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Cytopenia in adult brucellosis patients

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***Background & objectives*: Brucellosis can lead to haematological abnormalities including cytopenia confusing with haematological malignancies. The aim of this study was to compare the main characteristics of brucellosis patients without cytopenia (Group 1) and with cytopenia (Group 2).**

***Methods*: This five-year period study which was performed in two referral hospitals in Turkey, included all adult brucellosis patients. Abnormally, low counts of leucocyte or haemoglobin or platelets in a patient were considered as cytopenia. The demographics, clinical, laboratory, treatment and outcome data were analyzed.**

***Results*: A total of 484 brucellosis patients were enrolled. Among the cases, 162 (33.5%) of them had cytopenia. One hundred and four (21.5%) had anaemia, 88 (18.8%) had thrombocytopenia, 71 (14.6%) had leucopenia and 28 (5.8%) had pancytopenia. The mean age of group 2 was 35.01±16.05 yr and it was 33.31±14.39 yr in group 1. While there was no difference between the groups in terms of duration of treatment, the median length of hospital stay (LOS) was significantly longer in group 2 (9 vs 10 days; *P*<0.001). The most frequently applied combination therapy consisted of doxycycline plus rifampicin and doxycycline plus streptomycin regimens. No significant difference was observed in terms of duration of treatment, LOS and restoration time of cytopenia between the patients who received either of these combinations.**

***Interpretation & conclusions*: Our findings suggested that the patients with cytopenia should be investigated for brucellosis, especially if living in, or with a history of travel to, endemic areas, in view of the increase in world travel.**

Key words Anaemia - brucellosis - leucopenia - pancytopenia - thrombocytopenia

Brucellosis is a zoonotic disease frequently seen throughout the world. It is especially common in the Mediterranean region, the Middle East, the Arabian Peninsula, Central and South America, Asia and Africa. Although it has been brought under control in the majority of developed countries, it is still an important health problem in developing countries, including Turkey[1-3]. Vaccination of animals plays

an important role in the control of the disease. Transmission to humans is known to occur through the ingestion of contaminated meat and dairy products, infected animal tissue, direct contact of blood or bodily fluids with broken skin or conjunctiva and inhalation of infectious aerosols. Since the disease may involve a number of organs and systems in the body, it manifests with various symptoms. There are no disease-specific clinical, haematological or biochemical characteristics that help distinguish the condition from other infectious diseases. Therefore, its diagnosis may present a challenge[4].

Brucellosis leads to a number of non-specific haematological abnormalities. Although mild-to-moderate anaemia and leucopenia are frequently observed, it may also rarely present with pancytopenia, severe thrombocytopenia or severe leucopenia. Therefore, the condition may sometimes be confused with haematological malignancies[5]. The aims of this study were to evaluate the epidemiological, clinical and laboratory features of brucellosis in patients with cytopenia and the complications associated with the disease, and to compare the antibiotic combinations used, duration of treatment, normalization time of cytopenia, length of hospital stay (LOS) and cure or relapse in brucellosis patients.

Material & Methods

The South-eastern Anatolian region of Turkey is an endemic area for brucellosis[3]. One of the largest cities is Diyarbakir, and both the Gazi Yasargil Training and Research Hospital and the Dicle University Hospital are referral hospitals for the region. This study included all patients admitted to these two centres in Diyarbakir Province, Turkey, for brucellosis-associated cytopenia between 2009 and 2013. Only patients over the age of 14 yr with brucellosis were enrolled. Patients both with and without cytopenia were enrolled in the study, into separate groups. A standard questionnaire was administered to the participant centres, and data were collected through a digital database. A control group consisting of brucellosis patients without cytopenia was formed among the brucellosis patients concurrently diagnosed or treated at the participating centres. Dicle University Hospital's Review Board in Diyarbakir, Turkey, approved the study. All participants gave prior written informed consent.

