Original Article

TORCH infection in antenatal women: A 5-year hospital-based study

Kirti Nirmal[1], Rumpa Saha[1], V G Ramachandran[1], Amir Maroof Khan[2]

From Departments of [1]Microbiology, [2]Community Medicine, University College of Medical Science and Guru Teg Bahadur Hospital, Delhi, India

Correspondence to: Dr. Rumpa Saha, Department of Microbiology, University College of Medical Sciences and Guru Teg Bahadur Hospital, Delhi – 110 095, India. Phone: +91-9212116906. E-mail: rumpachatterjee@yahoo.co.in

Received - 12 August 2017 Initial Review - 09 October 2017 Published Online - 14 December 2017

ABSTRACT

Objectives: The diagnosis of acute TORCH infection in pregnant women being pertinent for the management of such infections prompted the current study due to lack of published data from India describing the seroprevalence of specific IgM antibodies to TORCH agents in this part of Northern India. **Material and Methods:** Blood samples of a total of 240 high-risk pregnant women attending the antenatal clinic of our tertiary care hospital during a 5-year period (2005–2009) were analyzed for specific IgM antibodies to *Toxoplasma gondii,* rubella, *Cytomegalovirus* (CMV), and combined herpes simplex virus (HSV) 1 and 2 by capture enzyme-linked immunosorbent assay. **Results:** Overall, seropositivity to TORCH infection in the present study was 98.8%. Seropositivity to *T. gondii* was 24.2%, rubella 9.2%, CMV 53.8%, and 11.7% were positive for combined HSV-1 and 2 infections. The average age of the study population was 27.5 years. Overall, 15.4% of women were seropositive for coinfections. **Conclusion:** The high seropositivity of 98.8% and presence of multiple infections seen in the present study communicate to all health authorities to screen routinely all pregnant women for TORCH infections for appropriate intervention in the proper management of these patients.

Key words: *Antenatal women, Bad obstetrics history, Coinfection, TORCH*

Maternal infections that are transmissible *in utero* at several stages of the pregnancy can be caused by many organisms, of which the members of the TORCH complex, namely, *Toxoplasma gondii*, rubella, *Cytomegalovirus* (CMV), and herpes simplex virus (HSV) occupy prominent positions [1]. These infections are associated with inadvertent outcomes such as multiple infections, abortions, infertility, fetal deaths, stillbirths, congenital malformations, and other reproductive failures, especially when they are acquired during the first trimester of pregnancy [2]. The diagnosis of acute TORCH infection in pregnant women, usually established by demonstration of seroconversion in paired sera or by demonstration of specific IgM antibodies, is pertinent for management of such infections [3,4]. TORCH screening in the antenatal period helps to identify high-risk mothers who alone or along with developing fetus are at an increasing risk of complications during/after pregnancy and birth. Infection may be asymptomatic or mild in the mother, but the outcome can be grave for the developing fetus [5]. In the absence of national screening program for TORCH, serological detection for TORCH infections during pregnancy remains the only means of revealing such infections [6-8]. Often treatment of maternal infections has no impact on the fetal outcome. Hence, the knowledge of these diseases will not only help obstetrician's counsel mothers on preventive measures to avoid these infections but will also aid in guiding parents on the potential for adverse fetal outcomes when these infections are present. Only few published data from India describing the seroprevalence of specific IgM antibodies to TORCH agents exist in this part of Northern India. This study was undertaken to look for serological evidence of the acute TORCH infections in high-risk pregnant women, by establishing the presence of specific IgM antibodies.

MATERIAL AND METHODS

A total of 240 pregnant women with previous unfavorable fetal outcome or bad obstetric history (BOH) attending the antenatal clinic of our tertiary care teaching hospital from November 2011 to October 2016 were included in the study. Cases with hypertension, diabetes mellitus, eclampsia of pregnancy, and Rh incompatibility were excluded from the study. Detailed clinical history, physical examination, and conventional laboratory investigations were conducted. This hospital caters mostly to the low socioeconomic class from this part of Northern India. The subjects mostly belonged to rural strata. Approximately 2–3 ml of blood was collected aseptically, and serum samples were analyzed for specific IgM antibodies to *T. gondii,* rubella, CMV, and combined HSV-1 and 2. All tests were capture enzyme-linked immunosorbent assay (ELISA) done according to manufacturer's instructions. All kits were from DIA.PRO Diagnostic Bioprobes SRL, Italy, having a sensitivity >98% and specificity >98%. All the patients, whose sera showed equivocal results, were retested after collecting fresh blood samples 2 weeks later.

