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Predictors of Blood Culture Positivity in Adult Patients with Brucellosis

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ABSTRACT

Human brucellosis is an infectious multisystem infection that damages the tissues and multiple organs. Frequency of positive blood culture (80-90%) in acute brucellosis is higher than in chronic brucellosis. Different studies measured the potential risk factors in seropositivity of brucellosis in pediatric population. At present, there is no study that evaluates the predictors of blood culture positivity in adult brucella patients. Aim of this study was to observe the predictors of blood culture positivity in brucella adult patients. This single-centered retrospective descriptive study was done in Makkah, Saudi Arabia for a 3 years period. We included all confirmed brucella patients of either gender with age >14 years. Diagnosis was confirmed on the basis of compatible clinical findings and above in serum agglutination test (SAT) titre 1:320 or positive blood culture (bacteremia) for brucella. The complete patients' data was extracted from the electronic medical records. The fisher exact test was applied for analysis. Data was analyzed on SPSS version 23. Analysis showed that patients with bacteremia has significant association with agglutination titre of brucella melitensis and brucella abortus (p= < .001, < .001 respectively). Similarly, co-morbid conditions has significant association (P= < .001). Laboratory parameters, like C - reactive protein, ESR, hemoglobin level, total leukocyte count , eosinophils %, and monocytes % has significance association with bacteremia (p= .002, .002, < .001, < .001, .011, < .001 respectively). So, it is concluded that anemia, leukocytopenia, eosinopenia, monocytosis, high ESR, high C-reactive protein, and high brucella agglutination titre could be considered the predictors of bacteremia in brucella adult patients.

Keywords: Human brucellosis, predictors, Bacteremia

INTRODUCTION

An infectious disease of animals and human "Brucellosis" is caused by gram negative bacteria brucella species (spp.) In Human this disease is spread by coincidently digesting the polluted food which includes the likes of unpasteurized dairy products, use of meat from the domestic livestock, and by direct contact with the infectious animal and its secretions. Occasionally the disease can be transferred to humans by the occupational vulnerability in the microbiology laboratories [1]. On the basis of host preferences and pathogenicity brucella genus is classified into six species that

includes brucella melitensis, brucella ovis, brucella melitensis, brucella suis, brucella neotomae and brucella canis [2]. Pathogenic bacteria have a variety of secretion systems. Virulence factors can be exported in the environment or in the infected host cell by these systems [3].

Worldwide human brucellosis is the huge common infectious disease, with the rate of five hundred thousand new cases reported annually [4]. In certain endemic countries its frequency is more than 10 in every 100000 people. But the disease is eliminated in some European countries of Northern region, England, Australia and Canada [4]. Human brucellosis is a multisystem infectious disease. Sometimes this disease is considered as local infections. These local infections include frequently in osteoarticular region, it involves hematological region, genitourinary system, gastrointestinal system, cardiovascular system and nervous system [5]. Most frequently involved part of the body is the liver. Because brucella is an intracellular bacterium so this fact is probably associated with higher incidence of relapsing[5]. Brucellosis diagnosis is made usually on the basis of symptoms presented clinically and the positive serology. There is a 30 to 90 percent rate of blood culture positivity in brucellosis [6]. In acute brucellosis there are a higher number (80% - 90%) of positive results but these decreases (30% - 70%) in cases of chronic disease and focal implications [6]. A modifies Standard agglutination test is a new serological test in use. In spite of the important progress that are made in the diagnosis of brucellosis in human after the introduction of blood culture procedures that are automated, still the diagnosis of the brucellosis is majorly dependent upon molecular and serological methods [7]. For focal problems in brucellosis, radiological imaging will produce a helpful topographic and anatomic evidence of presenting lesions to make enough plans for surgical and medical treatment [8, 9].

Treatment of brucellosis is given to decrease the symptoms' duration, to prevent the disease relapsing and the complications [10]. Monotherapies in the history are usually characterized by the increase in the relapse rates while combination of two drugs is used currently.

MATERIALS & METHODS:

Case files of 241 adults with brucellosis, who presented to our hospital in Makkah, KSA during August 1, 2016, to August 30, 2019 (3 years), were retrospectively evaluated. The included adults more than 14 years of age, with the diagnosis of brucellosis. Diagnosis of brucellosis was made on the basis of compatible clinical findings and above in serum agglutination test (SAT) titre in a single serum sample or a minimum fourfold increase within a 2-3 week interval or positive blood culture for brucella. BACTEC 9120 (Becton Dickinson, Sparks, MD, USA) was used for blood cultures. If no growth was observed on the 7th day, the cultures were incubated until the 21st day. Subspecies of Brucella could not be identified. So blood culture results were, therefore, released as Brucella organism without subspecies.

