



SEROPREVALENCE OF TORCH PATHOGENS IN PREGNANT WOMEN IN BAD OBSTETRIC HISTORY

Clinical Microbiology

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ABSTRACT

Background: TORCH complex also known as STORCH is a medical acronym for a set of perinatal infections for Toxoplasma, Others (Syphilis), Rubella, Cytomegalovirus (CMV), Herpes simplex virus-2 (HSV-2). They are one of the major contributors for Bad obstetric history (BOH), often associated with intrauterine infections causing adverse fetal malformations. **Aims:** The study aimed to evaluate the seroprevalence of STORCH infections among 90 pregnant women with BOH. **Settings and Design:** Cross sectional observational study carried out at Mahatma Gandhi memorial hospital (MGMH), Warangal. **Methods and Material:** Blood samples of BOH cases were collected among 19-36 years age group during March 2018 - August 2018 and tested for IgM and IgG antibodies of TORCH infections by ELISA method. Syphilis was initially screened by rapid plasma reagin test (RPR) and confirmed with modified Treponema Pallidum Hemagglutination (TPHA) test. **Results:** Seroprevalence for toxoplasma was 21.2%, rubella 37.8%, CMV 56.7%, HSV 17.8%. Seropositivity observed for toxoplasma 3.4%, rubella 12.2%, CMV 10%, HSV 7.8% and 2.2% reactivity for syphilis. Rubella was the most seropositive agent observed among TORCH infections. Mixed infections were seen in 39 (43.4%) cases. TORCH infections were identified among the age group of 19-24 years with 48 (53.4%) followed by 38 (42.2%) in 25-30 years and 4 (4.4%) in 31-36 years. **Conclusion:** Significant level of TORCH seropositivity in the present study among BOH cases suggests inclusion of TORCH testing along with syphilis in antenatal screening profile, will help in reducing the adverse fetal outcome and for the better reproductive outcome.

KEYWORDS

Bad obstetric history, IgG, IgM, Seropositivity, TORCH

INTRODUCTION:

TORCH complex¹ also known as STORCH, TORCHES or the TORCH infections are a medical acronym for a set of perinatal infections² i.e. infections that are passed from a pregnant woman to her fetus. TORCH acronym was first suggested by Andres Nahmias in 1971 to denote four congenital infections - Toxoplasma, Rubella, Cytomegalovirus and Herpes simplex virus.³ In 1975, Harold Fuerst proposed the new acronym STORCH, where Syphilis was added. Bad obstetric history (BOH) is defined as previous unfavourable outcomes in terms of two or more consecutive spontaneous abortions, history of intrauterine foetal death, intrauterine growth retardation, stillbirths, early neonatal death and/or congenital anomalies. TORCH infections have been ascribed to be one of the main causes of BOH.³ Serological status of TORCH infections in pregnant women provides information about the immune status which may help in identifying women at risk and aid in preventing congenital infections due to these agents.⁴

Subjects and Methods:

The present study was a cross-sectional study conducted in the Microbiology Department at a tertiary care hospital, Warangal, Telangana.

The study was approved by Institutional Ethics Committee. After taking written informed consent from 90 pregnant women of 19-36 years age group with BOH attending antenatal clinics, detailed history was taken and blood samples were collected during March 2018-August 2018.

History of Rh incompatibility, uterine anomalies, medical disorders were excluded from the study. Serum was separated and tested using the commercial kits for qualitative immunoenzymatic determination of IgM and IgG antibodies for toxoplasma, rubella, CMV and HSV-2 according to manufacturer's instructions using ELISA technique. The kits used were ENZYWELL, DIESSE Diagnostic, Monteriggioni (Siena)-Italy for IgG and IgM. The optical density (OD) was read at 450 nm on the ELISA reader and index value of each determination was calculated by dividing the value of each sample by calibrator values. Serotitres were interpreted as negative (<0.8), equivocal (0.8-1.2) and positive (>1.2) as per the literature supplied along with the kits. In case of equivocal result, test was repeated on fresh sample collected after 2 weeks and if still equivocal, it was not included in data

analysis. Rapid plasma reagin (RPR) test was done for syphilis using kit BEACON DIAGNOSTICS and reactive samples were confirmed with TPHA test using IMMUTREP TPHA from OMEGA DIAGNOSTICS to ascertain the true positivity. Interpretation of results in RPR test as large clump as Reactive (R), Small clumps as weakly reactive and no clumping as Non-Reactive (NR). Results in TPHA test interpreted as agglutinated cells form an even layer over the bottom of the well, non-agglutinated cells form a compact button in the centre of well and weakly agglutinated cells form a ring pattern. Only the cases positive for both RPR and TPHA were considered as reactive for syphilis.

