Summary & Conclusion
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The maternal infections that are transmitted in utero at several stages of the pregnancy caused by organisms viz., Toxoplasma gondii, Rubella virus, Cytomegalovirus and Herpes Simplex virus. The infectious disease threats during pregnancy are classified into three important issues. First, changes in immunity and physiology during pregnancy may make pregnant women more susceptible or more severely affected by infectious diseases. Second, the effects of infectious diseases on the fetus may be unknown and difficult to predict, and hence diagnosis of infection in the fetus or infant can be challenging. Third, prophylaxis and treatment appropriate for the general population cannot be afforded for pregnant women. Some maternal infections that when acquired during early gestation can result in fetal loss or malformations, this may be due to that the ability of the fetus to resist infectious organisms is limited and the fetal immune system is unable to prevent the dissemination of these organisms to various tissues.

TORCH is an acronym for a special group of infections that are either acquired during pregnancy or before pregnancy but produces disastrous consequences in infants. All these infections are grouped together as they can cause a cluster of symptomatic birth defects in newborn and are collectively referred as TORCH syndrome. The TORCH syndrome in infants includes congenital heart disease, cataract, blindness or significant visual impairment, hearing impairment including deafness, microcephaly (small head size), hydrocephaly (large head size), mental retardation, low blood counts (anemia), liver or spleen enlargement, pneumonia, skin rash usually appears as reddish-purple of brown, involvement of central nervous system (encephalitis, calcium deposits in the brain tissue and seizures, jaundice, in addition, each of the TORCH infections has its own characteristic differentiating symptoms in newborn.

These infections play an important role in pregnancy that can lead to the Bad Obstetric Complications (BOH). BOH can be defined in terms of either unfavorable fetal outcomes with one or more consecutive spontaneous abortion, history of intrauterine fetal death, intra uterine growth retardation, still births, early neonatal
death and other congenital anomalies. The recurrent pregnancy wastage is mainly due to the maternal infections that are transmitted in utero at various stages of gestation which includes the TORCH complex. In most cases the maternal illness is mild but the impact on the developing fetus is more severe. The degree of severity depends on the gestational age of the fetus when infected, virulence of the pathogen, the damage to the placenta and also the severity of the maternal disease.

Toxoplasmosis is caused by the coccidian parasite *Toxoplasma gondii*, worldwide in distribution. Cats are the definite hosts for the parasite and the human beings and other mammals serve as an intermediate hosts. Humans acquire the infection by handling infected cats or cleaning their litter box, drinking unpasteurized milk, eating raw or undercooked meat, by receiving the contaminated blood or blood products and through maternal transmission to the fetus. The infection when acquired transplacentally may mainly focus the fetus that can infect the eyes and central nervous system of the infants and also they can invade brain or muscle tissue and form tissue cyst (a resistant form the parasite). Toxoplasmosis when acquire during early in pregnancy may result in miscarriage or serious birth defects but when contracted later in pregnancy the higher probability is for the fetus to be infected. The prevalence of *T. gondii* in women of child bearing age was reported to be 10 to 80% and the incidence of toxoplasmosis in newborns is 1 in 1000 live births.

Rubella is the virus with seasonal outbreaks and most likely to occur during spring. Various epidemiological reports reveal that 10 – 20% of women in child bearing age are susceptible to rubella infection but it may lead to congenital malformations in 10 – 54% of cases. Rubella is said to be one of the important teratogen tend to cause fetopathy and embryopathy. The infection is characterized by fever, lymphadenopathy, sore throat and skin rash as these symptoms were common for other viral infections clinical rubella is difficult to diagnose. Congenital Rubella Syndrome (CRS) includes the signs of heart disease, retarded growth, hearing loss, blood disorders, vision problems or pneumonia and may develop problems later in childhood including autism, hearing loss, brain damage, immune disorders and thyroid disease.
Cytomegalovirus (CMV) belongs to the group of herpes viruses. In adults CMV infections are usually asymptomatic but its significance is increased in higher fold when it occurs during pregnancy. It is transmitted through body secretions, through sexual contact and even to newborn through breast milk. CMV is the most common intrauterine infection frequently associated with intrauterine growth retardation, sensorineural hearing loss, mental retardation, microcephaly, hepatosplenomegaly, petachiae, jaundice, chorioretinitis, thrombocytopenia, anemia and shortly after birth may develop pneumonia, hepatitis or various blood disorders. In certain populations of Asia and Africa even 100% seroprevalence were reported and in 0.2 – 2.5% of infants there is an evidence of the intrauterine infection but most of them were born without any clinical findings and may develop later in their life.

