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Original Research Article

Study of TORCH infections and its impact on newborn babies and infants: a retrospective study in a tertiary care hospital in Visakhapatnam, Andhra Pradesh, India

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ABSTRACT

Background: TORCH is an acronym for *Toxoplasma*, others (syphilis), *Rubella*, *Cytomegalovirus* and *Herpes simplex* virus. These are important causes of morbidity and mortality in new-borns, infants and children. Early diagnosis and treatment are essential to reduce the morbidity and mortality.
Methods: It was a cross sectional record based retrospective record-based study conducted in King George Hospital, Andhra Medical College, Visakhapatnam, Andhra Pradesh. Samples from clinically suspected cases (newborns and infants) for possible TORCH infections were tested in virology laboratory from January to November 2019 and the samples were collected and tested by EUROIMMUN kit for the respective IgM antibodies and analyzed. Clinical details of newborns and infants were gathered from the patients through telephonic communication.
Results: Total number of patients tested were 104 in which 54 (52%) showed positivity in which 36 were positive for CMV, 25 for HSV_2, 23 for Rubella, 12 for Toxoplasma and 11 for *Varicella zoster* infection. Out of 52 positive cases 20.4% were alive and normal, 20% were alive but severely affected, mortality was 16.7%. Out of 16.7% mortalities 22% of deaths were due to nephrotic syndrome. Clinical manifestations include hepato-splenomegaly in 33.3% cases, fever in 30%, low birth weight in 25%, heart disease in 13.7%, microcephaly in 13.7%.
Conclusions: Our study showed hepatomegaly, fever and low birth weight as common clinical manifestations. Fever and nephrotic syndrome were typically associated with CMV positive cases. Out of 52 % positively tested cases CMV was very common infection followed by HSV_2, Rubella and Toxoplasmosis.

Keywords: TORCH- *Toxoplasma*, Others, *Rubella*, *Cytomegalovirus*, *Herpes simplex*

INTRODUCTION

Toxoplasma gondii is an obligate intracellular protozoan parasite and is transmitted by eating under cooked meat and by ingestion of food or water contaminated with infected cat faeces. Other modes of transmission are through blood transfusion and organ transplantation. About one third of all women who acquire infection with *T. gondii* during pregnancy transmit the parasite to the foetus.[1] Infection is most lethal to the foetus if mother acquires infection during first trimester yet most infections occur in the third trimester which is usually asymptomatic or subclinical. The classical triad of congenital Toxoplasma includes chorioretinitis, and intra-cranial calcifications and symmetrical IUGR. Serological surveys help us understand the burden of disease in community.

Overall seroprevalence of *Toxoplasma* in Indian women of reproductive age was 22.4%, highest prevalence was in South India (37.3%) in East India (21.2%) and North India (19.7%). West Indian women had the lowest

seroprevalence (8.8%). Overall, the incidence rate of toxoplasmosis was 1.43%.[2]

Rubella virus (RV) is a member of Togaviridae family and the only member of the genus Rubivirus and humans are its only known reservoir. It is spread from person to person by respiratory droplets. Rubella is predominantly a childhood disease and is endemic throughout the world. Most commonly it causes polyarthralgia in adult women. However, the primary public health concern of RV infection is its teratogenicity like congenital cataract and congenital Rubella syndrome. *Rubella* is recognized as the most potent infectious teratogenic agent.[3] 10-30% of adolescent females and 12-30% of women in the reproductive age-group are susceptible to rubella infection in India.[4] Since *Rubella* is a vaccine preventable disease every effort should be made to achieve 100% vaccine coverage.

Cytomegalovirus (CMV) is a beta herpes virus has a double stranded DNA and sources of CMV infection include Congenital (acquired before birth from maternal source), Perinatl (acquired at or around time of birth from maternal sources, breast milk, cervico-vaginal secretions), postnatal (acquired after birth from non-maternal sources), blood product transfusions, organ transplantation stem cell transplantation, person-to-person transmission (close contact such as sharing food or drink, kissing, sexual contact.[5] In one study the maternal CMV seroprevalence ranged from 84% to 100%. CMV birth prevalence varied from 0.6% to 6.1% in developing countries.[6] Seroprevalence rates serve as a marker for the size of the reservoir of viruses. Human *Cytomegalovirus* (CMV) is a leading cause of congenital infections worldwide. It is the commonest nongenetic cause of childhood hearing loss and an important cause of neuro-developmental delay.[7] Women with flu like symptoms should be screened for TORCH infections and they should be educated about hand hygiene especially after attending to younger children attending day care centres who usually carry CMV infection.

Herpes simplex virus and *Varicella zoster* virus (HSV and VZV). These viruses are in Herpesviridae family. They have linear double stranded DNA genome. Mother with recurrent genital HSV lesions pose less of a risk for transmission to an exposed neonate than do mothers with primary infection. Mother to child transmission of HSV can occur during one of the three time periods in utero (5%), during delivery (85%) or post natally via direct contact within oral-labial or other cutaneous lesion (10%).

