

Seroprevalence of TORCH Infections in Pregnant Women with Bad Obstetric History in and Around Bikaner, Northern Western Rajasthan

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Abstract: The infections which are caused by *Toxoplasma gondii*, Rubella virus, Cytomegalovirus (CMV) and the Herpes Simplex Virus (HSV-2) during pregnancy are often associated with adverse foetal outcomes and reproductive failures. In the Indian context, the exact seroprevalence of these infections is not known due to unavailability of baseline data. TORCH infections are initially in apparent or asymptomatic and are thus difficult to diagnose on clinical grounds. The main aim of this study to detect specific IgM and IgG antibodies for *Toxoplasma*, Rubella, Cytomegalovirus and Herpes Simplex virus 2 by Enzyme Linked Immunosorbent Assay Test and also to know the outcome of TORCH infection in pregnant women with bad obstetric history in Bikaner region. Over a two-year period 75 serum samples were collected from pregnant women having bad obstetric history, attending Department of Obstetrics and Gynaecology department, P.B.M. hospital, Bikaner during the period of jan.2015 to feb.2017. IgM and IgG Anti TORCH antibodies were detected from serum by micro capture ELISA test kit in Department of Microbiology and Immunology, Sardar Patel Medical College, Bikaner. In the present study of 75 women with BOH, seropositivity of different TORCH agents (IgG and IgM) was *Toxoplasma gondii* 5.33% and 2.66%, Rubella was 84% and 6.66%, CMV was 82.66% and 9.33% and HSV was 38.66% and 8% respectively indicating recent infection which was maximum in CMV, HSV, Rubella and *Toxoplasma gondii*. The maximum number of 45 cases (60%) was of the age group 21-25 years followed by 20 cases (26.66%) 26-30 years age group, 05 cases (6.66%) 31-35 years age group, 03 cases (4%) 36-40 years age group and 02 cases (2.66%) in 16-20 years age group. The observations can be interpreted as incidence and prevalence indicating highest incidence of CMV followed by HSV, Rubella and Toxoplasmosis. The prevalence of Rubella was found highest followed by CMV, HSV and Toxoplasmosis. In conclusion this study has established that TORCH infection play an important role in adverse fetal outcome in pregnant women. Therefore, all the antenatal cases should be routinely screened for the TORCH infections, for carrying out early interventions to prevent foetal loss.

Keywords: TORCH, Bad obstetric history (BOH), IgG, IgM, Pregnant women.

INTRODUCTION

For thousands of couples, the joyous event of the birth of a child into a family may become the beginning of a long tortuous & tumultuous life. Human reproduction is a relatively insufficient process. Over one-fifth of the pregnancies are lost before implantation and the process of pregnancy loss continues thereafter. Recurrent pregnancy loss due to maternal infections transmissible in utero at several stages of the pregnancy can be caused by a wide array of organisms. TORCH complex (*Toxoplasma gondii*, Rubella virus, Cytomegalovirus, Herpes Simplex

virus) and other agents like *Chlamydia trachomatis*, *Treponema pallidum*, *Neisseria gonorrhoeae*, HIV (Human immunodeficiency virus), Human parvovirus B19, *Listeria monocytogenes* (bacteria) etc. are important causes of maternal infection associated with intrauterine or perinatal infection that may result in damage or even death of the fetus[1].

The acronym TORCH was coined by immunologist Andre Nahmias for *T. gondii*, Rubella, Cytomegalovirus and Herpes Simplex virus, these are capable of crossing the placenta and causing abortion,

stillbirth, congenital malformation, acute disease during neonatal period or chronic infection that often delay detection[2]. Infection with these agents can result in significant morbidity and mortality especially in developing countries [3].

Toxoplasmosis in humans is caused by an intracellular protozoan parasite *Toxoplasma gondii*, which is transmitted by contaminated food, water and undercooked meat. The incubation period for toxoplasmosis is 5–23 days [4, 5]. Toxoplasmosis acquired during pregnancy may cause damage to the fetus. Rubella infection is transmitted in mother to foetus by placenta and person to person by tiny droplets. The incubation period for Rubella infection is 2–3 weeks.⁶In India 10-20 % women in childbearing age are susceptible to Rubella infection.⁷Rubella infection during pregnancy may lead to 10-54% congenital malformation.⁸Cytomegalovirus is species-specific, ubiquitous and humans are reservoir hosts. The viruses are transmitted by direct contact with saliva, urine, and genital secretions. In pregnant women, the transmission is by direct contact with infected urine or saliva from young children or through sexual activity [8]. The incubation period of CMV infection ranges between 4-12 weeks. In adult CMV infection is usually asymptomatic but during pregnancy its significance is increased many times. So primary CMV infection significantly high in pregnant women from low socioeconomic group[9]. In world HSV is sexually transmitted viral disease (STD). HSV-1 is transmitted by non-sexual contacts & HSV-2 is transmitted sexually always. The mother is the usual source of transmission of HSV to the fetus or newborn[10, 11]. Incubation period for herpes is 4-21days[12].

