

# Seroprevalence of Toxoplasma, Rubella, CMV and HSV infection at a teaching hospital: A 7 year study from North India

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## ABSTRACT

**Objectives:** The present study was aimed to find seroprevalence in different age group population to explore the burden of TORCH (toxoplasma, rubella virus, cytomegalovirus [(CMV] and herpes simplex virus [HSV]) infection in the North Indian Population. **Materials and Methods:** It is a retrospective study carried out in the Microbiology Department, Institute of Medical Science, Banaras Hindu University (IMS, BHU), a tertiary care centre of North India. The blood samples of the suspected population of either sex or age group from different departments were analysed over a period of 7 years. The samples were tested for TORCH infections by the IgM ELISA kit following the manufactures instruction. **Results:** Out of total 4044 samples, 1353 (33.46%) cases were seropositive with maximum cases from the obstetrics and gynaecology department 39.46%. The highest seropositivity of TORCH (43.15%) was in the age group 15–25 years followed by 36.33% in the age group 25–35 years. This study revealed an overall male and female ratio of the total positive cases as 0.12 while it was 2.2 for pediatric cases (0–15 years). The overall seroprevalence was contributed as toxoplasma 1.38%, rubella 1.14%, CMV 13.63% and herpes 17.43%. The overall seropositivity (IgM) contributed as *toxoplasma gondii* with 4%, *rubella* with 3%, *cytomegalovirus* with 41% and *herpes simplex virus* with 52%. The coinfection of HSV with CMV was most abundant with 246 cases. **Conclusions:** The seropositivity of toxoplasma and rubella were comparatively more in infants while CMV and herpes were more prevalent in adults. Though, the incidence of TORCH has reduced over the past few years. Furthermore, knowing the epidemiology is an important aspect to develop strategies and appropriate implementation for the prevention of infection.

**Keywords:** Congenital malformations, epidemiology, high-risk pregnancy, seroprevalence, TORCH infection

## Introduction

The TORCH pathogens (toxoplasma, rubella virus, cytomegalovirus [(CMV] and herpes simplex virus [HSV]) generally cause asymptomatic or mild infections in the mother,<sup>[1,2]</sup> but may result in a serious sequel and congenital malformations in the foetus or years after birth such as spontaneous abortions,

intrauterine foetal death, congenital anomalies, intrauterine growth retardation, prematurity, stillbirth and live born infants with the evidence of disease.<sup>[1,3,4]</sup> Due to poor environmental and hygiene conditions, pregnant women may be exposed to a variety of these infections. Infection with TORCH pathogens may lead to significant morbidity and mortality in the health, especially in developing countries.<sup>[1]</sup> It is challenging to diagnose TORCH aetiology clinically, therefore diagnosis is usually established by seroconversion in paired sera or by the presence of specific antibody.<sup>[5]</sup> The prevalence of these infections varies with the geographical area.<sup>[6]</sup> Data for seroprevalence of TORCH agents in north India are very meager. With this background, the present study was carried out on a larger sample size to assess

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the prevalence to explore the burden of TORCH infection in this region.

## Material and Methods

### Settings and design

It is a retrospective study conducted in the Microbiology Department, Institute of Medical Science, Banaras Hindu University (IMS, BHU), a tertiary care centre of North India.

### Study sample and population

The samples belonged to patients for antenatal screening and clinically suspected of all age groups and either sex were sent in the serology laboratory as a part of routine diagnostic services from various departments of the institution from January 2011 to December 2017. A total of 4,044 samples were collected under aseptic conditions from the patients of outdoor and indoor. BHU is serving as a referral tertiary care centre for the patients of whole eastern Uttar Pradesh, nearby states such as Bihar, Madhya Pradesh and Nepal country also.

### Sample collection and processing

The serum was used for serological evaluation for TORCH infections. Sera were properly labelled and stored at 2–8°C for up to 7 days. IgM antibodies for the TORCH infections were detected by the ELISA test kit (NovaTec Immundiagnostica GmbH, Germany). The manufacturer instructions were followed in the performance and interpretation of the tests.

### Ethical approval

As it was a retrospective study, informed consents and clearance from the institutional ethical committee were not taken. Though, care was taken not to disclose patients' identity in any form.

