



BIOCHEMICAL AND HEMATOLOGICAL PARAMETERS IN RELATION TO INFECTED PATIENTS WITH BRUCELLA SPECIES AT KING FAHD HOSPITAL, RIYADH, SAUDI ARABIA.

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ABSTRACT

Objectives

To determine the prevalence and the intensity of infection with *Brucella* species among patients of different ages and sex at different months, and to evaluate the efficacy in normalizing the levels of some biochemical and hematological blood results.

Methods

This study was carried out at the Clinical Labs (Microbiology, Serology, Hematology and Biochemistry Departments) at King Fahd Hospital, King Abdulaziz Medical City (KAMC), Riyadh, Saudi Arabia.

Results

A total of 79 patients infected with *Brucella* were enrolled in this study. Males were outnumbered the females, 74.68% vs. 25.32%. Of the total number of isolates, 30 (37.97%) were from patients 46-71 years of age and 26 (32.91%) were from patients <20 years of age. The most common hematological changes observed were eosinopenia (91.14%), monocytosis (29.1%), anemia (22.8%), leukocytosis (15.2%), lymphocytosis (8.9%), leucopenia (7.6%), and lymphopenia (1.27%). Patients showed an increase in ESR level by 67.1%. The biochemical changes included a decline in sodium (54.4%), creatinine (19%), albumin (12.7%), and potassium (5.1%), however the total bilirubin was found to be elevated (6.33%). The patients showed increased serum aspartate transaminase (AST; 43.04%) and alanine transaminase (ALT; 27.85%).

Conclusion

Brucella disease causes significant hematological changes, and could lead to hepatic dysfunction. Despite the high incidence and serious nature of the hematological changes and liver involvement, these changes could be transient and responded favorably to a proper antimicrobial therapy.

Keywords: *Brucella*, Hematology, Biochemistry, Infection, Riyadh, Saudi Arabia.

Introduction

Brucellosis is a pyretic zoonotic infection and has a worldwide distribution among humans as well as animals [1, 2, 3], with a high prevalence in Mediterranean and Arabian Gulf countries [4, 5]. *Brucella* are Gram-negative coccobacilli, which doesn't contain capsules, endospores, or instinctive plasmid. The genus comprises different species such as *Brucella abortus*, *Brucella suis*, *Brucella melitensis*, and *Brucella canis*. *B. melitensis* reported to be of a high pathogenicity to humans. Moreover, *B. abortus* and *B. suis* were reported as causative agents of infectious abortion in cattle and swine [6]. *Brucella* is usually transmitted to humans via the ingestion of raw milk and its products such as milk cream, butter, and fresh cheese, or through the interaction with afterbirth products of the infected animals [7,8,9]. *Brucella* can enter the body

through digestive tract, lungs or mucosal layers, penetration of intact skin, and spread through blood and lymphatics to the body organs as well as causing localized disease [10]. Soon after entry into the body, this organism is phagocytosed by polymorphonuclear and mononuclear phagocytes [11]. Once in the blood stream, the organism is seeded to multiple organs, especially in those rich in reticuloendothelial tissue, such as liver, spleen, and skeletal and hematopoietic system [12] leading to various hemato-biochemical changes in the body [13]. Brucellosis usually leads to hemolytic anemia, leukopenia, thrombocytopenia or pancytopenia, neutropenia, lymphocytopenia, eosinophilia, and elevated transaminase and alkaline phosphatase [14, 15,16].

In Saudi Arabia, the disease cases recorded critical points when the reported cases reached 8000 cases [17, 18]. The

disease was reported in Central [19], Northern [20], Southern [21, 22], and Eastern [23] regions of Saudi Arabia. Several occupations are the major object of human brucellosis in Saudi Arabia. Brucellosis is considered a major threat for the laboratory workers of the Saudi hospitals [24, 25]. A study on 1290 abattoir workers indicated that human brucellosis among the veterinarian and veterinary assistants was 5.4%, butchers 8.9% and 1.1% among the administrative personnel [26]. The control of human brucellosis in Saudi Arabia is stalled by the importation of thousands of livestock especially during Hajj (Pilgrimage) season each year. The introduced livestock are usually permitted without proper verification on brucellosis [27, 28]. Moreover, it was reported by a study that was done at a tertiary-care hospital in Saudi Arabia that brucellosis led to spontaneous abortions in women in their first or second trimester, and caused intrauterine fetal death in the third trimester [29].

