

Seroprevalence of TORCH Infections in Pregnant Women Attending Antenatal Clinic in a Tertiary Care Hospital

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ABSTRACT

BACKGROUND

TORCH infections caused by *Toxoplasma gondii*, *Rubella virus*, *Cytomegalovirus (CMV)* and *Herpes simplex Virus (HSV-1 and 2)* are often responsible for many unfavourable foetal outcomes like intrauterine growth retardation, congenital anomalies, mental retardation, habitual abortions and still births. As these infections are mild and inapparent, they are rarely diagnosed clinically and are not tested in the pregnant women in the routine antenatal visits. Serological tests remain the method of diagnosis. There is no available baseline data regarding the exact seroprevalence of TORCH infections in our geographical area.

METHODS

An analytical cross-sectional study was carried out to assess the prevalence of TORCH infections among pregnant women who attended the Antenatal clinic at Government Medical College, Thrissur, Kerala, during a period of one year. Blood samples of 200 pregnant women were analysed for the presence of specific IgG antibodies against each agent of TORCH complex by Enzyme Linked Immunosorbent Assay (ELISA).

RESULTS

In the present study, specific IgG antibodies for *Toxoplasma gondii* were detected in 32.5%, for *Rubella* in 76%, for *CMV* in 89.5%, for *HSV-1* in 43% and for *HSV-2* in 8% of the pregnant women. It was noted that the pregnant women with bad obstetric history (BOH) showed a higher seroprevalence rate than the others. Statistical analysis was done by Chi square test.

CONCLUSIONS

This study proves that not only pregnant women with BOH but also normal pregnant women are affected by TORCH infections. We recommend that all antenatal cases with BOH even if they do not have any symptoms should be routinely screened for TORCH agents during the antenatal visits for the proper management of cases. The data reported in our study will be a contribution to the obstetricians and paediatricians of our geographical area to follow appropriate management protocols.

KEY WORDS

TORCH, Seroprevalence, IgG Antibody, ELISA

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BACKGROUND

Toxoplasma gondii, *Rubella* virus, *Cytomegalovirus* (CMV) and *Herpes simplex* virus (HSV) are the members of TORCH complex causing maternal infections transmitted in utero at different stages of pregnancy.^{1,2} These infections in pregnancy are commonly found in association with poor pregnancy outcomes like habitual abortions, neonatal deaths, intrauterine deaths, still births, intrauterine growth retardation, congenital malformations and other reproductive failures.^{1,2,3,4,5}

Toxoplasmosis in humans is caused by an intracellular protozoan parasite *Toxoplasma gondii*, which is transmitted by contaminated food, water and undercooked meat. *Rubella* infection is transmitted from mother to fetus through the placenta and from person to person by tiny droplets. Cytomegaloviruses are transmitted by direct contact with saliva, urine, and genital secretions. Transmission of these viruses in pregnant women is by direct contact with infected urine or saliva of young children or through sexual activity. The overall rate of transmission of toxoplasma and CMV infection to the foetus is about 40-45%.^{3,6} Seroepidemiological studies have shown that 10-20% of women in childbearing age group in India are susceptible to *Rubella* infection.⁷ HSV-1 is transmitted by non-sexual contacts while transmission of HSV-2 is always through the sexual route. The usual source of transmission of HSV to the foetus or newborn is the mother.²

The prevalence of the TORCH infections changes according to the nutritional factors, socio-cultural habits, geographic factors and route of transmission.^{3,4,6,8,9} TORCH infections usually cause minor illness in healthy individuals. As they are initially asymptomatic, they are rarely tested during pregnancy and an early diagnosis on clinical grounds is very unlikely to occur. But, the effect on the foetus can be so severe as these agents can cross the placental barrier to cause intrauterine growth retardation, prematurity, foetal loss or various developmental anomalies and are considered to be a major cause of bad obstetric history (BOH). It is particularly unfortunate as clinical evidence of infection may be detected at birth or not until years later.

Serological tests are the mainstay of diagnosis.^[1,2] The diagnosis of acute TORCH infection in pregnant women is usually established by demonstration of specific IgM antibodies or seroconversion in paired sera. Levels of specific IgM antibodies usually decrease after one to six months of infection and become undetectable within seven months. IgG may be detected one to three weeks after the initial rise in IgM level. IgG synthesis reaches a plateau within two or three months and then decreases more or less rapidly and persists lifelong at residual titers.^[10,11] A 4 to 8 fold rise in IgG titre in the serum samples taken two weeks apart also indicate a recent infection. A positive IgG titre alone is enough to prove a previous infection with TORCH agents.^[3,12]

The exact seroprevalence of TORCH infections in India is not known. Since no routine screening for TORCH infections is done for pregnant women in our hospital, no serological data was available regarding the baseline titres in our geographical

area. Most of the previous studies in the literature were focused to detect only one or two agents of TORCH complex. So, the present study was undertaken to evaluate the seroprevalence of the agents of TORCH complex- *Toxoplasma gondii*, *Rubella* virus, *Cytomegalovirus*, *Herpes simplex* Virus -1 and 2 among the pregnant women. This study gives serological evidence of TORCH infections by antenatal screening of specific IgG antibodies among pregnant women with or without BOH.

