

How to Cite:

Al-Bermani, O. K., Ibraheam, I. A., Shaalan, N. N., & Saad, A. M. (2022). Study of some microbial infections of recurrent miscarriage in women. *International Journal of Health Sciences*, 6(S5), 2042–2047. <https://doi.org/10.53730/ijhs.v6nS5.9074>

Study of some microbial infections of recurrent miscarriage in women

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Abstract---Background: some microbial infections can be passed to the fetus before or during birth and damage the fetus or cause a miscarriage, like infection with ToRCH agents and salmonella enterica. The current study aims to investigate the extent of the involvement of *salmonella enteria* serovars, *proteus* spp. and *Brucella* spp. in recurrent miscarriage in women during first trimester. Material and method: The 50 blood samples were collected from women age range (19-39), who had repeated miscarriages during the first trimester during periods extended from October 2021 to February 2022,. The study control includes the 20 fertile women with no miscarried history. Two tests were conducted which are ToRCH IgM and febril antigen slid test for identification infectious agents associated with pregnancy loss. Results: The present results showed that the most frequent recurrent miscarriage (RM) was in the age group 35-39 years at a percentage 34%, while the lowest abortion rate was 18% at the age group of 25-29 years. Out of fifty recurrent miscarriage women only three patients revealed positive result for current infection with cytomegalovirus and negative results for others pathogen of ToRCH panel test, as well as two patients were positive of infection with *Salmonella enterica* serotype *Typhi*.by using febrile antigen slid test. Conclusion: Pregnancy loss in the first trimester may involve even a small percentage of dangerous bacterial infections such as typhoid fever, which are not included in the clinical examinations established for cases of recurrent miscarriage.

Keywords---recurrent miscarriage, Typhoid fever, ToRCH test

Introduction

The pregnancy loss and miscarriage in women is a major public health concern around the world. Miscarriage, which occurs spontaneously in women before 12 weeks of pregnancy [1] or even when it occurs before 10 gestational weeks and fetal loss (or fetal miscarriage) is typically connected with the term reproductive lost [2,3]. According to literature, research suggests that between 10% and 20% of women with a medically confirmed pregnancy will end in miscarriage at first trimester [4]. In an Iraq study revealed that 77.27% of women had aborted in the 1st trimester of pregnancy and the lowest rate of abortion 3% was in the 3rd trimester[5]. The Aetiology and causes of miscarriage are identified in only ~50% of patients include Parental chromosomal anomalies, Uterine pathology, Prothrombotic state and antiphospholipid syndrome, Endocrinological disorders, Immunological factors (Autoantibodies; activated NK), Cervical weakness, Nutrition/environmental factors, Infections and other factors increase the risk of miscarriage like obesity, smoking excessive caffeine consumption and cocaine. [6,7]

Some infections, including listeriosis, toxoplasmosis, cytomegalovirus and primary genital herpes, cause sporadic pregnancy loss. Routine cervical cultures for Chlamydia or Mycoplasma, vaginal evaluation for bacterial vaginosis and ToRCH (toxoplasma, rubella, cytomegalovirus and herpes simplex) serology are not sufficient in the evaluation of recurrent pregnancy loss. [8]. The TORCH panel test is used to help diagnose infections that could harm the unborn baby during pregnancy [9].

Other microbes not on the TORCH list can also infect the human placenta and affect the fetus. Interestingly many of these same microbes cause abortion in cattle, sheep, goats. These microbes disseminate via the hematogenous route and have at least partially intracellular life cycles. It is important to consider these pathogens as a cause for septic abortion or preterm labor in addition to the pathogens that cause chorioamnionitis via the ascending route (e.g., *Escherichia coli* and *Streptococcus agalactiae*) [10]

Intestinal fever or typhoid fever caused by a variety of *Salmonella* serotypes is still one of the most important medical infections in developing countries. Hormonal changes and its inhibitory effect on the immune system in pregnant women may predispose them to various infections, including typhoid fever caused by *Salmonella enterica*. Gastroenteritis and septicemia caused by this bacterium can infect the placenta and fetus if they occur during pregnancy, and if not treated early, they may be associated with risks such as abortion [11]. The aim of this study is to investigate whether or not the presence of pregnancy loss and preterm birth was associated with infection with febrile bacteria and facultative intracellular bacteria like *Salmonella* spp. *Brucella* pp. and *Proteus* spp.