The aim of this study is to report the update in seroprevalence and hematological and biochemical changes associated with human affected with brucellosis in Riyadh, Saudi Arabia.

Methods

This was a hospital based descriptive study conducted at the Microbiology laboratory at King Fahd Hospital, Riyadh, Saudi Arabia, from January to December 2013. The study was designed to include demographics in addition to hematological and biochemical changes that were

observed in each patient. Only patients who showed positive blood culture for *Brucella* species were included in this study.

Hematological parameters including total white blood cells (WBC), total red blood cells (RBC), hemoglobin (Hgb), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), erythrocyte sedimentation rate (ESR), and Differential Leucocytes Count (basophiles, monocytes, eosinophils and lymphocytes) were estimated. Biochemical parameters including Sodium, potassium, creatinine, total bilirubin, albumin, ALT, and AST were estimated in serum by commercially available kits

Results

Patient Data

Data on 79 isolates of *Brucella*, corresponding to the same number of patients, were reported, including 59 (74.7%) male patients and 20 (25.3%) female patients. All isolates were collected from blood. Of the total number of isolates, 26 (32.9%) were from patients <20 years of age, 16 (20.3%) were from patients 20-45 years of age, 30 (37.9%) were from patients 46-72 years of age, and 7 (8.9%) were from patients >71 years of age. The peak of isolates was in December (12.7%). A total of 79 isolates were implicated in nosocomial infections (49.4% from Emergency Care Centre, 3.8% from Internal Medical Centre, 10.1% from Primary Health Care, and 36.7% from other departments (Table 1).

Table 1. Information of patients that were used in this study.

	Sex n (%)		Total
	Male	Female	
Number of patients with Brucellosis	59 (74.68)	20 (25.32)	79 (100)
Months			
January	5 (83.33)	1 (16.67)	6 (7.59)
February	4 (100)	0	4 (5.06)
March	2 (33.33)	4 (66.67)	6 (7.59)
April	4 (100)	0	4 (5.06)
May	8 (88.89)	1 (11.1)	9 (11.39)
June	6 (66.67)	3 (33.33)	9 (11.39)
July	3 (42.86)	4 (57.14)	7 (8.86)
August	8 (88.89)	1 (11.10)	9 (11.39)
September	6 (85.71)	1 (14.29)	7 (8.86)
October	3 (75)	1 (25)	4 (5.06)
November	2 (40)	3 (60)	5 (6.33)
December	8 (80)	2 (20)	10 (12.66)
Age			
<20	17 (65.38)	9 (34.62)	26 (32.91)
20-45	11 (68.75)	5 (31.25)	16 (20.25)
46-72	25 (83.33)	5 (16.67)	30 (37.97)
>72	6 (85.71)	1 (14.29)	7 (8.86)
Wards			
Emergency Care Center	30 (76.92)	9 (23.07)	39 (49.37)
Internal Medical Center	0	3 (100)	3 (3.8)
Primary Health Care	5 (62.5)	3 (37.50)	8 (10.13)
Others	24 (82.76)	5 (17.24)	29 (36.71)

Hematological Findings

Hematologic abnormalities were studied prospectively in 79 patients with brucellosis. The blood cell count findings

included leukocytosis in 12 (15.2%) and anemia in 61 (77.2%) patients. Moreover, the differential leukocytic count displayed lymphocytosis in 4 (5.1%), monocytosis in 23 (29.1%), and eosinopenia in 72 (91.1%) patients (Table 2). The ESR level was high in 53 (67.1%) patients.

Table 2. Hematological changes in brucellosis patients.