RESULTS

Overall seropositivity for IgM antibodies against *T. gondii*, rubella, CMV, and HSV for either a single organism or in combination, in the present study, was found to be 98.8% (n=237). Seropositivity for *T. gondii* was found to be 24.2% (n=58), rubella 9.2% (n=22), CMV 53.8% (n=129), and 11.7% (n=28) were seropositive for combined HSV-1 and 2 infections. On the whole, highest seropositivity (47.5%) was seen in the age group of 21–30 years. The proportion of seropositives for *Toxoplasma* (p=0.004), rubella (p=0.028), and HSV (p=0.001) was higher in the age group of <20 years as compared to other age groups, and this finding was statistically significant (Fig. 1). However, CMV seropositivity was found to be highest in the age group of 21–30 years and the association with age was statistically significant (p≤0.001). Multiple infections as compared to none or single infections were also more common (p≤0.000) in the <20 years of age group. Overall, 15.4% (37) of women were seropositive for coinfections, 14.5% (35) were dual infection while two cases (0.9%) had a triple infection (Table 1).

DISCUSSION

In the present study, seroprevalence of TORCH infections in high-risk pregnant females was found to be 98.8% contrasting with the 13.8% seroprevalence reported by Padmavathy *et al*. from Bengaluru [4]. However, Kaur *et al*. from Central Delhi reported high prevalence (93.4%), emphasizing the need for TORCH screening and adding further impetus to the need of immunization to evade the otherwise foreseeable fetal outcome [5].

It was observed that, in general, seroprevalence of TORCH infections was more common in 21–30 years age group analogous with a study from Gujarat, Bengaluru, Delhi, and Nepal probably because this is the most common childbearing age group [1,4,5,9]. In contrast to a study from Varanasi (19–25 years) and Bengaluru (25–30 years), the current study found a statistically significant association of seropositivity to *T. gondii*, rubella, and HSV with the <20 years age group [4,10]. A study from Croatia reports *Toxoplasma* seropositivity rate of 15% seen in the age group >40 years, highlighting the fact high-risk antenatal woman in all groups should be screened for TORCH infections to define the susceptible population.

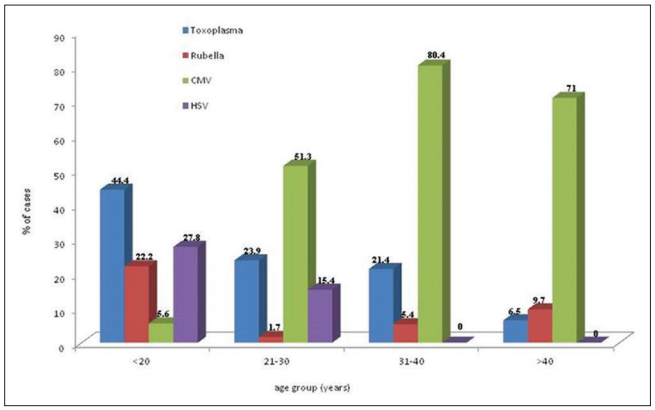

Figure 1: Age-specific distribution of seropositive TORCH cases

Seroprevalence of *Toxoplasma* IgM among high-risk pregnant women in different countries of the world had been found to range between 7.7 and 76.7% with Nigeria topping the list at 76%, closely followed by Brazil (50–75%), while India stands at 55% [11-13]. Our finding of 24% seroprevalence in the present study is in tune with a study from Gujarat (23.4%) [14]. Prevalence of IgM-positive *Toxoplasma* infection ranges from 9 to 55% in Indian studies [15]. Some of them proved that persistence of encysted forms of *T. gondii* in chronically infected uteri and their ruptures during placentation leads to infection of the baby in the first trimester and often to recurrent miscarriages [13,14,16]. As it remains the only TORCH infection which is treatable and completely curable in pregnancy by a single dose of spiramycin, toxoplasmosis should be diagnosed early in the antenatal period and treated to prevent complications. Women who show seroconversion during their pregnancies should be closely monitored clinically during their subsequent pregnancies and should be advised to avoid raw/undercooked meat and unpasteurized milk and to keep away from pets, mainly cats. Toxoplasmosis can also lead to infertility as has been documented from China and Palestine [17]. Zhou found that *Toxoplasma* was common in infertile couples possibly related to anti-sperm antibodies which were higher in *Toxoplasma*-infected couples [18].

