

Full Length Research Paper

Influence of TORCH infections in first trimester miscarriage in the Malabar region of Kerala

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To correlate the prevalence of TORCH (*Toxoplasma gondii*, Rubella, Cytomegalovirus and *Herpes simplex*) infections with incidence of abortion in pregnant women in the Malabar area of Kerala, in order to establish basic knowledge for future pregnancy care. Patients attending the Institute of Maternity and Child Health, Calicut Medical College, Kerala were subjected for the study. Seventy one miscarriage cases and thirty normal pregnant women were studied through their medical, clinical, and serological data. Results were analyzed using person's chi-square test. This study showed that general population of Malabar area has an infection susceptibility of 32.3% to *Toxoplasma gondii*, 9.6% to Rubella, 3.2% to CMV (Cytomegalovirus) and 61.3% to HSV (Herpes simplex virus) infections. This was revealed through the estimation of TORCH specific IgG. IgM specific to TORCH agents was also studied in abortion cases and was observed as *T. gondii*- 50.7% ($p<0.03$), Rubella-11.3% ($p<0.597$), CMV-28.2% ($p<0.231$) and HSV-59.2% ($p<0.022$). When 40.8% of the miscarriage cases were showing IgM specific to one or the other TORCH agents, only 20% of the control cases possessed IgM to TORCH agents. Cross infections with more than one of the TORCH agents was observed and 5.6% of the aborted mothers were infected with all the four pathogens. The significant role of *T. gondii* and HSV infection on spontaneous abortion, compared to CMV and Rubella, is provided here. The increased susceptibility of the general population of Malabar to these two pathogens, substantiates this observation further. Various abortion categories are also influenced by these pathogens differently. We also observed cross infections with two or more of the pathogens in the TORCH group, with a statistical significance of $p<0.003$.

Key words: Miscarriage, abortion, TORCH infection.

INTRODUCTION

The first trimester of pregnancy is an important period often fraught with complications like bleeding and pain, leading to severe apprehension in the mother (Florence et al., 1999). Pregnancy loss has been attributed to several factors involved in human reproduction. Genetic and uterine abnormalities, endocrine and immunological dysfunctions, infectious agents, environmental pollutants, psychogenetic factors and endometriosis are most important causes (Rock and Zacur, 1983; Dicker et al., 1992) of spontaneous abortion.

Spontaneous abortion is a new issue in terms of its social and economic impact. Today majority of women decide to conceive in their thirties or forties, since they are career-oriented during the age of maximum fecundity.

After the age of 30-35 years, potential fertility declines and the rate of spontaneous abortion increases (Harlap et al., 1989; Brock et al., 1990). But on the other hand, teenage pregnancy is a fairly common occurrence in countries like India. Bhalerao et al. (1990) had pointed out that pregnant teenagers are at greater risk and require additional care. Stress, pollutants, smoking etc. also increase the risk of miscarriage.

Some maternal infections, especially during the early gestation, can result in fetal loss or malformations because the ability of the fetus to resist infectious organisms is limited and the fetal immune system is unable to prevent the dissemination of infectious organisms to various tissues (Mladina et al., 2002). The fetus and/or neonate are infected predominantly by viral but also by bacterial and protozoal pathogens. Infections with various pathogens cause miscarriage or may lead to congenital anomalies in the fetus while others are associated with

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Table 1. Prevalence of TORCH infections in various abortion categories

Category	Toxoplasma (%)	Rubella (%)	CMV (%)	HSV (%)
Control	20	6.7	13.3	26.7
Complete Abortion	50	25	37.5	87.5
Incomplete Abortion	33.3	16.7	0	100
Missed Abortion	48.7	7.7	33.3	48.7
Threat Abortion	54.5	9.1	36.4	45.5

neonatal infectious morbidity. There are also reports saying that most of the infections of the mother will not result in fetal infection (Langford, 2002).

This study was conducted among the pregnancy cases in the Malabar area of Kerala, a place noted for its culture of early/childhood marriages, as per previous studies, with a view of assessing the role of TORCH (*T. gondii*, Rubella, Cytomegalovirus and *H. simplex*) infections in pregnancy related complications, especially miscarriage. Recognizing the prevalence infections with intrauterine and other pathogens in both mother and fetus is an important part of prenatal care.