METHODS

An analytical cross-sectional study was carried out to assess the seroprevalence of TORCH infections among pregnant women at Government Medical College Thrissur, Kerala. The study was done for a period of one year extending from March 2014 to February 2015. The study was started after getting approval from the Institutional Ethical Committee. Informed consent was obtained from all the pregnant women who were included in our study. The study group included pregnant women who attended the Antenatal clinic of our tertiary care teaching hospital with previous bad obstetric history including unfavourable foetal outcomes in terms of abortions, intrauterine foetal deaths, still births, preterm deliveries, neonatal deaths, intrauterine growth retardation and congenital anomalies and pregnant women without any previous BOH. Pregnant women with other known causes of bad foetal outcomes such as hypertension, diabetes mellitus, eclampsia of pregnancy, Rh incompatibility and physical causes of abortion were excluded from the study.

A total number of 200 pregnant women were enrolled in the study. Approximately 2-3 ml of blood was collected from each patient by venepuncture under aseptic precautions and transported to Microbiology laboratory for processing. The blood samples were centrifuged, sera were separated and transferred into sterile vials. As the serum samples were not tested immediately after collection, they were stored at -20°C till the test was performed. Three ELISA kits for each test were needed for the study. According to the availability of the kits and collection of serum, testing was done in three different months of the study year. All the serum samples were screened for the presence of specific IgG antibodies against *Toxoplasma gondii*, *Rubella* virus, *Cytomegalovirus*, *HSV-1* and *HSV-2* separately in a single serum test by commercially available ELISA test kits manufactured by DSI, Italy. The biomedical waste so generated were disposed-off as per the Bio-Medical Waste Management and Handling rules of 2014. The results were interpreted as per the manufacturer's reference values. All equivocal samples were retested. The results were compiled, and statistical analysis was performed by applying Chi-square test using the Epi Info software (Version 7.5.1.2). 95% Confidence Interval (CI) was calculated for the positive cases. The risk analysis was performed by calculating Odds Ratio (OR) at 95% CI. A p value of < 0.05 was considered to be statistically significant.

RESULTS

A total number of 200 pregnant women were tested for specific IgG antibodies against TORCH agents. Out of these, 70 pregnant women were found to have previous BOH and the rest 130 pregnant women had no previous BOH. In our study, we evaluated the seropositivity of 200 pregnant women for TORCH infections. IgG antibody seropositivity for *Toxoplasma gondii* was detected in 65 (32.5%), for *Rubella* virus in 152 (76%), for *CMV* in 179 (89.5%), for *HSV-1* in 86 (43%) and for *HSV-2* in 16 (8%) of the pregnant women. (See Table: 1) It was observed that the most frequent TORCH agent detected in the study was *CMV* (89.5%). Table: 2 depicts the seropositivity of specific IgG antibodies against TORCH infections among pregnant women with BOH and without BOH. It was worth noting that pregnant women with BOH showed a higher seropositivity than those without BOH. The history of the 70 BOH cases consisted of abortion in 45 (64.2 %), intrauterine growth retardation in (IUGR) in 21 (30 %), intrauterine death in 6 (8.6 %), premature labour in 6 (8.6 %), neonatal death in 4 (5.7 %), and still birth in 1(1.4 %). Odds ratio and 95% confidence interval was calculated in relation to BOH to know the risk of exposure of TORCH infections in previous foetal wastages [see Table: 3].

Serological Test	Total No. of Cases	No. of Positive Cases (%)	95% Confidence Interval
Toxoplasma IgG	200	65(32.5)	25.88-39.12
Rubella IgG		152(76)	69.9-82.04
Cytomegalovirus IgG		179(89.5)	85.16-93.84
Herpes simplex Virus-1 IgG		86(43)	36-50
Herpes simplex Virus-2 IgG		16(8)	4.16-11.84

Table 1. Seroprevalence of TORCH Infections in Pregnant Women

Causative Agent	No. of Positives for IgG among Pregnant Women with BOH (n= 70) (%)	No. of Positives for IgG among Pregnant Women without BOH (n=130) (%)
<i>Toxoplasma gondii</i>	30(42.9%)	35(26.9%)
<i>Rubella</i> virus	59(84.3%)	93(71.5%)
<i>CMV</i>	68(97%)	111(85.4%)
<i>HSV-1</i>	34(48.6%)	52(40%)
<i>HSV-2</i>	7(10%)	9(6.9%)