The WHO estimates that, worldwide, more than 1 lakh children are born with congenital rubella syndrome (CRS) each year, most of them in developing countries [16,19]. Seroepidemiological studies have shown that 10–20% of the women in the childbearing ages in India are susceptible to rubella infection [20,21]. On the other hand, the risk of the CRS following a maternal infection is documented to range from 5 to 50% in various studies, with increased severity if acquired in the first trimester of pregnancy [22]. The IgM seropositivity of rubella in India and other countries ranges between 4.7 and 28.6% in women of reproductive age groups. The present study reports a seropositivity of 10.4% for acute rubella infections. This is higher when compared to studies from South India (3–4.5%) [3,23]. However, studies from northern and western zones of India document acute infection rate up to 26% [13,24]. The paradox

Table 1: Prevalence of mixed etiology of TORCH infection

Age group in years n=number of cases recruited(%)	Only mono infected n (%)	Infected with two agents n (%)	Infected with three agents n (%)	No disease n (%)
<20 n=36 (15)	22 (61.1)	13 (36.1)	0 (0)	1 (2.8)
21–30 n=117 (48.8)	104 (88.9)	12 (10.3)	1 (0.9)	0 (0)
31–40 n=56 (23.3)	45 (80.4)	9 (16.1)	1 (18)	1 (18)
>40 n=31 (13)	29 (93.5)	1 (3.2)	0 (0)	1 (3.2)
Total (n=240)	200 (83.3)	35 (14.5)	2 (0.8)	3 (1.3)

lies in the fact that a large proportion of the cases (nearly 50%) are subclinical and that clinical diagnosis is often unreliable [20]. Moreover, there is a considerable variation in the prevalence of the rubella-specific IgG antibodies among the women of the childbearing ages, with studies suggesting a prevalence of 71.3% rubella immunity, thus leaving about one-third of the women susceptible to the rubella infection [21,22]. The screening for the rubella immunity was not done in this study. Further, the history of the vaccination against rubella could not be gathered from the study population. However, on the basis of the low socioeconomic status and poor educational background, it may be presumed that most of our subjects had not been previously vaccinated. Hence, vaccination of rubella at 1.5 years with measles, mumps, and rubella or at 14–15 years with rubella vaccine alone must be considered a priority to prevent subsequent maternal and fetal risk.

Primary CMV infection in pregnancy has a higher incidence, especially in women of rural population. This infection is usually asymptomatic, thus posing difficulty in clinical diagnosis. In the present study, the seropositive rate of CMV IgM in high-risk pregnant women was 52.9% which is markedly higher when compared to studies from Rajkot (4.7%) and Mumbai (8.4%) [1,14]. Studies from South India report an extremely low (0.8%) IgM seropositivity probably due to smaller sample size in their study [3]. However, a seroprevalence rate of 33–35% has been documented from Bengaluru and Varanasi [4,10]. Highest CMV seropositivity among the TORCH agents observed in the current study was similar to the Bengaluru study [4]. Pregnancy may reactivate the latent CMV leading to further reproductive wastages. Although serological surveys in different parts of India document 80–90% prevalence of IgG CMV antibodies in women of childbearing age [25], reinfection with a variant strain of CMV can cause infections even in the presence of detectable IgG levels [26]. The high seropositivity in the present study may be due to either primary infection in our economically less privileged population or reinfection with a variant strain of virus. Hence, screening of pregnant females for CMV-specific IgM antibodies is beneficial in alerting the obstetrician and pediatrician regarding possible infection of mother and newborn. The suspected newborn can further be subjected to the testing for CMV-specific IgM antibodies. Thus, timely medical treatment can be started to overcome various complications in an infected children.

