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SEROLOGICAL STUDY OF TORCH INFECTIONS IN WOMEN WITH HIGH DELIVERY RISK FACTORS

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ABSTRACT: OBJECTIVE: To evaluate the incidence of TORCH infections in women having history of pregnancy loss and women with high delivery risk factors (HDRF) in tertiary care hospital. **Duration:** A prospective study was conducted over a period of one year from January 2013 to December 2013. **METHODS:** The study included 100 women with HDRF and 50 clinically normal women with previous normal pregnancy and full term deliveries. Serological evaluation for TORCH infections was carried out by IgG and IgM ELISA method. **RESULTS:** The acronym TORCH (Toxoplasma, Other infections, Rubella, Cytomegalovirus, Herpes simplex virus) was introduced to highlight a group of agents which cause congenital and perinatal infections. The prevalence of TORCH infections in tertiary care hospital was studied over a period of one year. Since majority of congenital infections result from maternal infections during pregnancy, it was essential to evaluate the incidence of maternal infection like TORCH in child bearing age group. The present study showed toxoplasmosis was with a high risk seropositivity rate of 41%, followed by 27% seropositivity for Cytomegalovirus (CMV). Rubella infections still occur each year and it occurred in 18 % cases while Herpes simplex virus infection was comparatively low seen only in 14% cases among women of child-bearing age. But unfortunately the request for TORCH screening has been ignored and clinicians should be encouraged to send appropriate specimens for specific tests depending on the clinical features of the individual case so as to reduce the adverse fetal outcome.

KEYWORDS: TORCH, Seroprevalence, high delivery risk factors.

INTRODUCTION: The TORCH test, which is sometimes called the TORCH panel, included in the category of blood tests called Infectious-Disease Antibody Tests IDAT.⁽¹⁾

TORCH tests measure the presence of antibodies against a specific group of infectious diseases and their level of concentration in the blood. Toxoplasmosis, Other infections, Rubella, Cytomegalovirus (CMV), and Herpes simplex virus (HSV), may be acquired by a woman during pregnancy with disastrous consequences for the infant. All are grouped together because they can cause a cluster of symptomatic birth defects in new-borns, collectively called the TORCH syndrome.⁽²⁾ Rahway have suggested that this classification is too limiting and several additional infectious agents should be considered in the other category, such as enteroviruses, *Borrelia burgdorferi* (the cause of Lyme disease), and, of course, human immunodeficiency virus HIV⁽³⁾.

A positive Ig G antibody test is usually a sign of past-exposure to the TORCH agent and is not a marker for current active infection. Detection of Ig M antibody is more difficult, and false negative and false positive results may occur⁽⁴⁾.

Toxoplasmosis is caused by *Toxoplasma gondii*, and is found in human worldwide, a parasite that the mother can acquire from handling infected cats, drinking unpasteurized milk, or eating contaminated meat.

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The infection is carried to the infant through the mother's placenta, and can cause infections of the eyes or central nervous system. The later in pregnancy that the mother is infected, the higher the probability that the fetus will be infected. On the other hand, toxoplasmosis early in pregnancy is more likely to cause a miscarriage or serious birth defects^(2, 5, 6).

Syphilis was added to the TORCH panel because of a rapid increase in reported cases since 1990^(6, 7, and 8). It is also a potentially life-threatening infection for the fetus.

Rubella is a virus that has a seasonal pattern, with epidemics most likely in the spring. Between 0.1-2% of new-borns will be infected with rubella. The rate of foetal infection varies according to the timing of the mother's infection during pregnancy. Birth defects, however, are most likely (85%) in infants infected during the first eight weeks of pregnancy⁽⁹⁾.

