Original Article

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Seroprevalence of TORCH Infection in Paediatric Population and Women of Reproductive Age Group: A Cross-sectional Study

Paediatrics Section

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ABSTRACT

Introduction: The acronym 'TORCH' complex includes infections due to *Toxoplasma gondii*, as well as others such as Syphilis, Hepatitis B, Rubella virus, Cytomegalovirus (CMV), and Herpes Simplex Virus (HSV), respectively. Primary infections due to these agents during pregnancy are associated with congenital malformations in newborns. Seroprevalence data is important to gather estimates of immunity levels, vaccination status, as well as levels of exposure, and will correlate with the risk of acquiring infections during pregnancy.

Aim: To determine the seroprevalence of TORCH infections in paediatric populations with suspected clinical conditions and women of reproductive age group, and also to assess the associated risk factors in mothers and newborns, and evaluate their clinical outcomes.

Materials and Methods: This cross-sectional study was conducted between January 2019 and January 2022 in the Serology laboratory of the Department of Microbiology at the Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, Uttar Pradesh, India. A total of 92 consecutive antenatal females for whom TORCH antibody levels were determined and 343 suspected neonatal/paediatric populations were included in the study. The serum samples were subjected to IgM and IgG TORCH Enzyme Linked Immunosorbent Assay (ELISA). Demographic data and clinical details of patients were analysed from the Hospital Information System (HIS) and data records maintained in the department. Categorical variables are expressed as numbers and percentages.

Results: A total of 435 samples (343 paediatric and 92 women) were screened for TORCH infection in the laboratory. A total of 57 (13.1%) were seropositive for TORCH infection. The most commonly affected were infants (28 days- 1 year). Among the total screened population, the positive cases of CMV were 40 (9.1%), rubella 11 (2.5%), and toxoplasma 6 (1.3%). Biliary Atresia (BA) and neonatal cholestasis were the most common clinical conditions associated with CMV infection.

Conclusion: A high seroprevalence of IgM-specific CMV (9.1%) was observed in the present study. BA and neonatal cholestasis were the common complications in neonates associated with CMV infection.

Keywords: Enzyme linked immunosorbent assay, Herpes simplex, Neonatal cholestasis, Rubella cytomegalovirus, Toxoplasmosis

INTRODUCTION

The TORCH group of infectious agents commonly causes asymptomatic or mild infections in women of reproductive age but may result in adverse obstetrical outcomes such as spontaneous abortion, miscarriage, stillbirth, congenital anomalies, birth defects, intrauterine growth retardation, and prematurity [1]. The acronym 'TORCH' was coined by Nahmias A et al., in 1971 and includes *toxoplasma gondii*, as well as others (syphilis, varicella-zoster, parvovirus B19), rubella, CMV, and HSV [2].

The timing of maternal infection is a key epidemiologic factor as foetal damage usually depends on the gestational age [3]. Knowledge and awareness of TORCH infection can help clinicians in counselling the family regarding the prognosis and the preventive measures to avoid infections. Toxoplasmosis, caused by *Toxoplasma gondii*, an intracellular protozoan parasite, causes life-threatening events when the infection is acquired during the first or second trimester of pregnancy in the form of premature delivery, intrauterine death, stillbirth, and congenital malformations. Infections acquired in the third trimester and non pregnant individuals are usually asymptomatic or subclinical [3].

Rubella is transmitted through the respiratory route via droplets or from mother to foetus through the placenta [4]. It mostly causes an asymptomatic or mild infection in children [4]. Primary infection in pregnant women during the first trimester may lead to congenital malformations in infants including hearing loss, cataracts, and cardiac defects such as patent ductus arteriosus referred to as Congenital Rubella Syndrome (CRS) [4].

Human CMV, also known as beta herpes virus, is transmitted via direct contact with blood, saliva, urine, and genital secretions. The risk of foetal anomalies caused by CMV during the first trimester of pregnancy is highest and the outcomes include growth retardation, hearing loss, mental retardation, microcephaly, intracerebral calcification, hepatosplenomegaly, jaundice, chorioretinitis, thrombocytopenic purpura, and anaemia [5-7].