The diagnosis of brucellosis was based on positive agglutination titres (1:160 or higher) in the standard tube agglutination (STA) test and/or isolation of brucellae from blood or sterile body fluids in patients with signs and symptoms consistent with brucellosis. When the STA was negative, the test was repeated with Coombs serum to detect anti-*Brucella*-blocking antibodies (>1:160 in one serum sample or fourfold increase in two separate samples taken at least two weeks apart)[4]. Cases fulfilling the above-mentioned criteria were included, and cases having cytopenia of infectious aetiology other than brucellosis or non-infectious aetiology were excluded. According to the duration of symptoms, brucellosis was classified as acute (less than eight weeks), sub-acute (8-52 wk) and chronic (>52 wk). Blood haemoglobin values <12 g/dl for females and <13 g/dl for males, leucocyte count $<4\times10^9$/l and platelet count $<150\times10^9$/l were considered as anaemia, leucopenia and thrombocytopenia, respectively. Abnormally, low leucocyte and platelet counts and haemoglobin level together is accepted as pancytopenia[6]. Patients with more than five times the upper limit of normal for aminotransferases were placed in clinical hepatitis category. Reappearance of symptoms within six months of discontinuation of antibiotic treatment was considered as relapse.

For microbiological and serological analyses, the blood samples were inoculated into BacT/ALERT FA plus aerobic bottles (bioMérieux, France) and were analyzed in the BacT/ALERT 3D (bioMérieux, France) automated blood culture system. The other clinical samples including the cerebrospinal fluid, synovial fluid, abscess discharges and other bodily fluids were inoculated onto sheep blood agar and chocolate agar. *Brucella abortus* strain 99 was used for the agglutination test, which was produced in Pendik Animal Diseases Research Institute (Istanbul, Turkey). The Rose Bengal test (RBT; slide agglutination method), STA and Coombs agglutination test were used for the serological analyses[4].

All patients were evaluated on admission, daily during their hospitalization and six months after discharge, by the same physicians at the participating centres. For each patient, complete blood count, routine biochemistry parameters, serum C-reactive protein (CRP) levels (nephelometric method) and erythrocyte sedimentation rate (ESR) were measured at admission, and these were repeated when needed. In addition, double sets of blood cultures were drawn for each patient on admission. Response to treatment was monitored using clinical and laboratory data. Antibiotic combinations were continued until the resolution of all foci of brucellosis. Antibiotic treatment was modified

if therapeutic failure or adverse drug effects were observed.

The following data were collected from the participating centres and entered into a digital database for each patient: (*i*) Demographic and epidemiological data: age and gender; (*ii*) Clinical and laboratory data: duration of disease, symptoms and signs, comorbid conditions, foci of brucellosis, routine and microbiological and serological diagnostic test results for brucellosis, restoration time of the cytopenia to the normal range in the cytopenic group; (*iii*) Treatment data: drug combinations used, duration of treatment for each drug combination; and (*iv*) Outcome data: recovery, relapse or death (if any) and LOS in hospital.

All the patients diagnosed as brucellosis were enrolled for the study and were classified into two groups: those without cytopenia (Group 1) and those with cytopenia (Group 2).

Statistical analysis: Statistical analysis was performed using the SPSS for Windows v.16.5 (SPSS Inc., Chicago, IL, USA) software package. Descriptive statistics were presented as frequency and percentage for categorical variables or as mean±standard deviation (SD) and median [interquartile range (IQR)] for continuous variables according to the results of normality tests, as appropriate. Normality testing was done by the one-sample Kolmogorov–Smirnov test. For group comparisons, the Chi-square and Fisher's exact tests were used to compare the categorical variables, and numerical data were analyzed using Student's *t* test for the parametric data and the Mann–Whitney U-test for the variables of the non-parametric data.

Results

A total of 484 consecutive brucellosis patients over a period of five years were enrolled in the study. Among these patients, 233 (48.1%) were male and 251 (51.9%) were female (Table I). Their mean age±SD was 33.88±14.96 yr (data not shown), and 16.7 per cent patients were over the age of 50 yr. Among the patients, 162 (33.5%) were cytopenic and 70 (43.2%) of these were male while 92 (56.8%) were female (Table I). The mean age of cytopenic patients was 35.01±16.05 yr and 33.31±14.39 yr in patients without cytopenia (data not shown). No significant difference was observed in terms of gender between cytopenic and non-cytopenic patients groups (Table I). Of the 484 patients, 285 (60.9%) were identified as having the acute form, 105 (21.7%) the sub-acute form and 84 (17.4%) the chronic form of the disease. No significant difference was found regarding the number of patients with acute brucellosis between the groups.

A total of 61 (12.6%) of the 484 patients had at least one co-morbid condition, namely diabetes mellitus in 15 patients (3.1%), hypertension in five patients (1.03%), coronary artery disease in five patients (1.03%), congestive heart failure in one patient (0.2%), solid organ tumours in three patients (0.61%) and hypercholesterolaemia in one patient (0.2%). When the groups were compared in terms of the presence of at least one comorbidity, the cytopenic patient group outnumbered the other (33 vs 28; $P<0.001$).