Cytomegalovirus (CMV) belongs to the herpes virus group of infections. It can be transmitted through body secretions, as well as by sexual contact; some new-borns which acquire CMV through the mother's breast milk Infected infants may have severe problems, such as hearing loss, mental retardation, pneumonia, hepatitis, or blood disorders.⁽¹⁰⁾

Herpes simplex virus the virus enters the infant through his eyes, skin, mouth, and upper respiratory tract. Infants born with HSV infection, about 20% will have localized infections of the eyes, mouth, or skin. About 50% of infected infants will develop disease which spread throughout the body (disseminated) within 9-11 days after birth^(11, 12).

HSV-2 is sexually transmitted. Symptoms include genital ulcers or sores. In addition to oral and genital sores, the virus can also lead to complications such as infection of the lining of the brain and the brain itself (meningo encephalitis) or infection of the eye especially the conjunctiva and cornea.⁽¹³⁾

The aim of the present study is to confirm the presence of Ig M antibody for TORCH by ELISA method in women with high delivery risk factors.

PATIENTS AND METHODS: A prospective study was done from January 2013 to December 2013 on patients who had attended to the outpatient department (OPD) of department of Obstetrics and Gynecology in Tertiary health care hospital. A total of 150 women were investigated including 100 with high delivery risk factors and 50 clinically normal women with previous normal pregnancy and full term deliveries. Cases were included in the study depending on previous history of having 2-3 pregnancy loss, intrauterine growth retardation, intrauterine deaths, preterm labour, early neonatal death and congenital malformation.

From each woman 3 ml of venous blood was collected in a container with strict aseptic precautions. The serum was used for serological evaluation for Ig M antibodies for TORCH infections according to manufacturer's instructions using ELISA techniques^(9, 14).

TORCH index of each determination was calculated by dividing the value of each sample by calibrator values and TORCH M index of 1.0 or greater was considered positive for antibodies^(15, 16, 17).

RESULTS: From 100 cases with HDRF, the highest number of cases was in the age group of 21-30 years i.e. 55% followed by 29% in the age group of 31- 40 years and 16% in the age group more than 41 years. Out of 50 healthy control cases 14 (28%) were serologically positive in different age group as 9 (18%) the age group of 21-30 years followed by 3 (6%) in the age group of 31- 40 years and 2 (4%) in the age group more than 41 years as shown in table no. 1.

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Age in years	Seropositivity HDRF (n=100)		Seropositivity Controls (n= 50)	
	Number	%	Number	%
21-30	55	55	09	18
31-40	29	29	03	06
>41	16	16	02	04
Total	100	100	14	28

Table 1-Distribution of patients and controls according to age groups.

Table no. 2 shows out of 100 cases with HDRF, abortion occurred in 38, intrauterine growth retardation in 21, intrauterine death in 9, premature labour in 7, early neonatal death in 20 and congenital malformation in 5 cases.

HDRF	No. of patients
Abortion	38
Intrauterine growth retardation	21
Intrauterine death	09
Preterm labour	07
Early neonatal death	20
Congenital malformation	05
Total	100

Table 2 – Distribution of patients with different HDRF

Table no.3 displays all 100cases of HDRF were showing seropositivity for either one or two elements of TORCH infection while out of the 50 healthy controls 14 (28%) were serologically positive for only one of the TORCH infections. In HDRF cases the seropositivity for T. gondii was 41%, rubella virus 18% CMV 27% and HSV 14%, while in the control cases the seropositivity for T. gondii was 14%, rubella 4%, CMV 6%, and HSV was 4%.

TORCH agent	Seropositivity HDRF (n=100)		Seropositivity Controls(n=5)	
	Number	%	Number	%
Toxoplasma	41	41	07	14
Rubella	18	18	02	04
Cytomegalo virus(CMV)	27	27	03	06
Herpes Simplex Virus(HSV)	14	14	02	04
Total	100	100	14	28

Table 3 - Seropositivity of each infection agent within TORCH test.