HSV is the most common viral sexually transmitted infection. The virus is of two types, HSV-1 which manifests as mucocutaneous lesions, and HSV-2 which is transmitted sexually responsible for genital lesions. HSV infection acquired during the first and second trimesters is associated with high neonatal morbidity and mortality [8,9]. Genital herpes during pregnancy may cause miscarriage, prematurity, and congenital and neonatal herpes. Transmission in the above case occurs most frequently through direct contact with herpetic lesions in the birth canal [10]. It causes neonatal infection (skin, eye, central nervous system manifestations), systemic infection, and cutaneous lesions [11].

There is geographical variation in the prevalence of TORCH infections [12]. There is very little data available on the seroprevalence and clinical impact of TORCH infection in neonates in North India. With this background, the present study was conducted to determine the seroprevalence of TORCH infection in the paediatric population with suspected clinical conditions and women of reproductive age group along with the epidemiological profile and associated clinical conditions in neonates and mothers' risk factors and to analyse the clinical impact of TORCH infection.

MATERIALS AND METHODS

The cross-sectional study was conducted in the Serology laboratory of the Microbiology Department at Sanjay Gandhi Postgraduate Institute of Medical Sciences in Lucknow, India from January 2019 to January 2022, and the study was ethically approved.

Inclusion criteria: All neonates, infants, and women of reproductive age group tested for TORCH infection within the study duration were included in the study.

Exclusion criteria: Patients with infections other than TORCH were excluded from the study.

Study Procedure

A 2-3 mL blood sample was collected aseptically from clinically suspected TORCH infection cases from paediatric populations and antenatal women. The samples were processed in a serology laboratory according to the standard protocol. The serum was separated by centrifuging the blood at 3500 rpm for 10 minutes. ELISA (Diagnostic Bioprobes) was performed using the serum to detect IgM and IgG antibodies against Toxoplasma, Rubella, CMV virus, and HSV following the manufacturer's instructions. Demographic profiles as well as clinical data in terms of congenital conditions and risk factors of TORCH-positive patients were retrieved through the labouratory register and HIS.

STATISTICAL ANALYSIS

The data was compiled in Microsoft excel for primary analysis, and the results were analysed using Statistical Package for Social Sciences software version 20.0 (SPSS Inc., IBM Corp., Armonk, USA). Categorical variables are expressed as numbers and percentages.

RESULTS

A total of 435 samples (343 paediatric and 92 women) were screened for TORCH infection in the laboratory. Among these samples, 57 (13.1%) tested positive for TORCH infection. Out of the 57 positive cases, 45 (78.9%) were children, and 12 (21%) were adult females.

Among the 45 paediatric cases, the majority were in the 28-day to 1-year age group, followed by 4 (8.8%) in the 1-15 years age group, with a male predominance. Among the 12 adult females, 8 (66.7%) were in the 30-40-year-old age group, while 4 (33.3%) were between 20 and 30 years old [Table/Fig-1]. The total seroprevalence of TORCH infection in the present study was 13.1%. In the total screened population, 40 (9.1%) were seropositive for CMV, 11 (2.5%) for rubella, and 6 (1.3%) for toxoplasma [Table/Fig-2]. Out of 57 seropositive cases, the maximum seropositivity was found in CMV with 40 (70.1%), followed by rubella with 11 (19.2%) and toxoplasma with 6 (10.5%). No seropositivity was observed for the herpes virus. One neonatal case showed simultaneous seropositivity for both CMV and toxoplasma. IgM against TG, RV, CMV, and HSV was elevated in the serum sample. Based on the IgM and IgG positivity, overall, 92.9% of individuals showed IgM positivity for TORCH infection, with the highest proportion shown by CMV at 40 cases (70.1%) followed by rubella at 9 (15.7%) [Table/Fig-3]. Authors found that the majority of neonates seropositive for TORCH infection presented with BA (19 cases) and neonatal cholestasis (12 cases). These cases were related to high seropositivity for CMV infection. In the present study, various clinical manifestations were observed in children with TORCH infection [Table/Fig-4]. Among the risk factors associated with adverse foetal outcomes, birth asphyxia and premature delivery

Variables	Positive (n=45)
Age group of paediatric population	
0-28 days	8 (2.3%)
28 day-1 year	33 (9.6%)
1-15 years	4 (1.1%)
Gender of paediatric population	
Male	30 (66.6%)
Female	15 (33.3%)
Age group of reproductive adult female	**(n-12)**
20-30 years	4 (33.3%)
30-40 years	8 (66.7%)

[Table/Fig-1]: Age and sex-wise distribution of TORCH-positive cases in the paediatric population and adult females of reproductive age group.