RESULTS:

The IgM / IgG seropositivity to toxoplasma was n=3 (3.4%) / 16 (17.8%), rubella 11 (12.2%) / 23 (25.5%), CMV 9 (10%) / 42 (46.7%) and HSV 7 (7.8%) / 9 (10%). 2 cases (2.2%) were found to be reactive for syphilis. CMV was found to be the most seropositive infection observed (table-I). Majority of BOH cases were seen among the age group of 19-24 years 48 (53.4%) followed by 38 (42.2%) in 25-30 years and 4 (4.4%) in 31-36 years (graph-I). Among BOH cases, the obstetric history in various age groups was observed, where the major clinical presentation was abortion in 39 (43.4%) followed by intrauterine deaths (IUD) in 19 (21.1%) cases (graph-II). Majority of the seropositive cases were observed in the age group 19-24 years in toxoplasma 11 (12.2%), rubella 19 (21.1%), CMV 29 (32.3%). For HSV-2 infection, the seropositivity was found to be higher in the age group 25-30 years (table-II). In this study, and maximum reactivity for syphilis was observed among age group of 25-30 years. The predominant clinical presentation responsible for BOH in seropositive cases observed in abortions followed by intrauterine deaths. IgM seropositivity for abortions in toxoplasma (n=19), rubella (n=34), CMV (n=51), HSV (n=16), syphilis (n=2) were two (10.5%) and four (11.8%), three (5.9%), three (18.8%), two (50) respectively (table-III). Out of 39 (43.4) cases of mixed infections, individual IgG seropositivity was highest for CMV 42 (46.7) and IgM for rubella 11 (12.2). Combination of two TORCH agents for IgM seropositivity observed in toxoplasma with RUBV, CMV with RUBV. For IgG, two TORCH agents observed in TOXO with RUBV, TOXO with CMV and HSV, three agents for RUBV with CMV and HSV (table-IV).

DISCUSSION:

In the present study serological evidence for any one of the TORCH agents were detected in 78 (86.7%) of pregnant females. Kumari et al⁵ (2011) observed 83.3% seropositivity and Bhavesh R Faldy et al⁶ (2014) detected 90 (60%) of the pregnant women seropositive for any of the TORCH agents. Suryamani Chintapalli⁷, I Jyothi Padmaja (2013) and Shubangi Mande et al⁸ (2016) reported with maximum seropositivity of TORCH infections in the age group 20-24 years which is similar to the present study. Among BOH cases, the obstetric history in various age groups was studied, where the major clinical presentation was abortion in 39 (43.4) followed by intrauterine deaths (IUD) in 19 (21.1) cases where similar observations made by other studies as depicted in (table-V).

It is evident that maternal infections play a critical role in pregnancy loss and their occurrence in BOH is a significant factor. Toxoplasma gondii, an intracellular protozoan parasite transmitted through contaminated food or water and undercooked meat. An infected person is usually asymptomatic, but during pregnancy it can cause pregnancy loss, stillbirth and intrauterine malformations in fetus⁹. In the present study seropositivity for toxoplasma IgM/IgG was 3.4% / 17.8%. Singh M et al¹⁰ (2016) and Kusuma Nellimarla et al¹¹ (2017) have also reported as 23 (8.8%) / 40 (15.4%) and 20% / 30% respectively. Rubella infection is generally an asymptomatic childhood disease but during the first trimester of pregnancy, it can cause fetal death or severe congenital defects (CRS). The rubella seropositivity for IgM was 11(12.2%) and IgG 23 (25.5%) in this study. Ramana BV et al¹² (2012) and Jay Parikh et al¹³ (2016) reported overall IgM seropositivity of 12.67%, 12% respectively. Cytomegalovirus is a beta herpes virus has a double stranded DNA and sources of CMV infection include Congenital, Perinatal, postnatal, blood product transfusions, organ transplantation, stem cell transplantation, person-to-person transmission. The present study showed seropositivity rate of 10% / 56.7% for CMV IgM/IgG in women with BOH. Padmavathy M et al³ (2013) reported 9.2% seropositivity of CMV specific IgM, Tiwari et al¹⁴ (2016) concluded 12.6%. Several studies have reported between 84.5-95% prevalence of CMV IgG among pregnant women in Turkey.