TORCH agents are difficult to culture hence serodiagnosis is only modality available to detect their presence. In India baseline serological data regarding the presence of an antibody in the TORCH infection are not available because in India national screening programme are not governed by government. TORCH infections are initially in apparent or asymptomatic and are thus difficult to diagnose on clinical grounds. Therefore, diagnosis of TORCH infection in women, infants and newborns is usually established by demonstration of seroconversion in paired sera or by demonstration of specific IgM antibodies.

The main aim of this study to detect specific IgM and IgG antibodies for *Toxoplasma*, Rubella, Cytomegalovirus and Herpes Simplex virus 2 by

Enzyme Linked Immunosorbent Assay Test and also to know the outcome of TORCH infection in pregnant women with bad obstetric history in Bikaner region.

MATERIALS AND METHODS

Study design: A cross sectional study

Study period: January 2015 to February 2017

Sample size: 75 pregnant women with bad obstetrical history

Selection of cases:

Inclusion criteria

75 patients having a history of unfavourable fetal outcome in terms of two or more consecutive spontaneous abortion, history of intrauterine fetal death, intrauterine growth retardation, stillbirths, early neonatal death and or congenital anomalies were randomly selected and included in the present study on BOH from patients attending outpatient Department of Obstetrics and Gynaecology department, P.B.M. hospital Bikaner during the period of jan.2015 to feb.2017.

Exclusion criteria

Women with HIV positive, VDRL positive and diabetics were excluded from the study.

Institute's ethical committee approval was taken and an informed consent was obtained from all the patients.

Collection of samples: 5cc of blood collected aseptically from each woman in a duly labelled plain test tube. Blood was allowed to clot for 20 minutes and then serum was separated by centrifugation at 3,000 RPM for 10 minutes & transferred into sterile provials and stored at 20°C until the test was performed. Test was performed in Department of Microbiology and Immunology, Sardar Patel Medical College Bikaner.

IgM and IgG Anti TORCH antibodies were detected from serum by micro capture ELISA test kit. Separate kits for detection of antibodies to *Toxoplasma*, Rubella, CMV and HSV-2 for ELISA Test were used. ELISA kits used were manufactured by XEMA Co. Ltd. Moscow, Russia.

The optical density at 450 nm with a 620 nm filter dual wavelength mode was measured by micro well ELISA reader.

OBSERVATIONS AND RESULTS

Table-1: Distribution of BOH study cases on basis of age groups

S. No.	Age Group(years)	No. of cases studied and (%)
1.	16-20	02(2.66%)
2.	21-25	45(60%)
3.	26-30	20(26.66%)
4.	31-35	05(6.66%)
5.	36-40	03(4%)

	Total	75(100%)
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Table-2: Distribution of cases under study on basis of past BOH

S. No.	Group(past obstetric outcome)	No. of cases studied and (%)
1.	Abortion	40(53.33%)
2.	Intrauterine fetal death	16(21.33%)
3.	Intrauterine growth retardation	08(10.66%)
4.	Early neonatal deaths	06(8%)
5.	Congenital malformations	04(5.33%)
6.	Stillbirth	01(1.33%)
	Total	75(100%)

Table-3: Number of women of BOH with seropositivity to the TORCH agents

S. No.	TORCH agent	No. of IgG positive (%)	No. of IgM positive (%)
1.	T. gondii	04(5.33%)	02(2.66%)
2.	Rubella virus	63(84%)	05(6.66%)
3.	Cytomegalovirus (CMV)	62(82.66%)	07(9.33%)
4.	Herpes Simplex virus-2 (HSV)	29(38.66%)	06(8%)

DISCUSSION

The present study was conducted in Sardar Patel Medical College and associated hospital Bikaner from Jan. 2015 to Feb.2017. 75 cases of pregnant women having bad obstetric history were selected from those attending in P.B.M. hospital.

Bad obstetric history implies previous unfavourable outcome in terms of 2 or more consecutive spontaneous abortions, history of intrauterine fetal death, intrauterine growth retardation, stillbirth, early neonatal death/congenital abnormalities. Recurrent pregnancy wastage due to maternal infection transmissible in utero at various stages of pregnancy can be caused by a variety of organisms of which primary infection with TORCH complex (Toxoplasma, Rubella, Cytomegalovirus and Herpes viruses mainly Herpes 2) in pregnant women can lead to adverse outcome which are initially inapparent and thus difficult to diagnose on clinical grounds.