Infection	Total- 435	Positive=57
CMV	9.1% (40)	70.1% (40)
Rubella	2.5% (11)	19.2% (11)
Toxolasma	1.3% (6)	10.5% (6)
HSV	00	00

[Table/Fig-2]: Total seroprevalence and percentage positivity of TORCH infection.

Infection	IgM		IgG	
	Infants	Women	Infants	Women
CMV	35 (77.7%)	5 (41.6%)	0	0
Toxoplasma gondii	3 (6.6%)	1 (8.3%)	1 (2.2%)	1 (8.3%)
Rubella	5 (11.1%)	4 (33.3%)	1 (2.2%)	1 (8.3%)
HSV	0	0	0	0

[Table/Fig-3]: Specific TORCH IgM and IgG antibodies distribution.

Clinical manifestation	N=45
Biliary Atresia (BA)	19
Neonatal cholestasis	12
SNHL	3
RDS+ROP	2
Criggler syndrome	2
Disseminated TB	2
Infantile Hyalinosis syndrome	1
Down syndrome	1
Neonatal cholestasis+hydrocephalus, periventricular calcification, Alagille syndrome	1
Neonatal cholestasis+bilateral cataract, periventricular calcification	1
Biliary Atresia (BA)+ostium secondum ASD	1

[Table/Fig-4]: Clinical conditions associated with the TORCH infection in the paediatric population.
SNHL: Sensory neural hearing loss; RDS-ROP: Respiratory distress syndrome- Retina of prematurity; ASD: Atrial septal defect

before 32 weeks were common. These risk factors were most commonly associated with CMV infection. A history of repeated miscarriages and fever with rash was noted in mothers of children with TORCH infection. Other laboratory parameters like elevated alpha-fetoprotein levels were observed in patients with BA and neonatal cholestasis [Table/Fig-5]. CMV Polymerase Chain Reaction (PCR) was performed for four cases of neonatal cholestasis with CMV seropositivity, and the results were confirmatory.

Risk factors	Number	Risk factors (%)
Birth asphyxia	20	35.08%
Premature delivery (before 32 weeks)	25	43.85%
H/O repeated miscarriage	18	31.57%
H/O fever with rash	20	35.08%
Other laboratory investigation		
Alpha fetoprotein	20	35.08%
CMV PCR	4	7.02%

[Table/Fig-5]: Risk factors associated with TORCH infection and other laboratory parameters.
CMV PCR: Cytomegalovirus polymerase chain reaction

DISCUSSION

The TORCH infections during pregnancy carry a risk for intrauterine transfer which may lead to serious foetal consequences if the transmission occurs in the first trimester. Serological assays are helpful for screening antenatal TORCH infections [13]. An infected patient produces two types of antibodies (IgM and IgG) against the pathogen, which can be measured to identify the type of infection. The presence of IgM antibodies indicates recent or acute infection, while the presence of IgG antibodies indicates past infection or present active infection [14]. Present active infection is determined by a four-fold rise in the IgG antibody titer or low IgG avidity. Avidity means the aggregate strength by which IgG antibodies bind to the antigen; it gradually matures over the months. IgG antibodies produced during the first few months following primary infection have low avidity, while antibodies developed after six months have high avidity [15]. Congenital TORCH infection has been reported to be demonstrated by the presence of specific IgM and persistent IgG antibodies that do not decline with time (by 6 months) as expected for transplacentally derived maternal antibodies [16].

The overall seropositivity for TORCH infection in the present study was 13.1%, which is significantly less compared to a study from North India (33.46%) [17]. In the paediatric population, author report a prevalence of 13.11%, which is comparatively significantly less than stated by Biswas SK et al., (94.82%) [18]. Chilakala SP et al., reported 52% seropositivity in neonates and infants from Andhra Pradesh [19]. Though there are several published articles demonstrating seroprevalence in pregnant women, women of the reproductive age group, and women with a bad obstetric history. In present study, seroprevalence in women of the reproductive age group was 13.04%, while a study from central India demonstrated high (61.1%) seroprevalence among the same age group. Tiwari S et al., from New Delhi reported 45.56% IgM positivity in pregnant women [20]. Nirmal K et al., in their five-year study period, have reported an increasing trend of TORCH infections (98.8%) [21]. There is a wide variation in seropositivity due to geographical region, socio-economic status, living habits, and immunisation. As this study was conducted in a tertiary care centre, high-risk and referred patients come for consultation, which might be the reason for the low seroprevalence of the disease.