Herpes Simplex Virus (HSV) is among the most infections of human beings mainly spread either by oral or through genital contact. It is estimated that 1 in 1000 infants are born with HSV infections. Most of these infections are acquired during the birth process itself and the infections may be transmitted to the infants through its eyes, skin, mouth and upper respiratory tract. Among the infants infected infants 20% of them have localized infections of the eyes, mouth, or skin and about 50% may develop disease through the body (disseminated) within 9 – 11 days after birth. HSV – 2 is transmitted sexually and the symptoms include genital ulcers or sores and in addition to this virus may cause the lining of the brain leading to meningoencephalitis or infection of the eye especially the conjunctiva and cornea. Disseminated herpes leads to the entry of the virus to other organs such as liver, adrenal glands and other body organs. HSV without treatment may lead to 80% mortality rate, with treatment still mortality rate is found to be 15-20% and 40 – 55% of the survivors have long-term damage to the central nervous system.

The aim of the present study is to assess the serological status of the pregnant women against the TORCH infections through the detection of IgM and IgG antibodies. As these infections are initially inapparent or asymptomatic, they are difficult to diagnose on clinical background. Therefore the diagnosis of acute and latent infections among the pregnant women is usually demonstrated by the specific
IgM and IgG antibodies respectively. PCR has become the preferred method for rapid and more reliable viral diagnosis in recent years. To increase sensitivity some assays include a second round of amplification using nested or hemi-nested primers. They are highly sensitive especially for samples with very low concentration of virus, as was demonstrated by numerous research studies. The performance of PCR analysis is dependent upon the quality of the specimen. A total of 232 samples from pregnant women attending the antenatal clinic in and around Salem District, Tamil Nadu were included for the study. To demonstrate the association of TORCH infections with the infertility, 45 blood samples from women attending the antenatal clinic were also enrolled for the present study.

The prevalence of TORCH infections among the pregnant women was assessed with two different methods such as immuno-strip assay and ELISA technique. Further, the ELISA IgM positive samples were confirmed with the PCR assay. Out of 232 pregnant women participated in this study 9 (3.9%) were found to be positive for anti-toxoplasma IgM antibodies and 23 (9.9%) were positive for anti-toxoplasma IgG antibodies. Around 8 (3.4%) and 118 (50.9%) samples were positive for anti-rubella IgM and IgG antibodies respectively. A total of 11 (4.7%) samples were found to possess anti-CMV IgM antibodies and 139 (59.9%) women were positive for anti-CMV IgG antibodies and HSV prevalence rate was found to be 9.5% (22 out of 232) for IgM antibodies and 28% for anti-HSV IgG antibodies (65 out of 232). The presence of specific IgM and IgG was determined using the immuno-strip assay supplied by recomLine TORCH screening. Among the 232 pregnant women, 7 (3.01%) were found to be positive for toxo IgM and 18 (7.75%) for toxo IgG antibodies. A higher prevalence of 56.03% (n=130) and 43.1% (n=100) was observed for CMV and rubella IgG antibodies. A total of 6 and 9 women were found to be positive for IgM antibodies against rubella and CMV infections. The HSV positivity was recorded in 19 and 59 women with anti-HSV IgM and IgG antibodies respectively.

The efficacy of the immuno-strip assay with ELISA as a standard test was evaluated for the sensitivity, specificity and accuracy. The analysis revealed that the
immuno-strip assay showed 85 – 95 % sensitivity, 99 – 100% specificity and 98 – 100% accuracy against ELISA which is a standard test method. The ELISA positive samples were confirmed for the presence of the corresponding DNA (TORCH panel) by PCR assay. All the ELISA IgM antibody positive samples with either DNA or RNA of the respective infectious agents were amplified and visualized through gel electrophoresis. Through analysis of the PCR product revealed the presence of 233bp DNA fragment for 9 samples of *T. gondii*. Similarly, 143bp product of PCR for 8 positive cases of rubella, 263bp product for 11 samples of cytomegalovirus and 22 HSV positive samples amplified with 342bp PCR product. The results of PCR revealed that all the samples that were positive by IgM ELISA were found to possess specific DNA of the etiologic agent demonstrating the efficiency of the ELISA technique.