In a population-based study the seroprevalence rates of HSV_2 was 7.07% for women and 4.07% in men.[9]

Varicella zoster causes chicken pox as primary infection travels to dorsal root ganglion where it becomes latent and comes out years later as zoster. Mode of transmission is by respiratory droplets. If mother acquires chicken pox 5 days before to 2 days after delivery, the risk of infection to new born is highest.

Objectives

To know the impact of TORCH infections in neonates and infants who were tested positive to these infections and to analyse different clinical manifestations of TORCH infections in new-borns and infants.

METHODS

It was a cross sectional record based retrospective study conducted in King George Hospital, Andhra Medical College, Visakhapatnam, Andhra Pradesh. Samples from clinically suspected cases (new born and infants) for possible TORCH infections were tested in virology laboratory from January 2019 to November 2019 and the samples were collected and tested by EUROIMMUN kit for the respective IgM antibodies and analyzed. Clinical details of new-borns and infants were gathered from the patients through telephonic communication and electronic media. Reports were compiled in Microsoft excel and results were analyzed by SPSS software system.

Institutional Ethics Committee approval was taken prior to starting of this study. The reports of 104 samples were collected, tested and analyzed and patients' health details were obtained by phone (telephonic communication).

Inclusion criteria

All neonates and infants tested for TORCH were included.

Exclusion criteria

Infections other than TORCH were excluded.

RESULTS

Total numbers of patients tested were 104 in which numbers of positives were 54 (52%). Out of these 36 were positive for CMV, 25 were HSV_2, 23 were positive for *Rubella*, 12 were *Toxoplasma* positive and 11 were positive for VZV.

Table 1: Total tests positivity.

	Frequency	Percentage
TOXO plasma	2	1.9
Rubella	2	1.9
CMV	15	14.4

Continued.

	Frequency	Percentage
HSV_2	3	2.9
VZV	3	2.9
TOXO+Rubella+HSV_2	2	1.9
TOXO+Rubella+CMV	1	1.0
TOXO+Rubella+VZV	2	1.9
TOXO+Rubella+CMV+ HSV_2	3	2.9
TOXO+Rubella+CMV+ HSV_2+VZV	1	1.0
TOXO+CMV	1	1.0
Rubella + HSV_2	2	1.9
Rubella+VZV	1	1.0
Rubella+CMV+HSV_2+VZV	1	1.0
Rubella+HSV_2+VZV	1	1.0
Rubella+CMV	2	1.9
Rubella+CMV+HSV_2	5	4.8
CMV+HSV_2	5	4.8
CMV+HSV_2+VZV	2	1.9

Status of the babies: Out of 52% positive cases (54 out of 104 samples). Alive and normal were 20.4% (11 out of 54), alive and severely affected were20.4% (11 out of 54). Mortality- 16.7% (9 out of 54) and in remaining cases data was not available which accounts for 37.5% (23 out of 54).

Table 2: Mortality causes and its percentage.

Cause of death	Frequency	Percentage
Nephrotic syndrome	2	22
Severe anaemia	1	11
Congenital rubella syndrome	2	22
Hepatosplenomegaly and subsequent liver failure along with other causes	4	44

Out of 17% mortality, 22% of deaths were due to nephrotic syndrome. (2 out of 9), 12% due to severe anaemia (1 out of 9), 22% due to congenital rubella syndrome (2 out of 9), 44% due to hepato-splenomegaly and subsequent liver failure, bleeding in brain and other causes (4 out of 9).

Table 3: Clinical manifestations and its percentage.

Clinical manifestations	Frequency	Percentage
Hepato-splenomegaly	35	33.3
Fever	31	30
Low birth weight	26	25
Heart disease	24	13.7
Microcephaly	14	13.7
Nephrotic syndrome	10	9.8
Seizures	9	8.3
Hydrocephalus	4	3.9
Anaemia	4	3.9

Following clinical manifestations of congenital TORCH infections were found and they include, hepato-splenomegaly in 33.3%, fever- 30%, low birth weight- 25%, heart disease- 13.7%, microcephaly- 13.7%, nephrotic syndrome- 9.8%, seizures- 8.3%, hydrocephalus- 3.9% and anaemia in 3.9% cases.

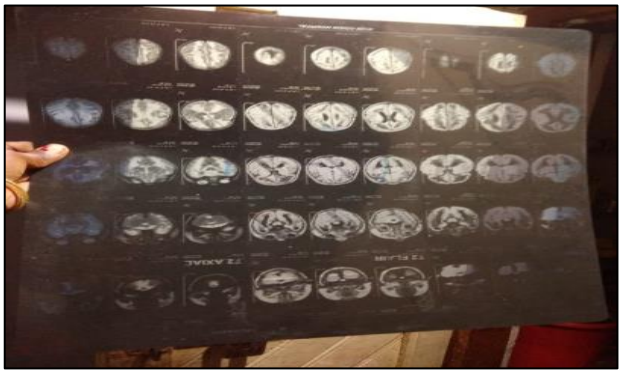

Figure 1: MRI showing intra cranial calcifications in *Toxoplasma gondii* infection.

