

The effects of maternal brucellosis on pregnancy outcome

Maged Elshamy,^{1,2} Amien Ahmed I.^{2,3}

¹Department of Obstetric and Gynecology, Faculty of Medicine, Mansoura University, Egypt.

²EL-Hasan National Hospital, EL-Rawad Clinic, Taif, Saudi Arabia.

³Laboratory of Biochemistry, Faculty of Science, Cairo University, Egypt.

Abstract

Background: Our aim was to assess the outcome of pregnancies complicated by *Brucella* infection.

Design: Prospective study.

Setting: EL-Hasan National Hospital, El-Rawad Clinic, TAIF, SAUDI ARABIA (where the practical part of the study was accomplished) and Obstetrics & Gynecology Department, Mansoura University Hospital (where the theoretical part of the study was completed).

Methods: This study was conducted from August 2005 to December 2007. Tube method for detection of antibody titre for brucellosis was performed on 450 pregnant women; 415 had no symptoms or signs of brucellosis and 35 had symptoms and signs of the disease. The antibody titre was positive in 55 pregnant women (group 1) and negative in 395 pregnant women (group 2). Both groups were followed up during pregnancy and the neonatal period to determine any type of reproductive failure. **Results:** The incidence of brucellosis was 12.2% among pregnant women included in the study. The incidence of abortion in group 1 was 27.27%; IUFD was 12.72%; and preterm labour was 10.90%. There were statistically significant differences in the abortion and IUFD rates but no significant difference in the preterm labour rates between the test and control groups. There was a statistically significant difference in abortion rates between patients with a titre more than 1/160 and those with a titre less than 1/160 ($p=0.03$).

Conclusion: The frequency of fetal loss among patients with brucellosis is very high. It is advisable to have a high degree of alertness for brucellosis in endemic areas.

Key Words: Brucellosis, *Brucella*, abortion, IUFD, preterm labour.

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Introduction

Brucellosis is a major zoonotic disease. *Brucella* is a coccobacillus, gram negative, non-sporing and non-motile aerobic bacterium whose hosts are mostly animals [1,2]. It has four species: *abortus*, *canis*, *melitensis* and *suis* [3]. The bacterium possesses an unconventional non endotoxic lipopolysaccharide that confers resistance to antimicrobial attacks and modulates the host immune response [4]. *Brucella* species are facultative intracellular pathogens that have the ability to survive and multiply in professional and non professional phagocytes and cause undulant fever in humans [5]. Control of brucellosis in agricultural animals is a prerequisite for the prevention of the disease in humans [6].

The interest of *Brucella* as a biological weapon lies in the fact that transmission through a spray is possible as has been reported with human

contamination during abortion of infected animals or bacterial spraying in laboratories. It is suggested that 10 to 100 bacteria would be sufficient to produce a contaminating spray for humans [7]. Farmers, meat processing workers, veterinarian and laboratory workers are at risk [3].

Human-to-human transmission is uncommon but it has been described after blood transfusion [8], bone marrow transplantation [9] and possibly during sexual intercourse [10]. Brucellosis is common in the Mediterranean region, East Africa, Arabian Gulf region. It is endemic in Saudi Arabia (national prevalence, 15%) [11]. Endemicity in Saudi Arabia results from the persistence of domestic animal reservoirs for *Brucella* species and the human consumption of unpasteurized products [12,13].

There is controversy about the relationship between brucellosis and the outcome of pregnancy

[14]. There is some evidence that brucellosis causes a higher rate of complications such as abortion, preterm labour and IUFD more frequently than do other bacterial infections [14]. It is postulated that maternal bacteremia, toxemia, acute febrile reaction and DIC are causes of spontaneous abortion and IUFD in brucellosis [15].

It is believed that brucellosis causes fewer spontaneous abortions in humans than it does in animals because of the absence of erythritol in the human placenta [16] which appears to be a preferential medium and growth factor for *Brucella* in the placenta of animals. An additional reason for the lesser role of *Brucella* infection in human abortion is the presence of anti-*Brucella* activity in human amniotic fluid [17].