The influence of sociodemographic factors and the associated symptoms and risk factors were assessed statistically for all the four types of infections and the results were recorded separately for each infection. To determine the influence of age, the patients were divided into four age groups. The results indicate a significant age dependent trend to TORCH seropositivity. Literacy level of the pregnant women plays a main role in the prevalence of these infections. Most of these infections show a statistical association for the literacy level and the seropositivity. The economic status influence among the anti-toxoplasma IgM and IgG positive pregnant women was found to be more in High and medium economic status (3/9 & 4/9 for IgM positivity and 10/23 for each high and medium class women in IgG positivity) and a lower prevalence was recorded among women with low economic status (2 and 3 for IgM and IgG respectively). The economic status of the women was found to have no significant association with the seropositivity. Among the 22 anti-HSV IgM positive women 12 (54.5%) were within the high economic class, 8 (36.3%) were within the medium class and 2 (9%) were from the low economic class. Most of these infections in this study is found to be more among the first trimester indicating the need for earlier treatment and also the cesarean delivery to protect the baby from exposure to these infections while delivery through the vaginal canal.
Pregnant women with the previous miscarriage, recurrent abortion, intrauterine growth retardation (IUGR), intrauterine fetal death (IUFD) and still birth were grouped as women with bad obstetric history (BOH). Pregnant women participated in this study are more susceptible to HSV and CMV compared to Toxoplasma and Rubella. These intrauterine pathogens have significant role in causing first trimester miscarriage. Significant relationship exists between TORCH mixed infections and miscarriage. Intrauterine growth retardation and Intrauterine fetal death has been influenced significantly by all the four TORCH infectious agents in this study. The seropositivity of the infertile women ranked higher than the pregnant women. The Immuno-strip assay was found to have higher level of sensitivity, specificity and accuracy which can be used for the primary screening of the TORCH infections.

The outcome of the study revealed that among the total population included in this study the awareness of congenital infections were nearly 20%. It was surprisingly documented that the 80% of the remaining participants which includes both the literate and illiterate pregnant women were unaware of these infections. The study indicates the necessity of educating the women. TORCH diagnosis are cost effective, time consuming and needs the expertise personnel to carry out the procedure as the screening test is not as easiest as other routine antenatal screening. The sensitivity, specificity and accuracy of Immuno-strip assay was found to be satisfactory and therefore this may also be considered for rapid detection of TORCH infections both in the private and in Government hospitals for women of reproductive age group. Immunoprophylaxis is available for susceptible pregnant women.

This study revealed that the seroprevalence of the TORCH infections were significantly noticed among the pregnant women residing in Salem District, Tamil Nadu. The epidemiology of TORCH infections is an important aspect in the development of strategies for the prevention of congenital infections. Hence from the study it is understood that the antenatal cases with bad obstetric history may be considered for routine screening of TORCH complex to avoid adverse fetal outcomes. Currently TORCH screening is performed only among the abnormal pregnancies and
with definite clinical presentation of the previous babies. Eliciting the risk factors for all relevant infections is time consuming and it is very difficult to identify the women’s those are at risk. *Toxoplasma* associated infection may be prevented by educating the women by avoiding the ingestion of raw or undercooked meat and poultry products. Preserving stringent practices in health and hygiene may also support in preventing the vicious cycle of TORCH transmission. Incorporation of rubella immunization may also be considered in the national immunization schedule for better immunological protection for the women of child bearing age. Alternatively, Human immune serum globulin may also be used for seronegative pregnant women. Awareness of CMV infection and their prevalence needs to be inculcated among the pregnant women. Necessary preventive measures needs to be taken while handling the toddlers during the first trimesters that will protect them from the spread of primary infections. Caesarian section is suggested for pregnant women with active genital herpes or early symptoms of HSV. Practicing safer sexual practices and sex education on genital herpes needs to be promoted.

Health education and counseling may have profound impact for the preventive strategies. The application of simple hygienic measures during pregnancy may reduce these congenital TORCH infections. Live vaccines may be given at 3-6 months before pregnancy. Early diagnosis and appropriate intervention may aid proper management of these infections. Hence new approaches to the prevention and treatment of congenital TORCH infections are necessary, including antiviral interventions and the development of a vaccine strategy.