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The highest seropositivity was seen with *T. gondii* 63.1% in cases of abortions followed by intrauterine growth retardation and preterm labour i.e., 42.8% each. Rubella showed highest seropositivity 30.0% in early neonatal death followed by 28.5% in preterm labour. In early neonatal death cases and in congenital malformation CMV showed highest seropositivity i.e. 55.0% and 40.0% respectively. HSV showed highest seropositivity in congenital malformation i.e. 20.0% followed by in abortion 18.4%. In intrauterine death *T. gondii* and CMV showed seropositivity of 33.3% each as shown in table no.4.

HDRF cases	Toxoplasma		Rubella		Cytomegalo virus(CMV)		Herpes Simplex Virus(HSV)	
	Number	%	Number	%	Number	%	Number	%
Abortion	24	63.1	04	10.5	03	07.8	07	18.4
Intrauterine growth retardation	09	42.8	03	14.2	07	33.3	02	09.5
Intrauterine death	03	33.3	02	22.2	03	33.3	01	11.1
Preterm labour	03	42.8	02	28.5	01	14.2	01	14.2
Early neonatal death	01	05.0	06	30.0	11	55.0	02	10.0
Congenital malformation	01	20.0	01	20.0	02	40.0	01	20.0
Total	41	41	18	18	27	27	14	14

Table 4 - TORCH agents with different presentations of HDRF cases.

Mixed infections were noted in 14 out of 100 patients (14.0%) in association with Toxoplasma Ig M antibodies in our study. Out of 14 patients of mixed infection 8 were with Rubella, 4 with CMV, 1 with Rubella plus CMV and 1 with CMV plus HSVII, similar observation of mixed infection has been made earlier.⁽¹⁷⁾

In cases of abortion, intrauterine growth retardation and preterm labour seropositivity with toxoplasma was predominant. In cases with early neonatal death and congenital malformation CMV was predominant. In cases with intrauterine death both toxoplasma and CMV were predominantly seen. Rubella and HSV were not predominant in any HDRF cases.

DISCUSSION: TORCH screening is now widely requested by clinicians, investigating suspected cases of congenital and perinatal infection. There is concern that such requests are appropriate and should be targeted more specifically.⁽⁵⁾

It is evident that maternal infections play a critical role in pregnancy loss and their occurrence in patients with HDRF is a significant factor. Persistence of encysted forms of *T. gondii* in chronically infected uteri, and their subsequent rupture during placentation lead to infection of the baby in the first trimester and often to recurrent miscarriages.⁽⁶⁾ In the present study *T. gondii*, which is a known etiological agent in recurrent pregnancy loss was found in 39% pregnant women with HDRF, this is similar to what has been reported earlier.^(14,18,19) Congenital transmission of *T. gondii* is known to occur during the acute phase of maternal infection and the Ig M antibodies are evaluated in the maternal sera.^(20,21)

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Ig M antibodies were found in 63.1% of present cases with recurrent abortions compared with other study reported previously showed 66.3% of women infected with *T. gondii* which is to accentuate my study.⁽¹⁹⁾

Pregnant women should have their blood examined for Toxoplasma antibody and those with negative results should take measure to prevent infection by avoiding exposure to cat feces, cooking meat thoroughly, and washing hands thoroughly after handling raw meat.⁽²²⁾

TORCH infections are unique in their pathogenesis and have potentially devastating clinical manifestations. Congenital toxoplasmosis remains an important cause of blindness, although avoiding exposure to cats and uncooked meat can prevent it ⁽²¹⁾.

Cytomegalovirus remains the most common cause of congenital infection in the United States, the possibility of effective treatment with Ganciclovir has emerged from recent studies done by Hoffman-La Roche, Basel, Switzerland.⁽²⁰⁾ In neonatal herpes, selective use of caesarean delivery and antiviral therapy can decrease incidence and improve outcomes.^(11,16,23)

Both CMV and HSV are known to have an intrauterine route of transmission with significant mortality and morbidity ⁽²¹⁾. The present study shows seropositivity rate of 27% for CMV specific IgM in women with HDRF. In other studies seropositivity ranges from 3 to 12.9 %. ^(11,12,20,21)

