improved due to better culture techniques. In the presence of appropriate signs and symptoms, a presumptive diagnosis of brucellosis is usually defined serologically as a standard tube agglutination titer of 1:160 or greater[5,9-11]. In our study IgA, IgG and IgM were positive in 11 (13.8%), 8 (10%) and 9 (11.3%) patients respectively. Investigators from the middle east have found that seroprevalence of brucellosis increases with age[5-7] and among persons with a high-risk occupation[12].

Brucellosis is quite common in Kuwait[13,14]. *Brucellosis* was the commonest cause of PUO (59%) in our study. Male patients were affected more than females. Notably more than 50% of the infected cases from Asian and GCC population in our study were at an exposure risk. Asians were affected with brucellosis in about 60% of the cases. The clinical pattern of 400 cases of brucellosis in Kuwait was presented in 1987[14]. The disease was acute in 77%, sub-acute in 12.5% and chronic in 10.5% of cases. Raw milk was the major source of infection. The major features on presentation, irrespective of the course of the disease, were fever, sweating, headache, rigors, arthralgia, myalgia, and low back pain.

In accordance with other studies[8,15], the present study demonstrates clearly that males are commonly affected by brucellosis. Few reports, however, have shown a higher incidence of brucellosis in females[16]. Probably this discrepancy is related to cultural and epidemiological factors. In developing countries females are in contact with domestic animals. Furthermore un-pasteurized milk and its products are widely consumed by such population. Socio-economic status of the population at risk is another important factor that might increase the risk of brucellosis. Large families are usually gathered in the same house and often sheep, goats and other domestic animals are at short distance which increases the risk of infection. Such populations are also of low educational level and history of exposure is difficult to extract from them. Therefore laboratory investigations are vital to reach to proper diagnosis.

CONCLUSION

Infections remain the most important cause of PUO in Kuwait. Brucellosis is the common infectious cause of PUO among Asians and patients in high-risk occupations in Kuwait. Health educations programs should be emphasized among high risk occupations.

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