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Seroprevalence of TORCH Infections in Pregnant Women with Bad Obstetric History in and around Kakinada Town, India

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A B S T R A C T

Pregnant women in India belonging to low socio-economic group are exposed to a variety of infections due to poor hygiene and environment. Though placental barrier prevents some microbes crossing from maternal into fetal circulation, TORCH agents cross the barrier and result in various clinical conditions. Objectives of the study are to study the seroprevalence of TORCH infections in pregnant women with Bad obstetric history (BOH) and also to know the outcome of these infections in newborn. This study was done on 120 pregnant women with Bad Obstetric History and 60 pregnant women with normal obstetric history attending Antenatal OP. Each group was screened for Anti TORCH antibodies by Micro ELISA method. The present study has shown IgM antibody seropostivity for *Toxoplasma* (20%), Rubella (5%), Cytomegalovirus (6.6%) among the BOH group where as in control group seropositivity was 10% for *Toxoplasma* and were negative for Rubella and CMV. In BOH group IgG antibody seropositivity was *Toxoplasma* (30%), Rubella (46.6%), CMV (93%) and HSV (6.66%) where as in control group IgG antibody seropositivity for *Toxoplasma* (16.66%), rubella (40%), CMV (66.66%), HSV-2 (3.33%). Higher rate of seropositivity for IgM and IgG antibodies was seen among pregnant women with BOH compared to those with normal obstetric history suggesting the relationship between TORCH infections and bad obstetric outcome. Thus prenatal screening programmes for TORCH infections over a period of time could be fruitful in decreasing perinatal morbidity and mortality.

Introduction

Recurrent pregnancy loss due to maternal infections transmissible in utero at various stages of gestation can be caused by a wide array of organisms. The acronym TORCH was first suggested by Nahmias *et al.,* (1971) to highlight a group of agents which cause congenital and perinatal infections. TORCH stands for *Toxoplasma gondii*, Others (*T. pallidum*, Varicella zoster (vzv), Parvo virus B-19, HIV), Rubella virus, Cytomegalo virus (CMV) and Herpes simplex virus-2 (HSV-2) (Tatjana *et al.,* 2010).

Bad obstetric history (BOH) implies pregnancy outcomes in terms of two or more consecutive spontaneous abortions, history of intrauterine foetal death, intrauterine growth retardation, still births, early neonatal death and/or congenital anomalies. Causes of BOH may be genetic, hormonal, abnormal maternal immune response or maternal infection.

During pregnancy, a highly efficient placental barrier prevents some infectious agents crossing from maternal into fetal circulation.

Nevertheless, TORCH agents cross the placenta to cause fetal loss or can result in Intrauterine Growth retardation (IUGR), Prematurity or Chronic Postnatal infection. In most cases the maternal illness is mild but the impact on the developing fetus is severe. The degree of severity is dependent on the gestational age at the time of infection, virulence of the organism, damage to the placenta and the severity of the maternal disease (Sue et al., 2004).

Clinical evidence of infection may be seen at birth, soon afterward, or not until years later. The infected newborn may present with growth retardation, developmental anomalies, or multiple clinical and laboratory abnormalities. The infection can also lead to late onset disease e.g. development of chorioretinitis in an adolescent with congenital Toxoplasmosis. Progressive tissue damage is seen in rubella, HSV, CMV, Toxoplasmosis, syphilis as the infective agents continue to survive and replicate in the tissue for months after initial infection. This is particularly unfortunate when treatment is possible.

Data on the serological status of these infections in pregnant women provides information about immune status that may help to identify women at risk and in preventing congenital infections due to TORCH agents (Tatjana et al., 2010). The prevalence of these infections varies from one geographical area to another (Canessa et al., 1987).

These maternal infections are initially inapparent or asymptomatic and are thus difficult to diagnose on clinical grounds. Therefore, diagnosis of acute TORCH infections in pregnant women is usually established by demonstration of seroconversion in paired sera or by demonstration of specific IgM antibodies.

Enzyme linked immunosorbent assay (ELISA) for IgM antibodies against these infections is highly sensitive and specific (Thapliyal et al., 2005).

In India, the exact seroprevalence of these infections is not known. There is no base line data on the antibody titres in various subpopulations of India. So, the present study has been undertaken to evaluate the seroprevalence of TORCH infections in pregnant women with Bad Obstetric History (BOH) attending antenatal OP of Government General Hospital. All the samples were screened for IgM and IgG antibodies against Toxoplasma, Rubella, Cytomegalovirus and IgG antibodies against Herpes simplex virus-2 by Enzyme Linked Immunosorbent Assay.

The main objectives of this study to detect specific IgM and IgG antibodies for Toxoplasma, Rubella, Cytomegalovirus and IgG antibodies for Herpes simplex virus-2 by Micro ELISA Test and also to know the outcome of TORCH infection in new born.