MATERIALS AND METHODS

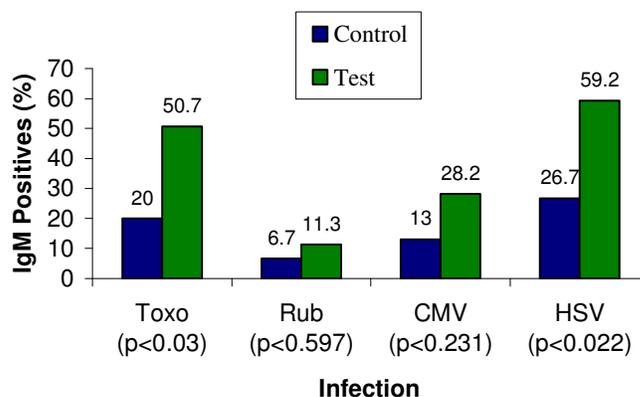
Seventy one miscarriage cases and 30 normal pregnant women attended the Institute of Maternity and Child Health, Calicut Medical College, Kerala, were subjected for this study. The approval of the institute's ethical committee was obtained prior to the sample collection. Informed written consent was obtained from all the patients considered under this study. Miscarriage categories like complete, incomplete, missed and threatened abortions were selected using medical, clinical and other diagnostic parameters. The patients' history was collected as per the proforma, which considered age, gravida, parity, previous miscarriages, pregnancy induced hypertension (PIH), diabetes and infections with HIV, Hepatitis virus etc.

Serum samples were collected at about 8 - 12 gestational weeks and stored in small screw capped vials at -20°C until serological analysis. Samples were screened for the presence of IgM and IgG antibodies against *T. gondii*, Rubella virus, Cytomegalovirus and *H. simplex* virus using ELISA kits from Equipar Diagnostics (Italy). The tests were done as per the directions given in the manual supplied along with the kits. The results were read at 450 nm in the ELISA reader (Sunrise Model, TECAN, Austria). Syphilis was diagnosed using VDRL test. Tests for presence of HIV and HBsAg were done in the Microbiology laboratory of Calicut Medical College and the results were recorded in the proforma.

The IgM levels were interpreted as negative, low positive or high positive. A positive IgM is an indication of recent infection. Statistical analysis is done using the SPSS software for microcomputers. The Chi Square test is used to assess statistical significance.

RESULTS

The incidence of miscarriages in various age groups was as 14.81% in 15 - 19 years group (teenagers); 49.38% in 20 - 24 years group; 24.69% in 25 - 29 years and 11.1% in the 30 - 34 years group. Here 39.4% were primigravida (G1) while 33.3% were G2, 16.7%-G3, 7.6%-G4 and 3%

**Figure 1.** TORCH infections in miscarriage cases.

-G5. Abortion had previously occurred in 32.3%. The parity of the group was as Nullipara -13.8%, Primipara (P1)-69%, P2 -10.3% and P3 -6.9%. None of the patients in the group had diabetes or infection with HIV and Hepatitis. One among the test group and none in the control group had PIH. Renal disease was observed in two patients.

The IgG prevalence against TORCH in normal population was found as *Toxoplasma*- 67.7%, Rubella- 90.4%, CMV- 96.8% and HSV -38.7%. The IgM levels observed against these pathogens are represented in Figure 1. The cases having infected with more than one of these agents are detailed in Figure 2. The miscarriage cases were studied under various categories like complete, incomplete, missed and threatened abortions, for the presence of infections with these pathogens. The results are presented in Table 1.

DISCUSSION

The incidence of first trimester miscarriage among the teenagers under this study was 14.3%. This is higher to the 5.5% miscarriage rate observed among the teenagers in other parts of India (Bhalerao et al., 1990). The teenage pregnancy rates reported from various parts of the world ranged from 8 - 14%. The mean age of the miscarriage cases here was 23.8 years, and is found as very close to that of normal pregnant women, which is 23.9 years.

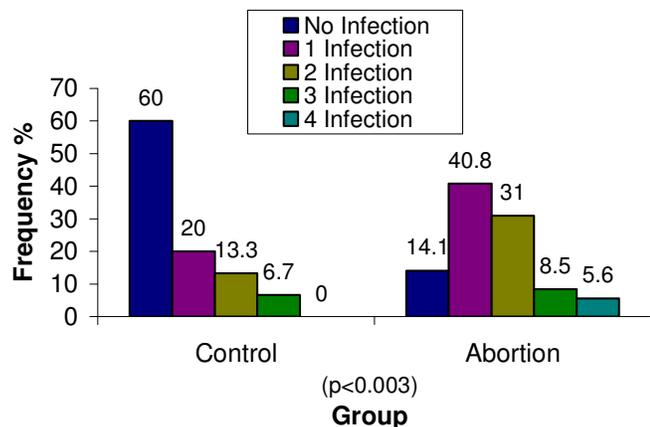


Figure 2. TORCH cross infections in miscarriage cases.

Though the parameters like age, gravida, parity and prevalence of infections like AIDS, hepatitis virus etc. of these patients were studied, no significant correlation was observed for these factors with the incidence of miscarriages. Though, as per previous studies (Regan et al., 1989; Alberman, 1988) maternal age and previous miscarriages had been reported as two independent risk factors for a further miscarriage, no evidence has been obtained from our study in this regard.