Materials & Methods

This study was conducted from August 2005 to December 2007 on 55 pregnant women with positive *Brucella* antibodies (group 1) and 395 matched pregnant controls (group 2) at Elhasan National Hospital and Elrawad Clinic, Taif, Saudia Arabia, (where the practical part of the study was accomplished), and the Obstetrics and Gynecology Department, Mansoura University Hospital (where the theoretical part of the study was completed).

All women were pregnant in the first trimester (up to 12 weeks’ gestation; second trimester = more than 12 weeks to ≤ 24 weeks). Fetal death that occurred less than 24 weeks gestation was considered spontaneous abortion while fetal death that occurred after 24 weeks’ gestation was designated “intrauterine fetal death.” Diagnosis of *Brucella* was done as follows: Fasting blood samples (5ml) were drawn from each subject in a clean dry tube then kept at room temperature for 15 minutes to clot. Serum was separated after centrifugation at 3000 rpm for 10 minutes and the biochemical tests were conducted. Serum antibody titre was evaluated by the method described by Freter [18]. Our patient *Brucella* test was considered positive when the titre was more than 1\160 [19].

Subjects infected with toxoplasmosis, CMV, rubella, syphilis, and HCV as well as diabetic patients and those with medical disorders were excluded from the study. Serum toxoplasmosis, CMV, Rubella and HCV antibodies were determined using enzyme linked immunosorbent

assay technique (ELISA) according to the methods of Wisdom [20], Engvall and Perlmann [21], Veheri and Salonen [22] and Alter *et al.* [23] respectively, while syphilis antibodies were determined using the indirect hemagglutination technique described by Tomizawa and Kamatsu [24].

We followed the pregnant women in the study for the occurrence of abortion, preterm labor or intrauterine fetal deaths. Patients who experienced abortion were classified into two categories: The first had a titre more than 1\160 and the second had a titer less than 1\160.

All statistical data were expressed according to Cochran [25] and Montgomery [26].

P value of 0.05 or less is considered significant.

Results

This study was conducted on 55 pregnant women positive for *Brucella* antibodies (group 1) and 395 matched pregnant controls (group 2).

Table 1 shows that no statistically significant difference in age or pregnancy duration was evident between both test and control groups.

Table 1. Age and pregnancy duration of the two groups.

Group	Group1 (n=55)	Group2 (n=395)	P value
Age (years)	27 ± 6	26 ± 8	0.2
Pregnancy duration (weeks)	9 ± 2	8 ± 6	0.1

There was no statistically significant difference between both tested groups.

Antibody titre for *Brucella* was performed on subjects of both groups (G1 and G2) and the percentage of abortion, IUFD and preterm delivery was calculated. As shown in Table 2, there was a statistically significant difference in the abortion and IUFD rates but no significant difference in the preterm labour rates between the test and control groups.

Results of percentage of abortion are shown in Table 3. Marked elevation can be seen in the percentage of abortion in patients with a titre more than 1/160 compared with those with a titre less than 1/160. As shown in Table 3, there was a statistically significant difference in abortion rates

between patients with a titre of more than 1/160 and those with a titre of less than 1/160 ($p=0.03$).

Table 2. Number and percentage of abortion, IUFD and preterm labour of the two studied groups.

Group	Group 1 (n=55)	Group 2 (n=395)	P value
Abortion	15 (27.27%)	60 (15.18%)	0.01
IUFD	7(12.72%)	15(3.79%)	0.002
Preterm labour	6 (10.90%)	35 (8.865)	0.3

Table 3. The relation of the percentage of abortion, IUFD and preterm labour and the titre of brucellosis.