Our aim was to investigate predictive contribution value of different factors in the positivity of blood culture in brucella adult patients.

The study was approved by the local Ethical Committee. Patients' data including social demographic (age, gender, place of residence, etc.), clinical (duration of symptoms, presence of fever, malaise, night sweats, etc.), and laboratory (leukocyte count with differential count, hemoglobin level, ESR, CRP. etc.) characteristics were retrospectively extracted from the electronic medical records. Anemia was defined as hemoglobin level <12.5gm/dl, leukopenia was defined as total leukocyte count <4x10^3/cu mm, lymphocytopenia was defined as a lymphocyte count of less than <20%, monocytosis >8%, and eosinopenia <0.6% of total leukocytes respectively. Thrombocytopenia was defined as a platelet count of less than 150,000 per cubic millimeter. Numerical variables are expressed as mean ± standard deviation and categorical variables as numbers (percentage). The fisher exact test was applied. P-value <0.05 was considered statistically significant. Data were analyzed on SPSS for Windows, version 23.0 software (SPSS, Chicago, IL).

RESULTS:

Totally 241 cases of brucellosis were documented of which 162 (67.2%) were male with a predominant (41.9%) young age group. The mean age of the adults in the study was 42.36 ±20.65 years, ranging between 4 and 94 years. Patients belonging to the

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rural areas were 42.7%. Forty-six patients (19%) had underlying comorbid conditions like type 2 diabetes mellitus and hypertension. Thirty-one patients (12.9%) had a significant risk of acquisition of brucellosis with direct exposure to livestock. Unpasteurized milk usage was observed in 57.3% and 28.1% of patients consumed local cheese. Frequencies, percentages, and means of the demographic features, clinical features, physical examination findings, and laboratory findings were shown in Table 1. Blood culture (brucella spp.) of 111 (53.1%) patients was observed positive, while 94 (45%) patients had negative blood culture and 4 (1.9%) patients' blood culture was not done. Univariate analyses showed that adults with isolation of brucella spp. in blood culture shown non-significant association with gender, direct contact with animals, family history of brucellosis, fever, and musculoskeletal pain**.** Analysis observed that adults with brucella spp. in blood culture has significant association with B. melitensis and B. abortus agglutination titre (p= <.001, <.001 respectively). Similarly co-morbid conditions has significant association (P= < .001) with brucella blood culture positivity.

On the basis of the laboratory parameters analysis, lower hemoglobin level, low leukocyte count , high CRP, and high ESR levels shows significant association (p .011, p <.001, p .002 and p .002, respectively) with isolation of brucella spp. in blood culture. While neutrophils %, and lymphocytes % has non-significant association with isolation of Brucella spp. in blood culture (p .817, .423 respectively). Eosinophil % and monocyte % has strong association with blood culture positivity (both has p value <.001) Two hundred twenty-three patients (92.5%) were improved. Death was reported in 2 patients (0.8 %) over this period.

DISCUSSION:

To our knowledge, this study appears to be the first to investigate the predictors of bacteremia in brucella adult population. Early diagnosis and cure of difficult cases is important to prevent the treatment failure, deaths due to relapsing disease, and drug resistance. Previous knowledge highlight that consumption of raw milk, age, gender, history of brucellosis in a family member and direct contact with animals or animal products/secretions are independent risk factors of seropositivity of brucellosis [11].

Previous literature document that death rate due to brucellosis is very low that is one in every hundreds of cases that is consistent with our study (0.8%) [12]. Previous studies reported a high blood culture positivity level in brucellosis of 86% than our study (53.1%) while others document levels between 17.6% and 50.8% [13]. Generally, there are multiple factors that influence the blood culture result. The micro-organism growth in blood culture depends upon previous use of antibiotics, culture methods, and the volume of the clinical specimen [14]. Blood culture results are also influenced by the stage of disease, presence of fever, and time when blood is drawn. Literature document that blood culture positivity levels are high as 80% to 90% in acute brucellosis, decreased to 30% to 70% in chronic cases [15]. In our study blood culture method and blood volume was standardized. A history of brucellosis in family members is not correlated with growth in blood culture in our study as seen in Kara SS study [13]. Although fever has been associated with bacteremia in our study as in previous research [16]. In our study, the serum agglutination test titre for B. abortus and melitensis emerged as powerful predictors of bacteremia as seen in previous studies [13, 16]

Hemoglobin level can also be considered a predictor of blood culture positivity for brucellosis. Anemia (hemoglobin level <12.5 gm/dl) is a common laboratory findings in brucellosis [17]. It is the anemia of chronic disease, characterized by low serum iron [18]. In this study, culture positive patients also had lower hemoglobin levels than culture negative patients [13]. Kadanali et al document that leukopenia has association with positive blood culture as in our study [19]. Increased CRP (C reactive protein) levels and high ESR (erythrocyte sedimentation rate) were determined in our patients with positive blood cultures, similarly to previous studies [13, 19].