## Results

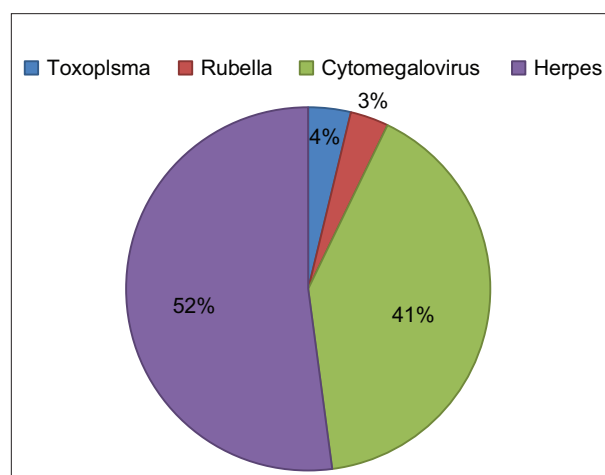
Out of 4,044 samples of either sex collected from various departments, 1,353 (33.46%) cases were seropositive. Most of the cases and positivity were reported from the obstetrics and gynecology department followed by paediatrics as 2,846 (1123) 39.46% and 1,095 (194) 17.72%, respectively. During 7 years, there were increasing trends in sample size except for a dip in the year 2012. On the other hand, the positivity of cases was reported highest in year 2011 (50.29%), followed by decreasing continuously till year 2016 [Table 1]. In a total of 4,044 samples, the highest TORCH seropositive 598 (43.15%) cases were in the age group 15–25 years followed by 530 (36.33%) cases in the age group 25–35 years. Out of 1,353 seropositive cases, 146 (10.79%) cases were male and 1207 (89.21%) cases were female. The male and female ratio was 0.12, on the other hand, it was 2.2 for pediatric cases (0–15 years). Males were predominant in the age group up to 15 years while most of the females were positive in age 15–25 followed by 25–35 years, age group. Maximum cases of toxoplasma were seen in age 15–25 years, rubella in the age group 0–15 years, cytomegalovirus and herpes in age 15–25

followed by 25–35 years [Table 2]. The overall seroprevalence was revealed as toxoplasma 1.38%, rubella 1.14%, CMV 13.63% and herpes 17.43% [Table 3]. During 7 years, total seropositivity was contributed with herpes as 52%, cytomegalovirus as 41%, toxoplasma as 4% and rubella as 3% [Figure 1]. In the year 2011, maximum positive cases were reported as 263 and lowest cases (127) in the year 2016. During the study period, HSV cases followed by CMV were most prevalent each year. Rubella was highest with 13 cases in the year 2014 and lowest with two cases in 2012. Toxoplasma was reported on the peak with 12 cases in the year 2012 while only two cases in the year 2016 [Figure 2]. Coinfection of HSV with CMV was most abundant with 246 cases and highest cases of 46 in each year 2011 and 2013 while HSV with toxoplasma was the second most common coinfection as 11 cases [Table 4]. Male sex was predominant in TORCH agents among paediatric age group [Figure 3].

## Discussion

In the present study, we had analysed retrospective data over the 7 years for TORCH agents (Toxoplasma, rubella, CMV and herpes) in a tertiary care hospital of North India. It is important, however to aware of the variation in the incidence of various TORCH infections in different parts of the country. The exact prevalence of TORCH agents is largely unknown.<sup>[7]</sup>

*Toxoplasma gondii*, an intracellular protozoan parasite that is 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 the foetus.<sup>[1,8,9]</sup> The incidence of congenital toxoplasmosis varies from country to country and estimated around 1–2 per 1,000 live births in the UK while 1–10 per 10,000 newborns in Europe and other countries.<sup>[5,9]</sup> Previous literature had shown seroprevalence of toxoplasma in different countries between 7.7 and 76.7% as as UK 9.1–17.8%, Norway 10.9%, Sweden 14–25.7%, India 45%, Iran 51.8%, France 71%



**Figure 1:** Overall contribution of seropositivity of TORCH (toxoplasmosis, rubella virus, cytomegalovirus [CMV], and herpes simplex virus [HSV]) for 7 years

**Table 1: Department-wise distribution of samples**

Department	2011		2012		2013		2014		2015		2016		2017		Total	
	T	P	T	P	T	P	T	P	T	P	T	P	T	P	T	P
Paediatrics	147	39	118	24	149	25	164	30	208	19	132	27	177	30	1095	194
Obstetrics and Gynaecology	371	223	312	170	398	186	463	180	442	148	413	91	447	125	2846	1123
Medicine	4	1	9	3	0	0	0	0	2	1	9	5	22	9	46	19
Ophthalmology	0	0	0	0	3	2	0	0	8	5	9	2	17	3	37	12
Others	1	0	0	0	0	0	0	0	1	0	10	2	8	3	20	5
Total	523	263	439	197	550	213	627	210	661	173	573	127	671	170	4044	1353
Positivity (%)	50.29		44.87		38.73		33.49		26.17		22.16		25.34		33.46	

**Table 2: Age-wise distribution of TORCH positivity**

Age/sex	Total samples	Positive samples	Male		Female	
			Total samples	Positive samples	Total samples	Positive samples
0-1	662	105 (15.87%)	416	78	246	27
1-15	438	96 (21.92%)	268	60	170	36
15-25	1386	598 (43.15%)	9	0	1377	598
25-35	1459	530 (36.33%)	22	2	1437	528
35-45	76	20 (26.32%)	5	3	71	17
>45	23	4 (17.39%)	11	3	12	1
Total	4044	1353 (33.46%)	731	146	3313	1207