Table 4: Comparison of maternal age and other factors with other studies.

Variables	Present study (104)	Prasoona et al[10]
Maternal age 20-30	89.4%	32%
Maternal age >30	3.8%	5%
Consanguinity	14%	25%
Secondary education	80%	65%

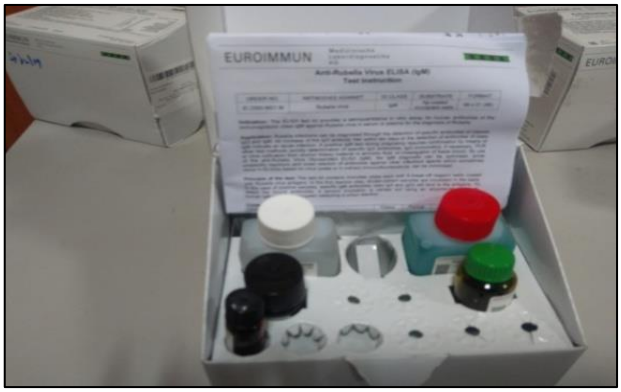

Figure 2: Euro-immune kit.

Figure 3: Infants severely affected with TORCH in this study.

Our study in comparison with Prasoona et al study showed similar incidence of maternal age of more than 3.8% in comparison with 5%. Consanguinity was present in 14 percent in our study as compared to 25% in Prasoona et al study. Majority of the women were educated and completed secondary education.[10]

DISCUSSION

In the present study 89.4% of women were in the age group of 20-30 years. 80% of them completed secondary education but were from poor economic status. Lack of proper sanitation and crowded conditions might have caused these infections.

In Prasoona et al study also showed a literacy rate of 68% as compared to 80 % of our study group.[10] Strong factor like history of consanguinity was found in 14% of babies as compared to 25% in Prasoona et al study.

Epilepsy in patients with congenital cytomegalovirus infection by Suzuki et al revealed 37% seizures where as in present study it is 8.3% and encompasses CMV, *Rubella* and *T. gondii* positive cases combined. Hence it is not quite comparable.[11]

In symptomatic congenital *Cytomegalovirus* infection neonatal morbidity and mortality by Bopannna et al showed hepato-splenomegaly in 70% where as in present study it is 33.3%.[12]

Cytomegalovirus-related congenital nephrotic syndrome with diffuse mesangial sclerosis by Besbas et al describes congenital nephrotic syndrome in a 2-month-old girl associated with cytomegalovirus infection.[13] Histological examination on renal biopsy showed diffuse mesangial sclerosis and cytomegalic inclusion bodies in the tubular cells and in some glomeruli. *Cytomegalovirus* (CMV) polymerase chain. (PCR) titre in serum was high.

However, in the present study no renal biopsy was done for confirmation.

This retrospective study is based on serology report of IgM antibody positivity for various TORCH infections. CMV specific IgM antibody though less specific and sensitive yet preferred method of preliminary screening of congenital infections deafness could have been a predominant symptom given the high positive results of CMV and *Rubella* but could not elicit such information from guardians because they were not aware of such and new born hearing tests were missing in available records. Clinical findings and adverse outcome in neonates with symptomatic congenital *Cytomegalovirus* (SCCMV) infection by Kylat et al revealed 7% of patients with symptomatic congenital CMV were without any deficits where as in present study 11% are alive and normal.[14]

Total number of deaths were 17 but only 9 of them were due to TORCH infections, 8 others were due to sepsis, anencephaly and other causes, so not included in the present study. Out of 9 deaths due to TORCH, three of them were due to CMV in which 2 babies died of nephrotic syndrome. One baby died at the age of 3 months and another at 6 months in spite of dialysis. Another baby with severe anaemia survived only 10 days.

Two succumbed to congenital Rubella syndrome with heart problems like ASD, VSD, and L-R shunt. Four deaths were due to hepato-splenomegaly with underlying biliary atresia and subsequent liver failure. They all tested positive for multiple infections, seizures, cerebral palsy, bleeding in the brain, hydrocephalus with poor brain development were noted in severely affected new-borns. Since the deaths have multiple causes and no autopsy was done, we cannot rule out the specific infection. To find the catalyst we must perform PCR or tissue biopsy.

This study is a unique study of its kind and similar studies were not found for comparison. Similar studies are needed to know the gravity of problem.

CONCLUSION

In our study majority of the babies are affected and died of cytomegalovirus infection and is mostly due to nephrotic syndrome and renal failure. To know the prevalence of other infections and cause specific mortality, we need to do extension of the study by increasing the sample size. Vaccination coverage should be increased to Rubella in adolescent girls. All pregnant women should be tested for Rubella in their first antenatal visit and if tested negative should be given vaccination after delivery. Women with Flu like symptoms should be tested for TORCH infections.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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