	Hematological Changes(%)								
	Male (n=59)			Female (n=20)			Total (n=79)		
	Normal	High	Low	Normal	High	Low	Normal	High	Low
Cell Blood Count (CBC)									
White Blood Cells (WBC)	46(75.4)	10(83.3)	3(50)	15(24.6)	2(16.7)	3(50)	61(77.2)	12(15.2)	6(7.6)
Red Blood Cells (RBC)	44(72.1)	0	15(83.3)	17(27.9)	0	3(16.7)	61(77.2)	18(22.8)	61(77.2)
Hemoglobin (Hgb)	41(97.6)	6(100)	12(39.2)	1(2.4)	0	19(61.3)	42(53.2)	6(7.6)	31(39.2)
Hematocrit (Hct)	32(76.2)	0	27(72.9)	10(23.8)	0	10(27.0)	42(53.2)	0	37(46.8)
Mean Corpuscular Volume (MCV)	50(87.7)	0	9(40.9)	7(12.3)	0	13(59.0)	57(72.2)	0	22(27.8)
Mean Corpuscular Hemoglobin (MCH)	53(82.8)	0	6(40)	11(17.2)	0	9(60)	64(81.0)	0	15(18.9)
Differential Cells Count (DCC)									
Basophils	58(75.3)	1(50)	0	19(24.7)	1(50)	0	77(97.5)	2(2.5)	0
Monocytes	41(73.2)	18(78.3)	0	15(26.8)	5(21.7)	0	56(70.9)	23(29.1)	0
Eosinophils	4(57.1)	0	55(76.4)	3(42.9)	0	17(23.6)	7(8.9)	0	72(91.1)
Lymphocytes	57(77.0)	1(25)	1(100)	17(22.9)	3(75.0)	0	74(93.7)	4(5.1)	1(1.3)
Erythrocyte sedimentation Rate (ESR)	19(73.1)	40(75.5)	0	7(26.9)	13(24.5)	0	26(32.9)	53(67.1)	0

Biochemical Results

Liver function tests were impaired in 91 patients. The abnormalities consisted basically of declined levels of sodium in 43 patients (54.4%), creatinine in 15 patients (18.9%), and serum albumin in 10 patients (12.7%). In

addition, 4 patients (5.5%) showed also a decrease in potassium level. Nevertheless, the level of total bilirubin was increased in 5 patients (6.3%). There was an increase in AST and ALT activities by 43.0% and 27.9%, respectively (Table 3).

Table 3. Biochemical changes in brucellosis patients.

	Biochemical Changes (%)								
	Male (n=59)			Female (n=20)			Total (n=79)		
	Normal	High	Low	Normal	High	Low	Normal	High	Low
Sodium	22(61.1)	0	37(86.1)	14(38.9)	0	6(16.7)	36(45.6)	0	43(54.4)
Potassium	57(76)	0	2(50)	18(24)	0	2(50)	75(94.9)	0	4(5.1)
Creatinine	42(73.7)	5(71.4)	12(80)	15(26.3)	2(28.6)	3(20)	57(72.2)	7(8.9)	15(18.9)
Total Bilirubin	54(72.9)	5(100)	0	20(27.0)	0	0	74(93.7)	5(6.3)	0
AST	34(75.6)	25(73.5)	0	11(24.4)	9(14.7)	0	45(56.9)	34(43.0)	0
ALT	41(71.9)	18(81.8)	0	16(28.1)	4(22.7)	0	57(72.2)	22(27.9)	0
Albumin	52(75.4)	0	7(70)	17(43.5)	0	3(30)	69(87.3)	0	10(12.7)

Discussion

The aim of the present study was to investigate the effect of brucellosis on the levels of selected hematological and biochemical parameters. The study indicated higher brucellosis incidents in males(74.7%) than females(25.3%) in Riyadh area in a ratio of 2.95:1. Similar results was obtained by Al-Ali and Alluwaimi [22] in Al-Ahsaa area and Al-Sekait [30] in Al-Medina region. A study on human brucellosis in the northern Saudi Arabia also confirmed the high brucellosis incidents among male than female in a ratio of 1.7:1, whereas in Tabuk (Northwest) the ratio was 1.8:1 [20, 31]. The high incident of brucellosis in male (70%) was also reported in Egypt [32]. In reference to age, the incidents in Riyadh were the highest in those 46-72 years old (37.9%). Nonetheless, in Al-Ahsaa the cases were mainly limited to the ages 28-33 years old. Moreover, the majority of incidents (60%) in the northern area were among 13-40 years old patients [19], while in Tabuk the median age was 13.9 [31]. The national health report of year 2006 indicated that the incidents of brucellosis was higher among 15-44 years old patients [33].

Brucella is a facultative intracellular pathogen that could

result, in some cases, in a persistent infection that may reactivate years after the initial exposure [34]. The most common hematological manifestations in our study were leukocytosis (39.2%), anemia (39.2%), eosinopenia (91.1%), monocytosis (29.1%), lymphocytosis (5.1%), and high ESR (67.1%). These results came in concordance with the study of Bukharie [35].