For the clinical findings among the patients (n=484), 411 (85%) had fever, 393 (81.2%) had arthralgia and 384 (79.3%) had night sweats. All the symptoms and findings are presented in Table I. When the groups were compared, headache was found to be more frequent in the cytopenic group ($P<0.01$), while backache was more common in the non-cytopenic group ($P<0.001$). Sacroiliitis (n=95; 19.6%) and spondylodiscitis (n=68; 14%) were the most frequently involved sites among the patients. While there was no significant difference regarding sacroiliitis between the groups, spondylodiscitis was significantly more frequent in the non-cytopenic group in association with backache ($P<0.01$).

Of the entire patients, 104 (21.5%) had anaemia, 88 (18.8%) had thrombocytopenia, 71 (14.6%) had leucopenia, 31 (6.4%) had leucopenia and thrombocytopenia, seven (1.4%) had anaemia and leucopenia, seven (1.4%) had anaemia and thrombocytopenia and 28 (5.8%) had pancytopenia (data not shown). In terms of the haematological parameters in the cytopenic group, the median (IQR) haemoglobin level was 11.2 (12.9-14.0) g/dl, the median leucocyte count was 4.4 (3.2-6.7)$\times 10^9$/l and the mean platelet count was 180±103$\times 10^9$/l. The groups were found to differ significantly for these parameters ($P<0.001$ for all comparisons). Furthermore, the differences in terms of the blood CRP and aspartate aminotransferase (AST) values were significant between the groups ($P=0.001$ and $P=0.01$, respectively) (Table II). Blood cultures yielded positive results in 111 patients (23%). Of the 111 isolates, 109 (98.2%) were *Brucella melitensis* and two (1.8%) were *B. abortus*. The RBT result was positive in 419 (86.5%) and the STA was positive in 482 (99.4%) patients. There were no significant

Table I. Comparison of some epidemiological and clinical features of brucellosis cases without cytopenia (Group 1) and with cytopenia (Group 2) at admission†

Variable	Total (n=484)	Group 1 (n=322)	Group 2 (n=162)
Male gender	233 (48.1)	163 (50.6)	70 (43.3)
Age (yr)			
≥40	151 (31.2)	98 (30.4)	53 (32.7)
≥50	81 (16.7)	51 (15.8)	30 (18.5)
Co-morbid conditions††	61 (12.6)	28 (8.7)	33 (20.3)***
Acute brucellosis	295 (60.9)	188 (58.3)	107 (66)
Symptoms and signs			
Fever	411 (85)	268 (83.2)	143 (88.3)
Night sweating	384 (79.3)	250 (77.6)	134 (82.7)
Arthralgia	393 (81.2)	264 (82)	129 (79.6)
Lack of appetite	270 (55.8)	183 (56.8)	87 (53.7)
Muscle ache	281 (58.1)	190 (59)	91 (56.2)
Backache	227 (46.9)	169 (52.4)	58 (35.8)***
Nausea-vomiting	227 (46.9)	149 (46.3)	78 (48.1)
Headache	231 (47.7)	143 (44.4)	88 (54.3)**
Chills	188 (38.8)	126 (39.1)	62 (38.3)
Skin rash	97 (20.1)	62 (19.3)	35 (21.6)
Depressive symptoms	97 (20.1)	67 (20.8)	30 (18.5)
Diarrhoea	28 (5.8)	19 (5.9)	9 (5.5)
Cough	38 (7.6)	25 (7.8)	13 (8)
Hepatomegaly	117 (24.2)	77 (24)	40 (24.7)
Splenomegaly	78 (16.1)	54 (16.7)	24 (14.8)
Lymphadenopathy	22 (4.5)	14 (4.3)	8 (4.9)
Involvement sites			
Sacroiliitis	95 (19.6)	67 (20.8)	28 (17.3)
Spondylodiscitis	68 (14)	55 (17.1)	13 (8)**
Meningitis/encephalitis	8 (1.7)	5 (1.5)	3 (1.9)
Brain abscess	10 (2.1)	7 (2.2)	3 (1.9)
Pneumonitis/bronchiolitis	17 (3.5)	12 (3.7)	5 (3.1)
Pleuritis	17 (3.5)	9 (2.8)	8 (4.9)
Hepatitis	38 (7.6)	27 (8.4)	11 (6.8)
Ascites	26 (5.4)	20 (6.2)	6 (3.7)
Pericarditis	7 (1.5)	7 (2.2)	0
Arthritis	21 (4.3)	16 (5)	5 (3.1)
Endocarditis	1 (0.2)	0	1 (0.6)

P **<0.01, ***<0.001 compared to group 1. †Data are expressed as n (%); ††Some patients have more than one co-morbid disease

differences in terms of frequency of positive blood culture for brucellae or positivity of RBT and STA tests between the groups (Table III).