TORCH: toxoplasmosis, rubella virus, cytomegalovirus [CMV], and herpes simplex virus [HSV]

**Table 3: Prevalence of TORCH**

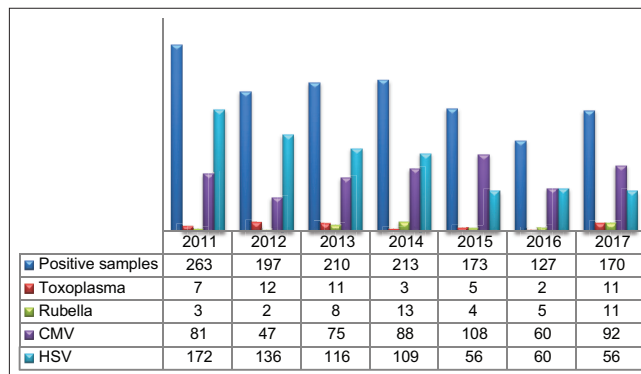
Age (yrs)	Total samples	Toxoplasma	Percentage	Rubella	Percentage	CMV	Percentage	Herpes	Percentage
<1	662	9	1.36	13	1.96	49	7.4	34	5.14
1-15	438	4	0.91	8	1.83	43	9.82	41	9.36
15-25	1386	25	1.8	11	0.79	227	16.38	335	24.17
>25	1558	18	1.15	14	0.9	232	14.89	295	18.93
Total	4044	56	1.38	46	1.14	551	13.63	705	17.43

**Table 4: Dominance of coinfection among cases during 7 years**

	2011	2012	2013	2014	2015	2016	2017	Total
CMV+HSV	46	28	46	39	35	25	27	246 (90.8%)
Toxo+HSV	-	5	4	-	1	-	1	11 (4.1%)
Rub+CMV	-	-	1	-	1	-	3	5 (1.8%)
Toxo+CMV	-	1	1	-	-	-	2	4 (1.5%)
Rub+HSV	-	1	-	-	-	-	-	1 (0.4%)
Toxo+Rub	-	-	-	1	-	-	-	1 (0.4%)
Toxo+CMV+HSV	-	-	-	-	1	-	-	1 (0.4%)
Rub+CMV+HSV	-	-	-	1	-	-	1	2 (0.7%)
Total	46	35	52	41	38	25	34	271

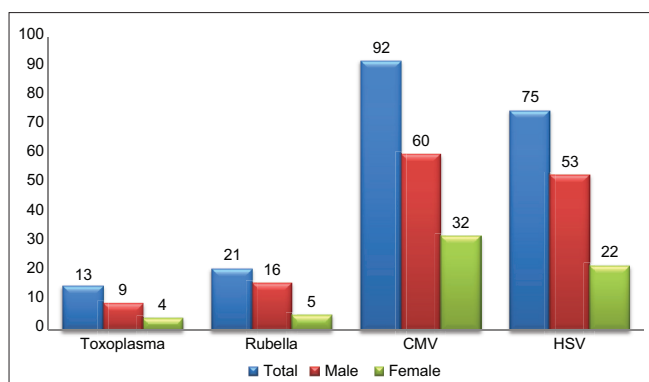
and Brazil 50–76%.<sup>[5,10]</sup> Few Indian studies had been reported a seroprevalence of toxoplasma as 14.66% in cases having a bad obstetric history of Nagpur,<sup>[6]</sup> 2.73% in reproductive age group females of Ludhiana.<sup>[3]</sup> Fortunately, the present study revealed low toxoplasma seroprevalence as 1.38% in whole population while 1.36% in infants.

Rubella causes asymptomatic or mild viral illness commonly in children and less common in adults.<sup>[3]</sup> It is transmitted from person to person by tiny droplets in air and mother-to-child through the placenta.<sup>[1]</sup> Primary virus infection during pregnancy



**Figure 2: Year-wise prevalence of TORCH**

may lead to miscarriage, foetal death, or an infant with serious birth defects including hearing impairment, cataracts and cardiac defects collectively called congenital rubella syndrome.<sup>[1]</sup> The prevalence of Rubella infection in pregnant women from the different country were reported as 87% in the USA, 93.3–94% in Saudi Arabia, 95–96% in Turkey, 98% in Spain.<sup>[5,11]</sup> In the present study, rubella was prevalent as 1.14% and infant with 1.96% which is comparatively low as reported in previous studies. A study from Chandigarh reported rubella as 2.8% in children, 4.66% in cases having bad obstetric history (BOH) in