Table 2. Comparison of Results of Pregnant Women with BOH and without BOH

Type of Torch Infection	Odds Ratio	95% Confidence Interval of Odds Ratio	p Value
<i>Toxoplasma gondii</i>	2.03	1.1-3.7	0.02(S)
<i>Rubella</i>	2.1	1.01-4.5	0.04(S)
<i>CMV</i>	5.8	1.3-25.7	0.19(NS)
<i>HSV1</i>	1.4	0.78-2.5	0.30(NS)
<i>HSV2</i>	1.4	0.5-4.1	0.62(NS)

Table 3. Association of BOH in TORCH Infections (S) Significant (NS) Non-Significant

DISCUSSION

The main aim of our study was to identify the pregnant women infected with TORCH agents. The study showed a high rate of seroprevalence for TORCH infections. We also identified women with BOH showing a higher IgG positivity for all TORCH agents which may be due to previous exposures (See Table: 2). In our study, the seroprevalence rate of *Toxoplasma gondii*

specific IgG antibody was found to be 32.5%. Turbadkar et al reported a seropositivity rate of 42.1% in women with BOH. Nearly 35.6% of the pregnant Saudi women exhibited specific IgG antibodies to *Toxoplasma gondii* as reported by Hani et al.¹³ High prevalence rates were obtained in studies done by Zemene et al (81.1 %)¹⁴ and Sroka et al (68.6%).¹⁵ A lower prevalence rates were reported in studies by Song et al (0.79%)¹⁶ and Jenum et al (10.9%).¹⁷ A decrease in the prevalence rates in these studies may be due to their very large sample size.

We found a high seroprevalence rate (76%) of *Rubella* IgG antibody. *Rubella* seroprevalence rate was high in studies reported from Jeddah (91.6%)⁸ and Tanzania (92.6%).¹⁸ We could not obtain a reliable history of immunisation status against *Rubella* from our patients. So, we could not exclude the possibility of a high prevalence rate of IgG antibody following *Rubella* vaccination. The high prevalence of *Rubella* IgG antibodies (93.3%) among pregnant women of Saudi suggesting a successful vaccination campaign was reported by Hani et al.¹³ Vaccination against *Rubella* in adolescence can result in adequate immunity in the women of childbearing age.

The high prevalence rate of *CMV* obtained in our study (89.5%) agreed with the study reported by Turbadkar et al (91.05%)² and Hani et al (92.1%).¹³ This denoted that *CMV* was very common and unidentified in our community. Even though the p value was not significant the high rate of *CMV* seropositivity in BOH cases shows the apparent risk of *CMV* infection in pregnant women with bad obstetric history. Interpretation of high rate of seropositive *CMV* required understanding the fact that *CMV* has the capability to persist as latent infection indefinitely in the human host particularly in several glands and kidneys.¹⁹ Serological surveys conducted in different parts of India has documented 80-90% prevalence of IgG *CMV* antibodies in the women of childbearing age.²⁰ In the current study, seroprevalence rate of *HSV-1* was 43% which was relatively low when compared to the study done by Obeid et al (93.2%).⁹ Regarding *HSV-2* positivity, rate of Ig G antibody was too high in a study done in Turkey (63%)²¹ compared to our study (8%). A study done at Northeast India has reported a seroprevalence rate of 8.7% which is similar to our findings.²² As *HSV-2* is a sexually transmitted disease, awareness of spread of HIV infection might have affected the prevalence rate of *HSV-2*. In a long term study spanning from 1989 to 2010 Delaney et al showed that there is a declining trend of *HSV-2* infection among pregnant women.²³ Also, he found that the seroprevalence of *HSV-2* infection has come down from 30.1% (During 1989 to 1999) to 16.3% (during 2000 to 2010).²³

95% Confidence Interval of the seroprevalence rate of all the TORCH agents (See Table: 1) showed a narrow range, therefore precision is more in descriptive results. We analysed the Odds Ratio of each TORCH components to find out the association of BOH against TORCH infections. This shows an apparent relationship between TORCH agents and BOH (See Table: 2). None of our subjects were previously symptomatic. It indicates that subclinical or asymptomatic infection was prevalent in our community.

Limitations

We could not test paired sera samples after two weeks to follow up the rise in titre of IgG antibodies. We could not test

for detection of IgM antibodies to exclude recent infection as a part of our study. We also could not do follow up of our cases till their obstetric outcome even though we enquired about BOH for their previous pregnancies. This could have given additional information about the actual burden of the infections.

CONCLUSIONS

This study proves that not only pregnant women with BOH but also normal pregnant women are affected by TORCH infections. In the absence of a national screening programme in India for TORCH infections during pregnancy, serological detection for TORCH infections remains the only means for detecting such infections. The pattern of investigations for pregnant women has to be changed by incorporating TORCH screening tests also in their routine antenatal check-ups. We recommend that all the antenatal cases with BOH even if they do not have any symptoms should be routinely screened for TORCH agents. This helps in the early diagnosis and appropriate intervention in managing the cases. The data reported in our study will be a contribution to the obstetricians and paediatricians of our geographical area to make appropriate management protocols. This knowledge will help the clinicians to counsel the mothers on preventive measures taken to avoid such infections.

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