The median duration of medical treatment in all patients was six weeks (6-8 wk) (maximum 24 wk), and the median LOS was nine days (7-12 days) (maximum 38 days). While there was no difference between the groups in terms of the duration of treatment, the LOS was significantly longer in the cytopenic group (9 vs 10 days; *P*<0.001; Table III). In the cytopenic group, median restoration time of

Table II. Comparison of laboratory findings of brucellosis cases without cytopenia (Group 1) and with cytopenia (Group 2) at admission*

Variable	Total (n=484)	Group 1 (n=322)	Group 2 (n=162)	*P*	Normal range
Haemoglobin (g/dl)	13 (12.6-13.8)	13.2 (10.2-12.9)	11.2 (12.9-14.0)	<0.001	14-18 (male) 12-16 (female)
WBC ($\times10^9$/l)	6.18 (4.8-8.0)	6.8 (5.4-8.4)	4.4 (3.2-6.7)	<0.001	4-11
Platelet ($\times10^9$/l), mean±SD	233±94	259±76	180±103	<0.001	150-450
CRP (mg/l)	12.8 (5.6-37)	11 (5-31.2)	18.2 (7.3-54.3)	0.001	0-8
ESR (mm/h)	24.5 (15-41)	24 (14-39)	27 (15.8-44)	0.064	≤15 (male) ≤20 (female)
ALT (IU/l)	33 (22-72)	31 (21-67)	36 (23-79.3)	0.102	17-63
AST (IU/l)	38 (23-71)	36 (22-60.3)	38 (23-71)	0.01	15-41
ALP (IU/l)	152 (98-248)	153 (97.8-241.5)	149.5 (94-254)	0.704	41-133
GGT (IU/l)	31 (19-51)	32 (19-53)	27.5 (18.8-41)	0.336	0-51
BUN (mg/dl)	27 (21-35)	28 (22-35)	26 (19.8-34)	0.357	7-20
Creatinine (mg/dl)	0.6 (0.5-0.8)	0.62 (0.5-0.8)	0.6 (0.5-0.8)	0.807	0.7-1.2
Total bilirubin (mg/dl)	0.6 (0.4-0.9)	0.6 (0.4-0.9)	0.6 (0.4-0.9)	0.799	0.3-1.9

*Data are presented as median (IQR) unless otherwise indicated. IQR, interquartile range; WBC, white blood cell; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; GGT, gamma-glutamyl transpeptidase; BUN, blood urea nitrogen; SD, standard deviation

Table III. Results of microbiological analysis, treatment and outcome data for brucellosis patients without cytopenia (Group 1) and with cytopenia (Group 2)

Variable	Total (n=484)	Group 1 (n=322)	Group 2 (n=162)
Methods, n (%)			
Blood culture	111 (23)	76 (23.6)	35 (21.6)
Rose Bengal test	419 (86.5)	277 (86)	142 (87.6)
STA ≥1:160†	482 (99.5)	320 (99.4)	162 (100.0)
Treatment and outcome			
Treatment duration (wk), median (IQR)	6 (6-8)	6 (6-8)	6 (6-8)
LOS (days), median (IQR)	9 (7-12)	9 (6.5-12)	10 (8-13)***
Relapse, n (%)	57 (11.8)	35 (10.9)	22 (13.6)

***P<0.001 compared to Group 1. †STA test ≥1:160, 36; ≥1:320, 310; ≥1:640, 114; ≥1:1280, 22. STA, standard tube agglutination test; IQR, interquartile range; LOS, length of hospital stay

cytopenia was 14.0 (9.0-18.5) days (data not shown) and the two most frequently administered combination therapy regimens were doxycycline plus rifampicin and doxycycline plus streptomycin. However, no significant difference was observed in terms of LOS, duration of treatment and the reversal of cytopenia to normal levels, between the patients who received either of these combinations (Table IV). Relapses were observed in 57 (11.8%) patients and the difference between the cytopenic and non-cytopenic groups was not significant. All of the relapsed patients responded to a second course of therapy. No death was observed in this study.