**Figure 3:** Sex-wise distribution among seropositive paediatric cases (up to 15 years)

Nagpur<sup>[6,7]</sup> and 5.66% in females of the reproductive age group of Ludhiana.<sup>[3]</sup>

Human cytomegalovirus (CMV), otherwise known as human herpes virus 5 is transmitted by direct contact with saliva, urine and genital secretions.<sup>[1,12]</sup> It can cause intrauterine growth retardation, microcephaly with intracranial calcification, hepatosplenomegaly, jaundice, chorioretinitis, thrombocytopenic purpura and anaemia in neonates while the loss of vision, hearing and cognitive impairment in childhood age.<sup>[1]</sup> In CMV infection, the fetus is affected in all stages of pregnancy but more severe damage is reported during the first half of the pregnancy.<sup>[12]</sup> It is highly prevalent in both developed and developing countries and remains the most common congenital infection worldwide with an estimated incidence of 0.2–2.2% with seroprevalence ranging between 45% and 100%.<sup>[12]</sup> Studies reporting seropositivity of CMV in pregnant women are 56.8% in Australia, 84% in Spain, 39–94.7% in the USA and 84.5–95% in Turkey.<sup>[5]</sup> The seroprevalence in Indian adult population ranges 80%–90% with some states of India reporting 15.98% CMV IgM in Kashmir and 12.9% in Delhi and 22.03% for CMV IgM in Punjab,<sup>[12,13]</sup> 5.33% in cases with BOH in the study of Nagpur,<sup>[6]</sup> 12.5% in children of Chandigarh<sup>[7]</sup> and 19.91% infertile females of Ludhiana.<sup>[3]</sup> The present study revealed CMV prevalence in infants as 7.4% while overall it was 13.63% which is near to previous studies.

Herpes is categorised into herpes type 1 (HSV-1 or oral herpes) and herpes type 2 (HSV-2 or genital herpes). Worldwide, HSV is the most common sexually transmitted viral disease. HSV2 is always transmitted by sexual contacts causing genital herpes, while HSV1 is transmitted by non-sexual contacts causing mucocutaneous disease largely involves the mouth and oral cavity.<sup>[1,14]</sup> Primary genital HSV infection remains asymptomatic or unrecognized in more than 75% of cases but during pregnancy, it may lead to spontaneous abortion, prematurity, congenital and neonatal herpes.<sup>[15,16]</sup> Primary HSV infection during the first half of pregnancy is associated with increased frequency of neonatal morbidity and mortality<sup>[17]</sup> while infection during the third trimester is associated with the highest risk of neonatal transmission.<sup>[18]</sup> Congenital malformations (organomegaly, bleeding and CNS abnormalities) are reported in the fetus due

to infection of both herpes virus as 30–50% due to HSV-1 and 50–70% to HSV-2.<sup>[18,19]</sup> A recent study of the United States assessed the epidemiological association between herpes simplex virus type 1 (HSV-1) and type 2 (HSV-2) infections from 1999 to 2016, and revealed a strong declining trend for at least two decades, for both sexes and for the different ethnicities.<sup>[20]</sup> The prevalence rate of HSV IgM in the present study was 17.43% in the whole study population and 5.14% in infants, while the study conducted in central India had reported a variation of prevalence as 1.56% in pregnant women,<sup>[5]</sup> 8.66% among BOH in Nagpur,<sup>[6]</sup> 24.84% in Ludhiana among studying females,<sup>[3]</sup> 9.46% in women of Hyderabad, Telangana.<sup>[12]</sup> Though, the incidence of herpes has reduced over the past few years as shown in studies conducted on different population groups. This is possibly due to improvements in hygiene level, better living standard and safer sexual contact.

The positive serology for toxoplasma (1.36%) and rubella (1.96%) were comparatively more in infants while CMV with 14.84% and herpes with 19.84% were more prevalent in adults. Among confectons in this study, the highest rate with 90.8% of CMV and HSV, followed by toxoplasma and HSV with 4.1% was reported. Besides this, maximum cases of herpes (52%) followed by CMV (41%), toxoplasma (4%) and rubella (3%) were distributed among overall TORCH seropositivity.

TORCH infections are a very annihilating group of infections. Its prevalence varies with different socioeconomic statuses on two different patient populations. Some of them can be preventable or curable if diagnosed on a regular basis of primary care. Thus, it is paramount to prevent TORCH and its associated serious sequels in mothers and infants by health promotion and better counselling of their patients by primary care physicians.

## Conclusion

In summarising context, TORCH pathogens have potentially devastating clinical manifestations. Hence, serological screening before pregnancy and early diagnosis of TORCH can diminish morbidity and mortality in both child and mother. Furthermore, knowing the epidemiology is an important aspect to develop strategies and appropriate implementation for the prevention of infection.

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## Conflicts of interest

There are no conflicts of interest.

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