Group	Titre More than 1/160 (n=34) G1	Titre Less than 1/160 (n=21) G2	P value
Abortion	15 (44.11%)	4 (19.4%)	0.03
IUFD	7 (20.58%)	4 (19.4%)	0.4
Preterm labour	6 (17.64%)	7 (33.33%)	0.09

Discussion

Brucellosis is a worldwide zoonosis and a common cause of economic loss and ill health among animal and human populations [27]. It is a major health problem throughout the Middle East, including in Egypt. The identification of risky patients with acute disease is challenging due to the diverse clinical presentations and the need of a specialized laboratory for confirming the diagnosis [28].

In the United States, there is a resurgence of interest in this disease because of its potential as a bioweapon. Also, in spite of aggressive public health measures to control brucellosis, its incidence is 8-fold higher in California, Texas and the other borderlands between the United States and Mexico compared with the international rate [29].

Acute febrile illness (AFI) including brucellosis is a very common problem in Egypt. In a study conducted in Egypt between 1999 and 2003 to evaluate 10,130 patients with AFI, 11 % of the study patients had brucellosis [28].

Maternal infection with *Brucella* during pregnancy can lead to significant morbidities such as abortion, IUFD and preterm labour [30]. Fallah *et al.* [12] stated that pneumonia, epididymo-

orchitis, human abortion and threatened abortion were complications of brucellosis in humans.

The high economic loss and public health implications of brucellosis prompted us to study the possible relation between *Brucella* infection and reproductive failure as assessed by the frequency of abortion, IUFD and preterm labour.

Our study showed that the incidence of brucellosis was 12.2% among pregnant women. This result is in agreement with the study done by Afifi *et al.* [28] in Egypt. However, another study by Sherif *et al.* [31] reported an incidence rate of 3.5% among Egyptian women.

Our study also shows that the incidence of abortion in pregnant women infected with brucellosis was 27.27%. This result exceeds the 10% rate reported by Crisculo and di Carlo [29] and that of Sarram *et al.* [32] who observed that among 51 pregnant women infected with brucellosis the incidence rate of abortion was only 11.6 %. Contrarily, the incidence rate of abortion in our study is less than that reported in other studies (Madkour *et al.*, Lulu *et al.* and Khan *et al.*, 40%, 35% and 43 %, respectively) [33-35].

Brucellosis is a major cause of abortion and IUFD. Our current study shows a statistically significant difference in the incidence of abortion and the incidence of IUFD but not the incidence of preterm labour between pregnant women with positive brucellosis antibodies and control pregnant women. This is consistent with Malone *et al.* (36), Makhseed *et al.* (37) and Khan *et al.* [35]; however, these results are contrary to the study of Seoud *et al.* [17] who stated that *Brucella* infection has a lesser role in human abortion.

There was a statistically significant difference in the incidence of abortion in pregnant women with brucellosis antibody titre of more than 1/160 compared to those women with titre of less than 1/160 (44.1 versus 19.4%, respectively, P value 0.03). There was no significant difference with regard to IUFD or preterm labour between the two groups. These results suggest that a brucellosis antibody titre higher than 1/160 indicates more susceptibility to abortion.

This result is in accordance with Sherif *et al.* [31] who concluded that if the titre was higher than 1/160 the incidence of abortion was 17.6% while the incidence was 7.7% if the titre was less than 1/160. However, our results are contrary to those of Khan *et al.* [35] who reported that occurrence of

abortion was not associated with either the magnitude of the serum agglutinin titre or the presence of *Brucella* bacteraemia.

Our results show that brucellosis is a risk factor for adverse reproductive outcomes. Therefore, it is advisable to have a high degree of awareness for brucellosis in pregnant women both in rural and in urban areas. In heavily infected areas a screening program may be warranted. Public health educational efforts should be directed to all people about the route of infection, the dangers of contact with infected animals, the dangers of consumption of raw milk and milk products, clinical manifestation of brucellosis, and the modes of treatment.

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Corresponding Author: Maged Ragheb Elshamy, Obstetrics & Gynecology Department- Mansoura University Teaching Hospital- El-Gomhorrea street – Mansoura, Egypt, Tel. (050) 2232553, (010) 1103162
E-mail: dr_maged66@yahoo.com

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