Toxoplasma IgM was observed in 50.7% of the miscarriage cases and this is significant, compared to its occurrence in 20% of the normal. This rate is higher when compared to the 11.6% *Toxoplasma* infection observed by Kaur et al. (1999) in Delhi. As per our study, 67.7% of the general population of Malabar region has *Toxoplasma* IgG, that is, immunity against *T. gondii*, leaving 32.2% susceptible to the infection. The immunity status found among this population is high compared to the 35.6% (Ghazi et al., 2002), 47.5% (Ustacelebi et al., 1986) and 53.6% (Rodier et al., 1995) observed in other populations.

The high rate of resistance against *Toxoplasma* may depend upon the environment and life style of the people here. A previous observation (Decavalas et al., 1990) that, '*Toxoplasma* antibodies are found to be higher in aborters from the rural areas, where contact with soil is common regardless of whether cats are kept pets or not', can be true here also.

Through the IgG estimation, this study has also revealed that 90.4% of our population have been pre-exposed and acquired resistance to Rubella virus, which is in agreement with the corresponding rates of 93.3% (Ghazi et al., 2002), 89.9% (Ustacelebi et al., 1986) and 85.5% (Rodier et al., 1995) observed in other populations. The Rubella IgM found in 11.3% of the miscarriage cases of this study is in accordance with the 9.6% susceptibility observed in our general population.. But, compared to the incidence in 6.7% of the normal, this is insignificant ($P < 0.597$).

As Rubella, role of CMV also is not very significant in the miscarriage cases. Here 28.2% of the miscarriage cases and 13% of normal pregnant women were seropositive to CMV. Only 3.2% of the general population is susceptible to this intrauterine pathogen as per their IgG estimation, since 96.8% were immune to it, as observed through their IgG estimation. Other workers have also observed more or less the same resistance rates as 92.1% (Ghazi et al., 2002), 87.8% (Ustacelebi et al., 1986) and 97.2% (Rodier et al., 1995) among their people. As per this study, CMV and Rubella infections have no significant role in causing miscarriage.

As *T. gondii*, *Herpes Simplex Virus* infections also have a statistically significant correlation with the incidence of miscarriages. A positive IgM observed in 59.2% of the cases is found as significant ($P < 0.22$) compared to the incidence in 26.7% of controls. This infection rate agrees well with our observation of 61.3% infection susceptibility to HSV in our general population. The HSV IgG level of 38.7% observed is much lower than the corresponding observations of 90.9% (Ghazi et al., 2002) and 87.5% (Ustacelebi et al., 1986) by previous workers.

On considering the effect of the pathogens on different categories of abortions, *Toxoplasma* and HSV were found to have high influence on the 'complete abortion' category. These have almost the same rate of effect on missed and threatened abortion also. HSV infection was noted in all cases of incomplete abortion, while Rubella and CMV were not found as very prevalent. CMV infection was totally absent in incomplete abortion category. Mihaela et al. (Ghazi et al., 2004) have recently reported that CMV infections have no role in miscarriage, which is partially true as per this study.

Another important finding was the cross infection or the condition where cases being infected by multiple pathogens, revealed through the IgM positivity to more than one of the TORCH pathogens (Figure 2). When 40.8% of the abortion cases and 20% of the normal were positive against any one of these, multiple positivity observed against two, three and four were as 31%, 8.5 and 5.6% among the miscarriage, and as 13.3, 6.7 and 0% among the control group, respectively. It is to be noticed that when 5.6% of the aborted mothers were infected with all the four pathogens, none of the control was infected to this extent. Gong et al. (1999) have reported cross infections with all the TORCH pathogens in only 2.6% of their study. A much higher rate (93.4%) of multiple sero conversion to the TORCH pathogens was also reported by some workers among pregnant women (Kaur et al. 1999). (Aubard et al). had reported double maternal seroconversion against *T. gondii* and Cytomegalovirus.

In conclusion, this study has established the general role of TORCH pathogens on miscarriage in first trimester pregnancy. When only 14.1% of the miscarriage cases were totally free of TORCH infections, 60% of the control group was free out of it. The role of *T. gondii* and *H. sim*

plex virus infection on miscarriage is well proved here. Rubella and Cytomegalovirus were not found to have influenced miscarriage, as per this study. The increased susceptibility of our general population to *T. gondii* and HSV, compared to Rubella and CMV, further supports these observations. Various abortion categories are also influenced by these pathogens differently. It is also observed that cross infections with two or more of the TORCH agents have a statistically significant ($p < 0.003$) prevalence in first trimester miscarriage cases.

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