Discussion

Brucellosis is an infectious disease that may manifest with various acute or chronic symptoms following an incubation period, which varies from 1 to 3 wk to a few months. Its prevalence among children is also high, and the disease is especially common in areas endemic to *B. melitensis* where children and animals share the same living spaces[7]. In two studies from Kuwait and Iran, more than 80 per cent of the patients were found to be below the age of 40 yr[8,9]. In our study, 68.8 per cent out of the 484 patients were below the age of 40 yr and the ratios between the cytopenic and non-cytopenic groups were similar. Most

Table IV. Antibiotic combinations used in brucellosis patients with cytopenia (n=162)

Antibiotic combinations	n	Median (IQR)		
		LOS (days)	Treatment duration (wk)	Normalization time of cytopenia (days)
DOX + RIF	64	10 (8-12.8)	6 (6-6)	12 (9-18)
DOX + SM	61	10 (7.5-14)	6 (6-6)	15 (10-20)
TMP/SXT + RIF	18	9.5 (7-12)	6 (6-6)	11 (8.5-15.2)
DOX + RIF + SM	14	10 (8.8-14.3)	8 (6-8)	16.5 (7.8-23.3)
Others	5	9 (7.5-14.5)	8 (6-14)	13 (10-17.5)

LOS, length of hospital stay; IQR, interquartile range; DOX, doxycycline; RIF, rifampicin; SM, streptomycin; TMP/SXT, trimethoprim/sulphamethoxazole; CFX, ceftriaxone; GEN, gentamicin; Others - CFX + RIF, 2; TMP/SXT + RIF + CFX, 2; DOX + GEN, 1

studies conducted in endemic regions demonstrated that males were more frequently affected by the disease, suggesting a relationship between the disease and occupation[10-13]. In our study, 51.9 per cent of the patients were females. The reason for this could be that females are more frequently occupied with animal husbandry than males.

Brucellosis presents as either acute or chronic infection. In this study, the acute form was more frequent (60.9%), and the symptoms during this phase, such as fever, were helpful in establishing an early diagnosis[14,15]. The results of this study showed that the clinical stage was not important for occurrence of cytopenia in brucellosis. A study from Turkey showed frequent anaemia and leucopenia but less frequent pancytopenia and thrombocytopenia, in patients with acute brucellosis[16]. Other reports from our country suggest more frequent fever, hepatomegaly, splenomegaly and epididymo-orchitis (in male patients) in the acute form and more frequent spondylitis in the chronic form of brucellosis[14,17]. Fever and arthralgia are the most frequently observed symptoms in patients with brucellosis, followed by sweating, anorexia, headache and backache[18,19]. In our study, fever and arthralgia were the most common symptoms. In general, the symptoms were similar in both groups. However, headache was more common in the cytopenic group, while backache was significantly more frequent in the non-cytopenic group. Lymphadenopathy was observed in 10-20 per cent of patients, while hepatomegaly and/or splenomegaly were observed in 20-30 per cent[20]. In our patients, the frequencies of hepatomegaly, splenomegaly and lymphadenopathy were 24.2, 16.1 and 4.5 per cent, respectively. Complications in brucellosis are important both with reference to the selection of antibiotics and the duration of treatment. Osteoarticular complications are the most common complications of brucellosis, and their prevalence was found to range between 10 and 80 per cent in various studies[21-23]. Sacroiliitis and spondylodiscitis of the lumbar vertebrae are frequently observed[21,22]. Sacroiliitis and spondylodiscitis were the most frequently observed complications in our patients.

Mild anaemia, leucopenia and thrombocytopenia are frequently observed haematological complications in brucellosis. In addition, pancytopenia may rarely occur. The exact causes of cytopenia in brucellosis are not well defined. Hypersplenism, haemophagocytosis, hypoplasia and granulomatous lesions of the bone marrow and immune destruction seem to be the possible causes of these anomalies in the peripheral blood[23,24]. Higher levels of interleukin (IL)-6, IL-8, interferon (IF)-gamma and tumour necrosis factor (TNF)-alpha in acute brucellosis patients suggest the presence of significant inflammation[25,26]. In this study, high CRP levels were found in cytopenic brucellosis patients. High CRP levels may be related to production of high levels of IL-6 secondary to *Brucella* infection or the existence of more co-morbid conditions in cytopenic patients. High CRP levels may show that brucellosis proceeds more severely in the cytopenic group. CRP is a biomarker of inflammation, and it is an important mechanistic link between inflammation and thrombosis in the host[27].