CMV infection is highly prevalent in both developed and developing countries, with prevalence ranging between 45 to 100% [12]. In the present study, the seroprevalence of CMV was observed to be 70.1% (40/57), which is comparable to the prevalence stated in various studies from India, i.e., 80-90% [17]. A 7-year study from Varanasi, North India showed a seroprevalence of 13.63% and 12.9% in Delhi [17,22]. In the present study, CMV-specific IgM antibodies were present in 70.1% of samples, Comparatively High that reported 36.5% CMV-specific antibodies [18]. A study by Gandhoke I et al., reported an 18.75% IgM positivity, which varied due to regional differences and the living conditions of individuals [23].

According to the World Health Organisation (WHO), the highest risk of developing CRS is in countries where adult women do not have immunity to the disease, either through vaccination or from having had rubella. Before vaccines were developed, every 4th baby was born with CRS, and 50% of CRS cases are reported from the South East Asia region where vaccination coverage is low [24]. There have been several studies in India that reported 5%-50% of cases of CRS following infection in mothers, and they are more serious if the infection occurs during the first trimester of pregnancy [25,26].

The current study reported a seroprevalence of rubella at 19.2%, comparable to Biswas S et al., who reported a 14% seroprevalence, and Chandy S et al., from Vellore, India, who reported a 9.4% IgM-positive rubella infection [16,18]. According to Nazme NI et al., from the Dhaka Shishu Hospital, there were 28% of cases with IgM rubella [27].

In the present study, authors demonstrated that the seroprevalence of toxoplasma infection was 10.5% compared to another study from Bangladesh that reported 5.17% [18]. Dinkar A and Singh J from Varanasi reported a low prevalence of toxoplasm, i.e., 1.38% [17]. In the present records, there is one case of double infection, seropositive for both CMV and Toxoplasma. Authors hereby, did not find any cases of HSV infection.

Based on current study, the most affected age group was 28 day to 1 year because these infections are transmitted mainly through the transplacental route during pregnancy. In women of reproductive age, TORCH is associated with mild morbidity but severe impacts on foetuses, such as stillbirth, growth retardation, birth asphyxia, and congenital malformations [1]. Based on information obtained from the HIS and medical records, birth asphyxia and preterm delivery were the most common risk factors in newborns with TORCH infection. The presence of these risk factors was more common in infants who were CMV-positive.

In the present study Neonatal cholestasis and biliary atresia were the most common clinical manifestations associated with TORCH infection. BA is a form of destructive cholangiopathy in which both intrahepatic and extrahepatic bile ducts are partially or completely obliterated in newborns [28]. The destruction of the biliary tree may be due to an autoimmune disorder, inflammation, and viral infection [29]. CMV is a hepatophilic virus that tends to affect the biliary tree. According to a series from England, Germany, Brazil, and Sweden, CMV infection has been found in 10-38% of infants with BA, but up to 60% have been reported from China [30-32]. In the present study, author have reported that 35.1% of BA cases have CMV infection. Approximately 1 in 2,500 infants suffer from

cholestatic jaundice. The cause of approximately 40% of infant cholestasis is neonatal hepatitis, mainly caused by the CMV virus [33]. Neonates with cholestasis and BA must be evaluated for CMV infection.

As TORCH infections are commonly associated with congenital malformations in newborns, it is important to know the seroprevalence of infection in the community and take appropriate measures to prevent infection.

Limitation(s)

This study is limited by the sample size, so further studies are needed with a large sample size and screening of antenatal women and neonates with congenital malformations attending the tertiary care hospital.

CONCLUSION(S)

This study showed a high prevalence of TORCH infection among neonates. The prevention of morbidity and mortality in mothers and children is greatly aided by antenatal screening and early diagnosis of TORCH infection in neonates. Mothers with flu-like symptoms during the first trimester should be tested for TORCH. Further studies with a large population size are needed to determine the seroprevalence. Understanding the seroprevalence is very helpful in developing strategies to prevent infection and strengthen the vaccination system.

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