In the present study 75 pregnant women were 16 to 36 years of age are included. The maximum number of 45 cases (60%) was of the age group 21-25 years followed by 20 cases (26.66%) 26-30 years age group, 05 cases (6.66%) 31-35 years age group, 03 cases (4%) 36-40 years age group and 02 cases (2.66%) in 16-20 years age group. A study done by Padmavathy M. *et al.* Bengaluru in april 2013 studied TORCH infections 67 cases. They reported majority of BOH cases 45 (51.9%) in age group 25-30 years followed by 30(34.4%) in 19-24 years[13].

A study also done by Munmun Das Sarkar *et al* at Andhra Pradesh in 2012 studies only toxoplasmosis in antenatal women. They had tested 105 sera and reported that 26.1% in the age group above 30 years followed by 37.1% cases in the age group 26-30 year, 24.7% in 21-25 year age group and 11.4% in the age group below 20 years[14].

Out of 75 women the bad obstetric history 40 (53.33%) had two or more abortions, 16 (21.33%) had intrauterine deaths, 08 (10.66%) had intrauterine growth retardation, 06 (8%) had early neonatal deaths, 04 (5.33%) had congenital malformations and 01 (1.33%) had a past history of stillbirth. Other study done by Munmun Das *et al.* 2012 and Rohini Suryawanshi *et al.* 2014 reported that 38, 9, 5, 21, 20 and 51.92, 36.53, 1.93, 1.93, 27.27 percentage of cases of abortions, intrauterine deaths, stillbirth, congenital malformations, intrauterine growth retardation and early neonatal deaths[14,15].

In the present study of 75 women with BOH, seropositivity of different TORCH agents (IgG and IgM) was Toxoplasma gondii 5.33% and 2.66%, Rubella was 84% and 6.66%, CMV was 82.66% and 9.33% and HSV was 38.66% and 8% respectively indicating recent infection which was maximum in CMV, HSV, Rubella and Toxoplasma gondii.

Among 04 cases of Toxoplasmosis observed 02 cases have IgM and IgG seropositivity and 02 cases shows only IgG positive. None of the case shows positivity to IgM alone indicative of 02 cases of recent infection and 02 cases of old infection.

We observe 63 cases of Rubella infection out of which IgM was alone not positive in any cases and IgG & IgM both are positive in 05 cases indicative recent Rubella infection. IgG seropositivity alone was seen in 58 cases suggestive old Rubella infection.

Cytomegalovirus infection was found in 62 cases out of 75 in which IgM alone was not positive in any cases while IgM and IgG both are positive in 07 cases suggestive of a recent CMV infection. IgG alone was found in 55 cases which indicates past CMV infection.

HSV seropositivity was observed in 31 cases of BOH out of which IgM alone was also found in 02 cases and IgG & IgM both were found in 04 cases suggestive of recent incidence of HSV infection, while IgG alone were found in 25 cases suggestive of an old infection.

The above observations can be interpreted as incidence and prevalence of Toxoplasmosis as 02 & 04, of Rubella as 05 & 63, of CMV as 07 & 62 and HSV as 06 & 31 respectively indicating highest incidence of CMV followed by HSV, Rubella and Toxoplasmosis. The prevalence of Rubella was found highest followed by CMV, HSV and Toxoplasmosis.

In Toxoplasmosis the IgM seropositivity of our study was 2.66% which correlates with the study of Padmavathy *et al.* 2013 Bengaluru 5.8%, Sadik *et al.* 2012 Hyderabad and Voona 2008 Chennai reported 0% IgM seropositivity of Toxoplasma [13,16,17]. Higher incidence of IgM seropositivity was also reported by other study like Suryawanshi *et al.* 2014 Satara 41% and Malik *et al.* 2014 Aligarh reported 28%[15,18]. The present study shows the IgG seropositivity of Toxoplasmosis to be 5.33% which nearly coincides with the study Padmavathy *et al.* 2013 Bengaluru 8% and Voona 2008 Chennai 7.14%[13,17]. However a higher IgG seropositivity of Toxoplasmosis were reported by Sadik *et al.* 2012 Hyderabad 20.93%[16].

Rubella a common infection in women. Sero epidemiologic studies have shown that 10-20% of women in India are susceptible to Rubella infection [19]. Infection rate to Rubella during pregnancy may lead to congenital malformations in 10-54% of cases.