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CONCLUSION:

Anemia, leukopenia, eosinopenia, monocytosis, high ESR, high C- reactive protein, high serum agglutination titre for brucella Melitensis and abortus could be considered as predictors of blood culture positivity in brucellosis patients of adult population.

REFERENCES:

1. Logan LK, Jacobs NM, McAuley JB, Weinstein RA, Anderson EJ. A multicenter retrospective study of childhood brucellosis in Chicago, Illinois from 1986 to 2008. IJID 2011;15 (12):e812-e17.
2. Cloeckaert A, Grayon M, Grépinet O, Boumedine KS. Classification of Brucella strains isolated from marine mammals by infrequent restriction site-PCR and development of specific PCR identification tests. Microb Infect 2003; 5 (7):593-602.
3. Christopher S, Umapathy B. Ravi umar KL. Brucellosis: review on the recent trends in pathogenicity and laboratory diagnosis J Lab Physicians 2010; 2 (2):55-60.
4. Pappas G, Papadimitriou P, Akritidis N, Christou L, Tsianos EV. The new global map of human brucellosis. The Lancet infectious diseases 2006; 6 (2):91-2.
5. Aygen B, Doğanay M, Sümerkan B, Yildiz O, Kayabaş Ü. Clinical manifestations, complications and treatment of brucellosis: a retrospective evaluation of 480 patients. Medecine et maladies infectieuses 2002; 32 (9):485-93.
6. Hasanjani Roushan MR, Ebrahimpour S. Human brucellosis: An overview. Caspian J Intern Med 2015 Winter; 6 (1): 46-7.
7. Memish Z, Oni G, Mah M. The correlation of agglutination titer with positive blood cultures in brucellosis: A comparison of two study periods. Journal of chemotherapy 2001;13(1):60-1.
8. Asaad AM, Alqahtani JM. Serological and molecular diagnosis of human brucellosis in Najran, Southwestern Saudi Arabia. J. Infect. Public Health 2012 Apr 1;5 (2):189-94.
9. Franco MP, Mulder M, Gilman RH, Smits HL. Human brucellosis. Lancet Infect Dis 2007; 7 (12):775-86.
10. Sen P, Demirdal T, Nemli SA. Predictive Value of Inflammation Markers in Brucellosis. Archives of Iranian Medicine 2019; 22 (11):640-45.
11. Njeru J, Wareth G, Melzer F, Henning K, Pletz MW, Heller R. Systematic review of brucellosis in Kenya: disease frequency in humans and animals and risk factors for human infection. BMC Public Health 2016;16 (suppl 1):853.
12. Hull NC, Schumaker BA. Comparisons of brucellosis between human and veterinary medicine. Infect Ecol Epidemiol. 2018 Jul 24;8 (1):1500846.
13. Kara SS, Cayir Y. Predictors of blood culture positivity in pediatric brucellosis. Journal of the College of Physicians and Surgeons Pakistan 2019; 29 (7):665-70.
14. Aliskan H. The value of culture and serological methods in the diagnosis of human brucellosis. Mikrobiyol Bul 2008; 42:185-95.
15. Al Dahouk S, Nöckler K. Implications of laboratory diagnosis on brucellosis therapy. Expert Rev Anti Infect Ther 2011; 9:833-45.
16. Apa H, Devrim I, Memur S, Günay I, Gülfidan G, Celegen M, Bayram N, Karaarslan U, Bağ O, Işgüder R, Oztürk A, Inan S, Unal N. Factors affecting Brucella spp. blood cultures positivity in children. Vector Borne Zoonotic Dis 2013;13 (3):176-80.
17. Buzgan T, Karahocagil MK, Irmak H, Baran AI, Karsen H, Evirgen O, et al. Clinical manifestations and complications in 1,028 cases of brucellosis: A retrospective evaluation and review of the literature. Int J Infect Dis 2010; 14:469-78.
18. Silva-Gomes S, Vale-Costa S, Appelberg R, Gomes MS. Iron in intracellular infection: To provide or to deprive? Front Cell Infect Microbiol 2013; 3:96.

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19. Kadanali A, Ozden K, Altoparlak U, Erturk A, Parlak M. Bacteremic and nonbacteremic brucellosis: clinical and laboratory observations. Infection 2009; 37:67-69.