In our study 43.0% and 27.9% of patients exhibited increased enzyme activities in both AST and ALT. This was similar to the observations that were obtained by Bukharie [35], as the study showed 29% increase in enzymes activity for both enzymes (AST and ALT). Jaundice due to the increase in total bilirubin was observed only in 5 patients (6.3%). This result came in contrast of that obtained by Bukharie [35]. Forty three patients showed elevated sodium levels (54.4%), while 15 patients had a decrease in creatinine (18.9%), and 10 patients were low in serum albumin level (12.7%).

In conclusion, the study has confirmed the continuous risk of brucellosis in Riyadh area. The current results highlight the importance of optimizing animal vaccination program and improving the public awareness activities that could

assist in minimizing the risk of the infection. Moreover, this study emphasizes on applying strict measures on the imported livestock especially during Hajj (Pilgrimage) season. Furthermore, safety policies and procedures should be also applied strictly at the abattoirs to assure the protection for the workers against *Brucella* infection or any other infection.

REFERENCES

- Hussain, I., Arshad, M.I. Mahmood M.S. and Akhtar M. 2008. Seroprevalence of brucellosis in human, cattle and buffalo populations in Pakistan. *Turk. J. Vet. Anim. Sci.* 32:315-318.
- Maadi, H., Moharamnejad, and M.Haghi, M. 2011. Prevalence of brucellosis in cattle in Urmia, Iran. *Pak. Vet. J.* 31:81-82.
- Akhtar, R., Y.O. He, C.B. Larson, Chaudhary, Z.I. and Ahmad, M.U.D. 2012. Differential stimulatory activities of smooth and rough *Brucella abortus* lipopolysaccharide in murine macrophages. *Pak. Vet. J.* 32:339-344.
- Apan, T.Z., Yildirim, M. and Üstanbulluoğlu, E. 2007. Seroprevalence of brucellosis in human, sheep, and cattle populations in Kirikkale (Turkey). *Turk. J. Vet. Anim. Sci.* 31:75-78.
- Gul, S.T., and Khan, A. 2007. Epidemiology and epizootology of brucellosis: A review. *Pak. Vet. J.* 27:145-151.
- Young, E.J., 2006. *Brucella* spp. In Gillespie SH, Hawkey PM. Principles and practice of clinical bacteriology, 2, pp.265-71.
- Khorasgani, M.R., Esmaeili, H. Pourkarim, M.R. Mankhian, A.R. and Salehi, T.Z. 2008. Anti-*Brucella* antibodies in blood donors in Boushehr, Iran. *Comp. Clin. Pathol.* 17:267-269.
- Behzadi, M.A. and Mogheiseh A. 2011. Epidemiological survey of *Brucella canis* infection in different breeds of dogs in Fars province, Iran. *Pak. Vet. J.* 32:234-236.
- Abubakar, M., Mansoor, M. and Arshed, M.J. 2012. Bovine brucellosis: old and new concepts with Pakistan Perspective. *Pak. Vet. J.* 32:147-155.
- Lapaque, N., Moriyon, I. Moreno E. and Gorvel J.P. 2005. *Brucella* Lipopolysaccharide acts as a virulence factor. *Curr. Opin. Microbiol.* 8:60-66.
- Young, E.J. 2005. *Brucella* species. In: Mandell, Douglas and Bennett's Principles and Practice of Infectious Diseases. Mandell GL, Bennet JE, Dolin R, (Eds), Elsevier, Churchill, Livingstone; Philadelphia, pp: 2669-2674.
- Greenfield, R.A., Drevets, D.A. Machado, L.J. Voskuhl, G.W. Cornea P. and Bronze M.S. 2002. Bacterial pathogens as biological weapons and agents of bioterrorism. *Am. J. Med. Sci.* 323: 299-315.
- Al-Eissa, Y. and Al-Nasser, M. 1993. Haematological manifestations of childhood brucellosis. *Infection* 21:23-26.
- Dimitrov, A., Goranov, K. and Antonov, S. 1978. Biochemical study of serum from sheep infected with *Brucella ovis*. *Vet. Med. (Nauki)* 15:107-112.
- Galanaxis, E., Bourantas, K.L., Leveidiotou, S. and Lapatsanis, P.D. 1996. Childhood brucellosis in northwestern Greece: a retrospective analysis. *Eur. J. Pediat.* 155:1-6.
- Pourbagher, M.A., Pourbagher, A. Savas, L. Turunc, T. Demiroglu, Y.Z. Erol, I. and Yalcintas, D. 2006. Clinical pattern and abdominal sonographic findings in 251 cases of brucellosis in southern Turkey. *Am. J. Roentgenol.* 187:191-194.
- Elfaki, M. G., Al-Hokail, A.A., Nakeeb S.M., Al-Rabiah, F.A. 2005. Evaluation of culture, tube agglutination, and PCR methods for the diagnosis of brucellosis in humans. *Med Sci Monit*; 11: MT69-74.
- Memish Z. A. and Venkatesh, S. 2001. Brucella epididymo-orchitis in Saudi Arabia: a retrospective study of 26 cases and review of the literature. *BJU Int. Jul*; 88(1): 72-6
- Cooper, C. W. 1991. The epidemiology of human brucellosis in a well-defined urban population in Saudi Arabia. *J Trop Med Hyg.* 94: 416-422.
- Fallatah, S. M., Oduloju, A.J., Al-Dusari, S.N., and Fakunle, Y.M. 2005. Human brucellosis in Northern Saudi Arabia. *Saudi Med. J.* 26:1562-1566.
- Malik G.M. 1997. A clinical study of brucellosis in adults in the Asir region of southern Saudi Arabia. *Am J Trop Med Hyg.* 56:375-377.
- Alballa, S.R. 1995. Epidemiology of human brucellosis in southern Saudi Arabia. *J Trop Med Hyg.* 98: 185-189.
- Al-Ali, A.M. and Alluwaimi, A.M. 2009. The incident of human brucellosis in Al-Ahsaa area, Saudi Arabia. *Scientific Journal of King Faisal University (Basic and Applied Sciences)*, 10: 115-121
- Kiel, F. W. and Khan, M. Y. 1993. Brucellosis among hospital employees in Saudi Arabia. *Infect Control Hosp Epidemiol.* 14:268-272.
- Memish, Z. A. and Mah, M.W. 2001. Brucellosis in laboratory workers at a Saudi Arabian hospital. *Am J Infect Control.* 29:48-52.