Primary infection with HSV-2 acquired by women during pregnancy accounts for two-thirds of the morbidity and mortality from HSV-2 among neonates while the rest results from reactivation of an old infection [27,28]. Despite the higher risk of transmission of HSV from mother experiencing first episode of genital herpes, most neonates are infected because of asymptomatic viral shedding and undiagnosed disease of the mother. Both these reasons make it important to determine the predominant HSV antibody type. In this study, the prevalence of anti-HSV IgM antibodies among pregnant women was 11.7% comparable to data from Aligarh (16.8%) [27]. Reports from Varanasi (33.6%) show higher prevalence, whereas Rajkot (2%), Mumbai (3.6%), and Lucknow (3.3%) document the lower prevalence of HSV IgM [14,1,15,26]. Although, a 1982, American study reveals that despite frequent recurrences of genital HSV infection during pregnancy, if delivery is done through ceserian section, the outcome in their infants are reliably better [29]. Studies suggest that primary HSV infection occurring in first or second trimester causes an increase in spontaneous abortion or prematurity and fetal growth restriction [30]. An antenatal screening for HSV among the pregnant women is, therefore, required for carrying out effective interventions on delivery and in the lifestyle practices.

In the present study, a coinfection rate of 15.4% was found to be 2-fold higher compared to a study from Rajkot (7%) and Bengaluru (6.8%) [1,4]. A 0.9% rate of triple infection (rubella+CMV+*Toxoplasma*) seropositivity was comparable with 1.1% infection rate reported from Bengaluru (*Toxoplasma*+CMV+HSV) [4]. Mixed infection with TORCH complex has a very unfavorable outcome, and these cases have to be, especially, kept in mind by obstetricians when pregnant patients with BOH present to them.

CONCLUSION

All antenatal cases with BOH should be routinely screened for TORCH. Early diagnosis and appropriate intervention will help in proper management of these patients. Finally, the high seroprevalence of these agents, in our society, calls for the need for preventive strategies such as reproductive hygiene and immunization for circumventing the otherwise inevitable fetal outcomes. In developed nations such as France, a structural antenatal screening program to identify specified infections and instituting appropriate intervention is part of their national healthcare delivery system. In India, this aspect of health care has not received the attention it deserves, especially in the context of high birth rate and population growth. Effective programs to ensure maternal and fetal health would greatly contribute to population control measures and maintaining equilibrium. One of the pre-requisites for implementation of an effective control program is the availability of accurate data generated through long-term studies. Data reported in the present study are a small contribution toward this end.

ACKNOWLEDGMENT

The authors acknowledge the help of Mr Narendra Singh Mogha and Mr Roop Ram Premi, Senior Technical Assistants, Department of Microbiology, for their help in putting up the ELISA tests.

REFERENCES

1. Parikh J, Chaudhary A, Kavathia GU. Prevalence of serum antibodies to TORCH infection in women with bad obstetric history (BOH) attending tertiary care hospital, Gujrat. J Dent Med Sci 2016;15:14-6.
2. Li Z, Yan C, Liu P, Yan R, Feng Z. Prevalence of serum antibodies to TORCH among women before pregnancy or in the early period of pregnancy in Beijing. Clin Chim Acta 2009;403:212-5.
3. Yashodhara P, Ramlaxmi BA, Naidu AN, Raman L. The prevalence of the