The present study reports the IgM seropositivity of 6.66% for Rubella. Nearly similar observations were shown by Padmavathy *et al.* 2013 Bengaluru 4.6%, Sadik *et al.* 2012 Hyderabad 4.65% and Voona 2008 Chennai reported 0% IgM seropositivity of Rubella [13,16,17]. While higher IgM seropositivity of Rubella was reported by Suryawanshi *et al.* 2014 Satara 18%, Turbadkar *et al.* 2003 Mumbai 26.85%, Sen *et al.* 2012 Varanasi 30.4%[15,20,21]. The present study shows that IgG seropositivity of Rubella to be 84%. Nearly similar observations were shown by other authors Padmavathy *et al.* 2013 Bengaluru 90.8%, Turbadkar *et al.* 2003 Mumbai 61.3%[13,20]. Lower IgG seropositivity of Rubella was reported by Sadik *et al.* 2012 Hyderabad 29% and Voona *et al.* 2008 Chennai to be 17.85%[16,17].

Primary CMV infection in pregnancy has a higher incidence of symptomatic congenital infection and fetal loss. This infection is commonly asymptomatic in adults hence difficult to diagnose [20]. The present study shows a 9.33% IgM seropositivity for CMV infection. A similar observations was reported by Padmavathy *et al.* 2013

Bengaluru 9.2%, Turbadkar *et al.* 2003 Mumbai who reported IgM seropositivity for CMV to be 8.42% [13,20]. Other authors have reported a higher IgM seropositivity of CMV Suryawanshi *et al.* 2014 Satara 27%, Sen *et al.* 2012 Varanasi 34.7%[15,21]. Lower IgM seropositivity also reported by Voona *et al.* 2008 Chennai 3.57% and Sadik *et al.* 2012 Hyderabad reported a zero percentage IgM positivity rate [17,16]. Present study shows 82.66% of CMV IgG seropositivity. A similar observations was also made by Padmavathy *et al.* 2013 Bengaluru 95%, Turbadkar *et al.* 2003 Mumbai 91%.[13,12] However a lower seropositivity of CMV was reported by Sadiq *et al.* 2012 Andhra Pradesh and Voona *et al.* 2008 Chennai reported a IgG positivity rate of 23%[16,17].

Primary infection with HSV acquired by women during pregnancy accounts for about 50% morbidity and mortality among neonates, the other half result from reactivation from an old infection[22]. In the present study the IgM seropositivity of HSV 2 was found to be 8% which is in accordance to study of Nidha Abdul *et al.* 2009 Iraq 8%, Surpam *et al.* 2006 Nagpur 8.66%, Suryawanshi *et al.* 2014 Satara 14% [23,24,15]. On the contrary other studies have reported a higher IgM seropositivity by Thapliyal *et al.* in 2005 at Nainital 26.7%, Sen *et al.* 2012 Varanasi 33.5%[25,21]. A lower IgM seropositivity of HSV was also reported by Padmavathy *et al.* 2013 Bengaluru 2.3%, Voona *et al.* 2008 Chennai 1.78%, Sadik *et al.* 2012 Hyderabad 1.69% [13,17,16]. In the present study the IgG seropositivity of HSV 2 was found to be 38.66% which correlates with the other studies of Turbadkar *et al.* 2003 Mumbai who reported 33% positivity with IgG[20] A higher IgG seropositivity of HSV was also reported by Sulochana *et al.* 2008 from Imphal 67% and Thapliyal *et al.* 2005 from Nainital 73% [26,25] However a lower IgG seropositivity of HSV was also reported from 6% to 18% by Padmavathy *et al.* 2013, Ranjith Voona 2008 Chennai and Sadiq *et al.* from Hyderabad in 2012[13,17,16].

The variation in the percentage of seropositivity to IgM and IgG, IgM alone and IgG alone indicative of incidence and prevalence of TORCH infections reported by various authors from India and abroad may be likely due to different country and different geographical areas of India including their urban and rural background and their behaviour, the occupation of women and the sample size of the study.

Maternal infection play a critical role in pregnancy wastage and their occurrence in BOH and complicated pregnancy is a significant risk factor. These infections cause fetal and neonatal mortality and an important contributor to early and major childhood morbidity. All viral pathogens usually cause a primary maternal viraemia which infects the placenta and there

by the fetus with the exception of HSV which causes an ascending infection via genital tract to the fetus.

Women affected with any one of these diseases during pregnancy are at high risk for miscarriage, stillbirth, or for a child with serious birth defects. Thus there is need of performing the TORCH test as early as possible for diagnosing and determining the mother's exposure to Toxoplasma, Rubella virus, Cytomegalovirus and Herpes Simplex virus infection.

CONCLUSION

In conclusion this study has established that TORCH infection play an important role in adverse fetal outcome in pregnant women. In order to prevent the morbidity and mortality of fetus all antenatal cases with bad obstetrical history even if not having any symptoms should be screened for TORCH agents as early as possible for early diagnosis and appropriate management.

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