Genital herpes infection during pregnancy may lead to spontaneous abortion, prematurity, congenital and neonatal herpes. Seropositivity rate of HSV IgM 7 (7.7%) and IgG 9 (10%) in this study. Namrata Saxena et al,¹⁵ Maimoona Mustafa et al¹⁶ (2017) and Tiwari et al¹⁴ had shown seroprevalence of HSV-2 IgM as 8.57% - 10% and comparative studies were shown as in (table-VI). Syphilis remains a significant cause of perinatal mortality and morbidity in many parts of the world and seroprevalence varies widely. In India, the prevalence of syphilis ranges between 2.0-4.8% among women of reproductive age.

Maternal syphilis has a severe impact on outcome primarily as spontaneous abortions, stillbirth and congenital syphilis. In the present study the predominant obstetric history in seropositive cases of syphilis was abortion one (1.1%), preterm labor one (1.1%) Mathai E et al (2001) reported abortions 16 (32%) of the 50 seropositive women. The reactivity of syphilis in this study was 2 (2.2%). Archana et al¹⁷ (2007) study ranged from 0.57 to 0.78% and Hiral K Patel et al¹⁸ reported 0.28% seropositivity of syphilis.

CONCLUSION:

The present study had reported a significant seroprevalence of IgM and IgG antibodies for TORCH infections among pregnant women in BOH cases. ELISA method is more efficacious than any other methods in demonstrating TORCH antibodies. Educating the public about avoidance of ingestion of raw meat and poultry, keeping away from cats may be the best approach to prevent toxoplasma associated infection. As the rubella (IgM) had shown to be the highest seropositivity, which indicates acute infection in this study.

Thus it emphasizes the need to modify the vaccine strategies in rubella by providing routine childhood vaccination, mass vaccination of adolescent girls and women of childbearing age or a combined strategy. Active surveillance of rubella and congenital rubella syndrome (CRS) is needed to redress the burden in India.

High seroprevalence of CMV in our study, reflects the low hygienic standards as well as faulty practices running in especially low socio-economic group. In the light of the substantial burden on society conferred by CMV infection, a modest reduction of this disease is an important public health goal, and justifies aggressive clinical evaluation of vaccines currently in the pipeline. The risk of

transmission of maternal-foetal-neonatal HSV-2 can be decreased by performing caesarean section in genital herpetic lesions. Women should be tested for syphilis during each pregnancy even if they tested negative in a previous pregnancy. When access to prenatal care is not optimal or laboratory capacity is limited, rapid tests have been shown to be beneficial in detecting and treating syphilis in pregnant women. Guidelines recommend that after delivery, neonates should not be discharged from the health facility unless the serological status of the mother had been determined at least once during pregnancy and preferably again at delivery. Efforts must be made towards ensuring complete follow up as well as adequate treatment of reactive cases, universal access to early antenatal care, recommends husbands of pregnant women get screened at the first antenatal visit and that the test should be repeated early in third trimester.

A previous history of pregnancy wastage and the positive serological reaction for TORCH infection during current pregnancy must be considered while managing the BOH cases to reduce the adverse foetal outcome. Understanding the epidemiology of TORCH infections is an important element in the development of prevention strategies and medical interventions for the prevention of congenital infections.

Abbreviations:

BOH = Bad obstetric history, HSV = Herpes simplex virus, CMV = Cytomegalovirus, IUD = Intrauterine death, RUBV= Rubella virus, TOXO=Toxoplasma

Declarations:

- Approval was obtained from the ethics committee of Kakatiya medical college. The procedures used in this study adhere to the tenets of the Declaration of Helsinki.
- Informed consent was obtained from all individual participants included in the study.
- Funding: nil
- There are no conflicts of interest.

Table-I: Positive serological evidence of TORCH agents (N=90)

Torch agent	IgM (%)	IgG (%)	Total (%)	IgM+ IgG (%)
Toxoplasma	3 (3.3)	16 (17.8)	19 (21.1)	1 (1.1)
Rubella	11 (12.2)	23 (25.5)	34 (37.8)	3 (3.3)
Cytomegalovirus	9 (10)	42 (46.7)	51 (56.7)	3 (3.3)
Herpes Simplex Virus-2	7 (7.8)	9 (10)	16 (17.8)	1 (1.1)
Syphilis	02 (2.2)			