Primary CMV infection in pregnancy has a higher incidence of symptomatic congenital infection and foetal loss. This infection, being asymptomatic in adults it is difficult to diagnose clinically. Demonstration of Ig M antibodies is indicative of primary infection. The need of serological evaluation of CMV specific Ig M during pregnancy has been supported by various investigators.^(12,24)

Patients with HIV disease should have toxoplasma antibody titres checked. If the results of the blood test are positive and if the CD4 count is less than 100, patients should be given prophylactic antibiotics (trimethoprim-sulfamethoxazole is the medication of choice) with antiretroviral therapy until the CD4 cell count has risen.⁽²²⁾

Primary infection with HSV II acquired by women during pregnancy accounts for half of the morbidity and mortality from HSV II among neonates, the other half results from reactivation of old infection. Seropositivity rate of HSV Ig M among the HDRF patients in our study was 14%, while HSV in asymptomatic women with recurrent infection during pregnancy was found to be 2% previously.⁽²⁵⁾

Seropositivity rate for HSV Ig M among HDRF patients in our study was 14%, similar to what has been reported in other study ⁽²⁶⁾.

Rubella is a mild viral illness in children but can occasionally infect adults. Primary virus infection during pregnancy may cause foetal damage. In our study seropositivity for rubella was 18% while other workers reported seropositivity ranging from 4 to 17.7% ^(11, 12).

Episodes of increased incidence of Rubella are reported to occur every 3-4 years,⁽²⁵⁾ since 10-20% of women in child bearing age are susceptible to Rubella.⁽⁴⁾ Increased incidence of Rubella will lead to increased reporting of pregnant women with Rubella infection. About 26.8% of pregnant women were positive for Rubella Ig M as has been reported earlier ⁽²⁷⁾. The observation therefore suggests an increased incidence of Rubella infection in pregnant women.

The Ig G antibody in the pregnant woman may be a sign of past infection with one of these infectious agents. By testing a second blood sample drawn two weeks later, the level of antibody can be compared. If the second blood sample shows an increase in Ig G antibody, it may indicate a recent infection with the infectious agent ^(5, 17).

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Ig M is never zero as it cross-reacts with many other IgMs and other proteins. We have to follow the reference range provided by the private laboratories^(13,19).

There is no direct relation between an active infection and ultrasound growth and, therefore ultrasound not be relied upon as the diagnostic criteria either to confirm or refute the diagnosis of Rubella. In fact it gives us no information at all. You cannot take a decision based on the ultrasound report therefore Ig M is more specific and reliable.⁽⁴⁾

The unborn child cannot be tested for infection by ultrasound. If there is a reasonable suspicion of a foetal infection the only way to check would be to take the blood from the foetus at twenty weeks and analyse it for Ig M against Rubella and do a Polymerase Chain Reaction (PCR) diagnosis of Rubella.^(13,28)

Ig M is a specific class of antibodies that seeks out virus particles. It is, therefore, the most useful indicator of the presence of a TORCH infection.⁽⁹⁾ The general abnormal, or positive finding give high levels of Ig M antibody.⁽²⁰⁾ The test can be refined further for antibodies specific to given disease agents. The TORCH screen, however, can produce both false-positive and false-negative findings.⁽¹²⁾

Ig M antibodies against TORCH organisms usually persist for about three months, while Ig G antibodies remain detectable for a lifetime, providing immunity and preventing or reducing the severity of reinfection.⁽²⁶⁾ Thus, if Ig M antibodies are present in a pregnant woman, a current or recent infection with the organism has occurred. If Ig M antibodies are absent and Ig G antibodies are present and do not demonstrate an increase on serial testing several weeks later, it can be assumed that the person has had a previous infection by the corresponding organism⁽²⁴⁾ or has been vaccinated to prevent an infection. If the serum of a person has no evidence of either Ig M or Ig G antibodies specific for the organism, then the person is at risk of infection because they do not have any demonstrable immunity.⁽⁷⁾

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