26. Al-Sekait M. A. 1993. Prevalence of brucellosis among abattoir workers in Saudi Arabia. *J. R. Soc. Health.* 113:230-233.
27. Memish Z. 2001. Brucellosis control in Saudi Arabia: prospects and challenges. *J Chemother.* 13:11—7.
28. Al-Eissa, Y. A. 1999. Brucellosis in Saudi Arabia: past, present and future. *Ann Saudi Med,* 19:403-405.
29. Khan, M.Y., Mah, M.W. and Memish, Z.A. 2001. Brucellosis in pregnant women. *Clin. Infect. Diseases,* 32: 1172-1177.
30. AL-Sekait, M.A. 2000. Epidemiology of Brucellosis in Al-Madina region, Saudi Arabia. *Journal of Family and Community Medicine,* 7: 47-53
31. Elbeltagy, K.E. 2001. An epidemiological profile of brucellosis in Tabuk Province, Saudi Arabia. *Eastern Mediterranean Health J.* 7(4/5):790- 798.
32. Jennings, G. J., Hajjeh, R.A. Girgis, F. Y., Fadeel, M. A., Maksoud, M.A., Wasfy, M O., El Sayed, N., Srikantiah, N.P., Luby, S. P., Earhart, K., and Mahoney, F.J. 2007. Brucellosis as a cause of acute febrile illness in Egypt. *Trans. Roy. Soc.Trop. Med. Hyg.* 101: 707-713.
33. Ministry of Health Annual Report. 2006. <http://www.moh.gov.sa/statistics/S1427/Chapter%201.pdf>
34. Billard, E., Dornand, J., and Gross, A. 2007. Brucella suis Prevents Human Dendritic Cell Maturation and Antigen Presentation through Regulation of Tumor Necrosis Factor. *Infect. Immun.* 75: 4980-4989.
35. Bukharie, H.A. 2009. Clinical features, complications and treatment outcome of Brucella infection: Ten years' experience in an area. *Tropical journal of Pharmaceutical Research,* 8: 303-310.