Table 1: Frequencies of Demographic and Clinical Data of Brucella patients

Variables	Frequency	Mean	SD	Percentage
Age.				
< 14 yrs.	20			8.3
15-40 years	101			41.9
41-60 years	64	2.65	0.929	26.6
>60 years	56			23.2
Total	241			100
Gender.				
Male	162	1.67	0.470	67.2
Female	79			32.8
Residence.				
Rural	103			42.7
Urban	138	1.43	0.496	57.3
H/O contact e animals	31	1.87	0.335	12.9
H/O Raw milk intake	138	1.43	0.496	57.3
H/O Local Cheese intake	64	1.72	0.450	28.1
Family H/O Brucellosis	33	1.86	0.344	13.7
H/O Co- morbidity:				
DM+ HTN	46			19
No H/O co-morbidity.	192	2.06	0.722	79.7
H/O Others diseases	03			1.3
H/O Fever	230	1.05	0.209	95.4
H/O Musculoskeletal Pain	145	1.40	0.491	60.2
H/O Wt. Loss	13	1.94	0.230	5.6
Agglutination Titre: Brucella Abortus.				
<1:320	07			2.9
1:320	59			24.5
1:640	58	2.57	1.182	24.1
1:1280	59			24.5

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1:2560	58			24.1
Brucella Melitensis.				
<1:320	07			2.9
1:320	42	2.65	1.109	17.4
1:640	72			29.9
1:1280	63			26.1
1:2560	57			23.7
Blood Culture.				
Positive	111			53.1
Negative	94	1.49	0.541	45
Not done	4			1.9

Table 2: Factors Related to Blood Culture Positivity in Adults with Brucellosis.

PARAMETERS **Gender**	**Blood culture** **Positive**	**Blood culture** **Negative**	**Blood culture** **not done**	**Total**	**P-VALUE**
Female	46	30	4	80	.285
Male	79	78	4	161	
H/O Direct contact e animals					
Yes	18	12	3	33	.680
No	108	96	4	208	
Family H/O Brucellosis					
Yes	21	11	3	35	.221
No	104	98	4	206	
Fever					
Yes	122	100	5	227	.170
No	3	8	3	14	
Musculoskeletal pain					
Yes	74	66	5	145	.186
No	51	42	3	96	

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Agglutination Titre: B. Melitensis					
1;320	13	29	2	44	
1;640	28	42	2	72	
1;1280	38	21	2	61	.000
1;2560	41	14	1	56	
<1;320	5	2	1	8	
Agglutination Titre: B. Abortus					
1;320	14	44	2	60	
1;640	27	29	2	58	
1;1280	36	20	1	57	.000
2560	42	14	1	57	
<1;320	6	2	1	9	
Diagnosis: Focal/Non Focal disease					
Non-Focal	108	84	5	197	.333
Focal	17	24	3	44	
Co-morbidities					
Diabetes & Hypertension	13	14	0	27	
No Disease	102	83	4	189	
Hypertension	6	3	0	9	.000
Diabetes mellitus	3	7	0	10	
Chronic liver disease	1	1	1	3	
Bronchial asthma	2	1	0	3	

Table 3: Laboratory factors related to blood culture positivity in adults with brucellosis.

Laboratory findings	**Blood culture**				
ESR	**Positive**	**Negative**	**Not done**	**Total**	**P-value**
<15	24	83	4	111	
15-30	75	14	1	90	.002
>30	26	11	3	40	
CRP (mg/dl)					

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<0.9	0	18	0	18	
1-3	103	79	5	187	
3.1-5	15	5	0	20	.002
5.1-7	3	1	1	5	
7.1-10	2	3	1	6	
>10	2	2	1	5	
Hemoglobin (gm/dl)					
<10	11	1	1	13	
10.1 -12.5	15	18	1	34	.011
12.6-15	79	60	3	142	
>15	20	30	2	52	
WBCs x10^3 /cu mm					
<4	42	12	1	55	.000
5-11	76	95	5	176	
>11	7	1	2	10	
Neutrophils %					
<50	73	56	4	133	
50-70	49	51	1	101	.827
71-80	1	1	1	3	
81-90	1	0	1	2	
>90	1	1	0	2	
Platelets count x10^3/cu mm					
<100	1	0	0	1	
100-150	19	19	1	39	
151-400	104	84	7	195	.0562
>400	1	5	0	6	
Lymphocytes %					
21-40	11	14	0	25	
>40	16	13	0	29	.413
Eosinophil %					
0.0-0.1	38	4	2	44	
0.11-0.6	39	22	1	62	.000
0.61-1.0	8	3	0	11	
>1.1	40	79	5	124	

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Laboratory findings	Blood culture				
Monocytes %	**Positive**	**Negative**	**Not done**	**Total**	**P-value**
0-8	10	49	6	65	
9-12	102	48	4	154	.000
13-20	11	7	4	22	

ESR: Erythrocyte sedimentation rate. CRP: C - reactive protein

WBCs: White blood cells.

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