Bone marrow examination of brucellosis patients with haematological involvement has revealed hypercellularity, non-caseified granulomas, and haemophagocytosis[28]. Brucellae also have a directly suppressive effect on bone marrow, which may lead to a reduction in the production of erythropoietin. In the majority of brucellosis patients, the haematological findings are normal[29]. Therefore, in patients with anaemia, leucopenia and/or thrombocytopenia, brucellosis may be overlooked. In a study conducted in Turkey, 43 per cent of the patients had anaemia,

14 per cent had thrombocytopenia, 12 per cent had leucopenia, seven per cent had leucopenia and anaemia, five per cent had pancytopenia, six per cent had anaemia and thrombocytopenia and four per cent had leucopenia and thrombocytopenia[16]. In our study also, 21.5 per cent of the 484 patients had anaemia, 18.8 per cent had thrombocytopenia, 14.6 per cent had leucopenia, 5.8 per cent had pancytopenia, 6.4 per cent had leucopenia and thrombocytopenia, 1.4 per cent had anaemia and leucopenia and 1.4 per cent had anaemia and thrombocytopenia.

Blood culture, the gold standard for laboratory diagnosis of brucellosis, was positive in 111 (23%) of 484 patients. Positive blood cultures occur in 10-70 per cent of suspected infections, depending on the duration, localization of the infection, the type of *Brucella* species and the culture techniques used. It is more often positive during the acute phase[7,15,29]. Moreover, automated culture systems are much more often positive than conventional cultures for sterile body fluids[30]. In this study, more patients (60.9%) being in the acute phase and the use of an automated culture system may both have affected the blood culture results. However, they are in agreement with the current literature[15]. We detected that 482 (99.5%) patients had positive STA test, with 446 (92.1%) of them having STA test titres ≥1:320, which was consistent with the expectation in endemic areas due to frequent contact with brucellosis infection. Turkey is an endemic area for brucellosis, and in a previous study from our region of Turkey (district of Van), the STA test was found to be positive in 99 per cent (779/787) of brucellosis patients[16]. The test was also reported positive in 86.2 per cent of Iranian brucellosis cases[12].

The treatment of brucellosis is difficult due to the side effects of the antibiotics, relapses and development of resistance. The World Health Organization recommended regimen is doxycycline plus rifampin for six weeks for the treatment of adult brucellosis. However, the regimen of doxycycline for six weeks plus streptomycin for 2-3 wk is reported to be the most effective therapy[4,30]. In patients with serious localization, a triple antibiotherapy should be administered and the duration of treatment should be extended[31]. Although the relapse rate in cytopenic patients was found to be slightly higher than that of the non-cytopenic group, the groups were not different for relapse rates. Relapse rates for brucellosis are reported between 5 and 15 per cent depending on drug combinations[30]. In our study, doxycycline plus rifampicin and doxycycline plus streptomycin were the two most common treatment options in the cytopenic patients group. Both median treatment duration (six weeks) and median LOS (10 days) were found to be the same for both combinations of drug regimens. Other treatment regimens showed similar results for treatment duration and LOS. In addition, in cytopenic patients with brucellosis, the median LOS was significantly longer compared to patients without cytopenia. Significant additional co-morbid conditions may have contributed to longer LOS in this group of patients and this will also be reflected in the treatment costs. Although data on the hospitalization period for brucellosis patients are limited, the LOS was reported to range between 7 and 14 days in Iranian brucellosis patients[5]. Dilek *et al*[16] showed that the thrombocytopenia and leucopenia returned to the normal range within one week, while anaemia took 3-4 wk. In another study, the normalization time for the cytopenia was observed to be 2-6 wk[32]. In our study, it was 14 days, and the longest duration (35 days) was observed in a patient treated with the doxycycline plus rifampicin plus streptomycin therapy regimen.

In conclusion, our study showed that the epidemiological, clinical and treatment features and relapse rates of adult brucellosis patients with cytopenia and those without cytopenia were similar. Further, both time span until normalization of the cytopenia was 14 days and the LOS was longer in cytopenic patients than the non-cytopenic patients. It is recommended that patients with cytopenia should be investigated for brucellosis, especially if living in, or with a history of travel to, endemic areas, in view of the increase in world travel.

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Conflicts of Interest**:** None.

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