Material and methods

The study subject

This case-control study was conducted from October 2021 to February 2022 in Babylon university/college of science for women /Biology department . All

patients agreed and signed the free and informed consent form. In total, fifty women age range 19-38 years with recurrent miscarriage (RM) who attended to the infertility center at Babylon Hospital for Maternity and Children and to private laboratory. The women in the RM group had primary infertility and had no children. RM was defined as having two or more consecutive abortions in the first trimester of pregnancy. Control study group includes the 20 fertile women with no miscarried history. Inclusion criteria this study was limited with women experienced with first trimester pregnancy loss.

Specimen collection

Samples were collected from the patients by drawing 5 ml of venous blood where serum was obtained by centrifugation of blood at 3500 rpm for 10min and stored in freezing until use for ToRCH IgM rapid and febrile bacterial antigen tests .

ToRCH IgM rapid test

ToRCH screening works on the principle of immunochromatography. It was done according to the instructions of the manufactured company (AccuBioTech, Spanish). The results was examined at 15 -20 minutes.

Febrile antigens slid test

This examination was carried out according to the steps established by the producing company(LINEAR CHEMICALS, S.L.U. SPAIN) the composition of this kit are: Febrile Antigen which are stabilized suspension of stained killed bacteria in a buffered solution; positive Control which are Animal serum containing the corresponding febrile antibodies against *Brucella*, *Salmonella* and *Proteus* additionally to the negative control which are non-reactive animal serum. The results was read according to the principle of test design, which is the presence or absence of agglutination comparison with positive and negative controls

Results and Discussion

Maternal Age and Miscarriage Rate

The present results showed that the highest rate of miscarriage occurred in age group 35-39 years at a percentage 34%, While the lowest abortion rate was 18% at the age group of 25-29 years. Table-1

Table-1: Distribution of No. miscarriage cases according to the age groups of patients

Age group(years)	Miscarriage No.	Percentage%
19-24	10	20
25-29	9	18
30-34	12	24
35-39	17	34

There is a difference in a maternal age risk associated with miscarriage frequency as documented by current study and by previous study [12] the authors found that lowest risk (9.5%) at age 27, and then rising nearly linearly after the age of 30 to reach 54% at ages 45 and over. Early pregnancy loss in women is a relatively common event, occurring in 15%–25% of pregnancies, and increasing in prevalence with maternal age[7]

The increase in the rate of miscarriage in women with progressing age may be due to chromosomal abnormalities of egg, contributes to the age-related risk of miscarriage[13]

Infection- related risk of miscarriage

Of fifty ToRCH screening, three patients were positive for current infection with cytomegalovirus and all the patients revealed negative results of other ToRCH pathogens. As well as the febrile antigen screening of fifty RM women explained only two patients were positive of infection with *Salmonella enterica* serotype *Typhi*.

During pregnancy, a woman has a specialized immune system that prevents the process of rejecting the foreign antigens of the fetus and this is due to the change in the percentage of proportions of Th1/ Th2 the immune system tends to increase the Th2 immune response but at the same time makes the mother is prone to infection with ToRCH agents, leishmaniasis, malaria and salmonellosis, where the host is dependent to Th1 immune response for eradication of these pathogens [14,15] the infection with any pathogen of ToRCH may be cause pregnancy wastage at any stage of gestation. Serological assays can be an important tool for diagnosis [9]

The five miscarriage cases under present study explained current infection with Cytomegalovirus. Mothers can get CMV by sexual contact or contact with bodily fluids such as saliva from a person who has CMV. CMV can cause long-term problems in infants, including problems with vision, hearing, and mental development and in some cases pregnancy loss especially during first trimester[16]

During pregnancy, Salmonella infections are associated with complications such as septicemia, choriarnionitis, fetal infection, preterm labor, fetal growth restriction and abortion [17]. Typhoid fever in pregnancy was a well-known and dreaded disease, associated with a 60–80% risk of abortion and premature labor and a maternal mortality of 15% [18]

The current results is consistent with [10] who record case suffering from abortion during first trimester when infected with salmonella serovar Typhi. Jain and coauthors 2020 [19] recorded that fetal loss occurred at 14 weeks with *Salmonella enterica* serovar *Typhi* (S. Typhi), found in the fetus at autopsy. The patients was first trimester pregnant women with symptoms of gastroenteritis about a month before abortion and was discharged without antibiotics. Although Widal serological test and blood culture of the patient were negative, the bacterium was isolated from placenta in culture.

Most of the information we have about the pathogenesis typhoid fever in pregnancy is derived from experiments with *S. typhimurium*, a serovar that causes gastroenteritis in humans but produces a disseminated disease similar to typhoid fever in mice. Infections of pregnant mice with *S. typhimurium* result in 100% fetal loss and 60% maternal mortality. *S. typhimurium* proliferates in the

infected placenta and causes widespread placental necrosis and inflammation leading to fetal death and maternal disease [20,21]

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