specific IgM which is caused by the toxoplasma, rubella, *Cytomegalovirus* and the *C.trachomatis* infections during pregnancy. Indian J Med Microbiol 2001;19:79-82.
4. Padmavathy M, Mangala G, Malini J. Seroprevalence of TORCH Infections and adverse reproductive outcome in current pregnancy with bad obstetric history. J Clin Biomed Sci 2013;3:62-71.
5. Kaur R, Gupta N, Nair D, Kakkar M, Mathur MD. Screening for TORCH infections in pregnant women: A report from Delhi. Southeast Asian J Trop Med Public Health 1999;30:284-6.
6. Shashi C, Usha A, Aruna A. Prevalence of IgM antibodies to toxoplasma, rubella and *Cytomegalovirus* infections during pregnancy. JK Science 2004;6:190-3.
7. Binnicker MJ, Jespersen DJ, Harring JA. Multiplex detection of igM and igG class antibodies to *Toxoplasma gondii*, rubella virus, and *Cytomegalovirus* using a novel multiplex flow immunoassay. Clin Vaccine Immunol 2010;17:1734-8.
8. Kishore J, Misra R, Paisal A, Pradeep Y. Adverse reproductive outcome induced by parvovirus B19 and TORCH infections in women with high-risk pregnancy. J Infect Dev Ctries 2011;5:868-73.
9. Pradhan SV. Epidemiological and serological profiles of TORCH infection in pregnancy. J Pathol Nepal 2015;5:705-8.
10. Sen MR, Shukla BN, Tuhina B. Prevalence of serum antibodies to TORCH infection in and around Varanasi, Northern India. J Clin Diagn Res 2012;6:1483-14.
11. Allain JP, Palmer CR, Pearson G. Epidemiological study of latent and recent infection by *Toxoplasma gondii* in pregnant women from a regional population in the U.K. J Infect 1998;36:189-96.
12. Nash JQ, Chissel S, Jones J, Warburton F, Verlander NQ. Risk factors for toxoplasmosis in pregnant women in Kent, United Kingdom. Epidemiol Infect 2005;133:475-83.
13. Tamer GS, Dundar D, Caliskan E. Seroprevalence of *Toxoplasma gondii*, rubella and *Cytomegalovirus* among pregnant women in western region of turkey. Clin Invest Med 2009;32:E43-7.
14. Turbadkar D, Mathur M, Rele M. Seroprevalence of torch infection in bad obstetric history. Indian J Med Microbiol 2003;21:108-10.
15. Srirupa P, Nibedita D, Pal D. Seroprevalence and risk factors of *Toxoplasma gondii* in pregnant women in Kolkata, India. J Recent Adv Appl Sci 2011;26:27-33.
16. Sadik MS, Fatima H, Jamil K, Patil C. Study of TORCH profile in patients with bad obstetric history. Biol Med 2012;4:95-101.
17. Li S, Cui L, Zhao J, Dai P, Zong S, Zuo W, *et al.* Seroprevalence of *Toxoplasma gondii* infection in female sterility patients in china. J Parasitol 2011;97:529-30.
18. Al-Hindi A, Al-Helou T, Al-Helou Y. Seroprevalence of *Toxoplasma gondii*, *Cytomegalovirus*, rubella virus and chlamydia trachomatis among infertile women attending *in vitro* fertilization center, Gaza strip, Palestine. J Egypt Soc Parasitol 2010;40:451-8.
19. Vijayalakshmi P, Anuradha R, Prakash K, Narendran K, Ravindran M, Prajna L, *et al.* rubella serosurveys at three Aravind eye hospitals in Tamil Nadu, India. Bull World Health Organ 2004;82:259-64.
20. Rubella and Pregnancy. ACOG technical bulletin number 171 - August 1992. Int J Gynaecol Obstet 1993;42:60-6.
21. Lever AM, Ross MG, Baboonian C, Griffiths PD. Immunity to rubella among women of child-bearing age. Br J Obstet Gynaecol 1987;94:208-12.
22. Singla N, Jindal N, Aggarwal A. The seroepidemiology of rubella in Amritsar (Punjab). Indian J Med Microbiol 2004;22:61-3.
23. Miller E, Cradock-Watson JE, Pollock TM. Consequences of confirmed maternal rubella at successive stages of pregnancy. Lancet 1982;2:781-4.
24. Ballal M, Bangar RP, Sherine AA. Seroprevalance of rubella in BOH cases a 5 year study. J Obstet Gynecol India 2007;57:407-9.
25. Gandhoke I, Aggarwal R, Lal S. Congenital CMV infection in symptomatic infants in Delhi and surrounding areas. Indian J Pediatr 2006;73:1095-7.
26. Boppana SB, Rivera LB, Fowler KB, Mach M, Britt WJ. Intrauterine transmission of *Cytomegalovirus* to infants of women with preconceptional immunity. N Engl J Med 2001;344:1366-71.
27. Haider M, Rizvi M, Khan N. Serological study of herpes virus infection in female patients with bad obstetric history. Biol Med 2011;3:284-29.
28. Sebastian D, Zuhara KF, Sekaran K. The influence of the TORCH infections in the first trimester miscarriages in the Malabar region of Kerala. Afr J Microbiol Res 2008;2:56-9.
29. Vontver LA, Hickok DE, Brown Z, Reid L, Corey L. Recurrent genital herpes simplex virus infection in pregnancy: Infant outcome and frequency of asymptomatic recurrences. Am J Obstet Gynecol 1982;143:75-84.
30. Deborah M, Vancouver BC, Marc S, Montreal QC. Guidelines for the management of herpes simplex virus in pregnancy. J Obstet Gynaecol 2008;30:514-19.

Funding: None; Conflict of Interest: None Stated.

How to cite this article: Nirmal K, Saha R, Ramachandran VG, Khan AM. TORCH infection in antenatal women: A 5-year hospital-based study. East J Med Sci. 2017;2(4):54-57.