Table-II: Seropositivity of TORCH agents in age wise distribution of BOH cases

TORCH Agent	Age group (years)	IgM no.	IgM positive %	IgG positive no.	IgG positive (%)	Total positive no.	Total positive (%)
Toxoplasma	19-24	2	2.2	9	10	11	12.2
	25-30	1	1.1	6	6.7	7	7.8
	31-36	0	0	1	1.1	1	1.1
	Total	3	3.4	16	17.8	19	21.2
Rubella	19-24	6	6.7	13	14.5	19	21.2
	25-30	4	4.4	8	8.9	12	13.3
	31-36	1	1.1	2	2.2	3	3.3
	Total	11	12.2	23	25.5	34	37.7
Cytomegalovirus	19-24	5	5.6	24	26.7	29	32.3
	25-30	3	3.4	16	17.8	19	21.1
	31-36	1	1.1	2	2.2	3	3.3
	Total	9	10	42	46.7	51	56.7
Herpes simplex virus	19-24	2	2.2	3	3.4	5	5.6
	25-30	4	4.4	5	5.6	9	10
	31-36	1	1.1	1	1.1	2	2.2
	Total	7	7.7	9	10	16	17.8

Table-III: Clinical presentation of BOH cases with positive serological evidence of TORCH agents

Type of BOH	Toxoplasma (n=19)				Rubella (n=34)				Cytomegalovirus (n=51)				Herpes simplex virus (n=19)			
	IgM %	IgG %	IgG+ IgM %	Total %	IgM %	IgG %	IgG+ IgM %	Total %	IgM %	IgG %	IgG+ IgM %	Total %	IgM %	IgG %	IgG+ IgM %	Total %
Abortion	7 (36.8)	2 (10.5)	1 (5.3)	10 (52.6)	4 (11.8)	13 (38.2)	1 (2.9)	18 (52.9)	3 (5.9)	25 (49.2)	1 (1.9)	29 (56.9)	3 (18.8)	4 (25)	1 (6.2)	8 (50)
IUD	4 (21)	1 (5.3)	0 (0)	5 (26.3)	2 (5.9)	8 (23.5)	1 (2.9)	11 (32.4)	1 (1.9)	13 (25.4)	1 (5.3)	15 (29.4)	1 (6.2)	3 (18.8)	1 (6.2)	5 (31.2)
Preterm labor	2 (10.5)	0 (0)	0 (0)	2 (10.5)	0 (0)	0 (0)	0 (0)	0 (0)	2 (3.9)	3 (5.9)	1 (5.3)	6 (11.8)	0 (0)	0 (0)	0 (0)	0 (0)
Stillbirth	1 (5.3)	0 (0)	0 (0)	1 (5.3)	1 (2.9)	2 (5.9)	0 (0)	3 (8.8)	0 (0)	1 (1.9)	0 (0)	1 (1.9)	1 (6.2)	2 (12.5)	0 (0)	3 (18.8)
CM	1 (5.3)	0 (0)	0 (0)	1 (5.3)	1 (2.9)	0 (0)	1 (2.9)	2 (5.9)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Total	15 (78.9)	3 (15.8)	1 (5.3)	19 (100)	8 (23.6)	23 (67.6)	3 (8.8)	34 (100)	6 (31.6)	10 (52.6)	3 (15.8)	51 (100)	5 (31.2)	9 (56.3)	2 (21.5)	16 (100)

IUD = intrauterine deaths CM= congenital malformations

Table-IV: Mixed infections among TORCH agents

TORCH AGENT	INDIVIDUAL REACTIVITY		PLE REACTIVITY								RUBV + CMV		RUBV + HSV		CMV+ HSV		TOTAL	
	IgM	IgG	IgM	IgG	IgM	IgG	IgM	IgG	IgM	IgG	IgM	IgG	IgM	IgG	IgM	IgG	IgM	IgG
Toxoplasma (TOXO)	3	16	XX	XX	1	1	0	3	0	1	1	2	1	1	1	2	9	
Rubella (RUBV)	11	23	1	1	XX	XX	1	7	0	1	0	0	0	0	0	2	9	
Cytomegalovirus (CMV)	9	42	0	3	1	7	XX	XX	0	2	0	0	0	0	0	1	12	
Herpes simplex virus-2 (HSV-2)	7	9	0	1	0	1	0	2	XX	XX	0	0	0	0	0	0	4	

Table-V: Obstetric History of BOH cases -Comparison with other Studies

Authors Name	Year of study	Obstetrical History No. & %
Shashi Chopra et al	2004	Abortions 61 (71.8%)
Rajendra Surpam B et al	2006	Abortions 44 (29.33%)
Janak Kishore et al	2011	Abortions 28 (59.5%)
Sarkar MD et al	2012	Abortions 11 (52%)
Padmavathy M et al	2013	Abortions 47 (54.1%)
Bhaves R Faldu	2014	Abortions 86 (57.3%)
Namrata saxena et al	2015	Abortions 30 (42.8%)
Shubangi Mande et al	2016	Abortions (54%)
Present Study	2018	Abortions 52 (57.8%)

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