Materials and Methods

This study was done on pregnant women attending Antenatal OP, Government General Hospital, for a period of 6 months. Two groups of subjects were included in the study: 1st group included Pregnant women with Bad Obstetric History (N=120) and 2nd group included pregnant women with Normal Obstetric History (N=60). After obtaining clearance from Institutional Ethical committee and consent from the pregnant women detailed information on education, occupation, socio-economic status, previous obstetric history and medical history was recorded. Nutritional status and general conditions like anaemia and blood pressure were also recorded. Prior delivery outcome with reference to gestational age at the time of abortion, delivery information on still birth

and congenital malformations was recorded. Type of delivery and any other complications was also recorded. All the samples were screened for IgM and IgG Anti TORCH antibodies by ELISA (Table 4).

Method

5ml of venous blood was collected using disposable syringes under sterile conditions. Blood was centrifuged, serum separated and transferred into sterile provials and stored at -20ºC until the test was performed.

All the samples were screened for IgM and IgG specific antibodies for *T. gondii*, Rubella, CMV, and type specific IgG antibodies of HSV-2 (g G2) by ELISA. ELISA Test for detection of antibodies to *Toxoplasma*, Rubella, CMV and HSV-2 was done using separate kits for each agent. EUROIMMUN KITS Medizinsche Labordiagnostika AG, Lubeck (Deutschland). Imported by CPC Diagnostics PVT LTD, Chennai were used. Photometric measurement of the colour intensity was made at a wavelength of 450nm and a reference wavelength of 650nm by ELISA Reader. Calculation of results was done by semiquantitative method for the detection of IgM antibodies and by quantitative method for the detection of IgG antibodies. The results were compiled and statistically analysed.

Results and Discussion

The results are expressed as percentage and analysed using chisquare test. The present study showed IgM antibody seropostivity for *Toxoplasma* (20%), Rubella (5%), Cytomegalovirus (6.6%) among the BOH group where as in control group seropostivity was 10% for *Toxoplasma* and were negative for Rubella and CMV. In BOH group IgG antibody seropostivity was *Toxoplasma* (30%), Rubella (46.6%), CMV (93%) and HSV (6.66%) where as in control group IgG antibody seropostivity for *Toxoplasma* (16.66%), rubella (40%), CMV (66.66%), HSV-2 (3.33%). The difference in the seropostivity between BOH and control group was found to be statistically significant.

Infections by TORCH agents in women are usually asymptomatic and chronic. Maternal infections transmissible in utero at various stages of gestation lead to recurrent pregnancy wastage. Infections caused by TORCH agents – *Toxoplasma*, Rubella virus, cytomegalovirus (CMV) and Herpes simplex virus-2 (HSV-2) are the major cause of BOH. Many sensitive and specific tests are available for serological diagnosis of TORCH complex. ELISA for antibodies against these infections is highly sensitive and specific. *T. gondii* is an obligate intracellular protozoan parasite that causes toxoplasmosis. Infection is found worldwide, particularly in warm and moist climates. About 20 – 90% of the world adult population is exposed to *T. gondii*.

Table.1 Seropositivity of anti-TORCH IgM antibodies in BOH and control groups

GROUP	Number studied	Seropostivity for IgM Antibodies for TORCH	
		Number Positive	Positive Percentage
BOH	120	38	31.6
CONTROL	60	6	10

(Chi-Square =10.167; df =1; P= 0.001)

Table.2 Seroprevalence of TORCH infections in BOH and control groups

Sl. No	Causative agent	BOH Group (N=120)		Control Group (N=60)	
		Number Positive for IgM	Number Positive for IgG	Number Positive for IgM	Number positive for IgG
1	*T. gondii*	24(20%)	36(30%)	6(10%)	10(16.66%)
2	Rubella virus	6(5%)	56(46.6%)	0(0%)	24(40%)
3	Cytomegalo virus	8(6.6%)	112(93%)	0(0%)	40(66.66%)
4	Herpes simplex-2	--	8(6.66%)	---	2(3.33%)

Table.3 Seropositivity for anti TORCH IgM antibodies among BOH group in relation to previous obstetric history

Sl. No	Previous Obstetric History	Number of Pregnant women tested	Seropositive for ANTI-TORCH IgM antibodies.	
			Number	Percent
1	Spontaneous abortion	58	21	36.2
2	Intra uterine deaths (IUD)	10	3	30
3	Congenital anamolies	5	1	20
4	Neonatal death	14	3	21.4
5	Abortions and congenital anamolies	28	10	35.6

(Chi-Square=1.633, df =4, P=0.803)

Table.4 Outcome of pregnancy in seropositive women of BOH group

Seropositive for IgM	No of patients followed	NVD	Abortions	IUD	Congenital anomalies/ Neonatal death
T. gondii	10	4	3	1	2 babies with IUGR, LBW, Chorioretinits, Hydrocephalus
Rubella	2	-	1 1st trimester Abortion	-	1 baby had Cleft lip and palate, ascites, pleural effusion, died in NICU.
CMV	3	1	4th month abortion	-	1 baby had Microcephaly, seizures, chorioretinitis and intracranial calcification.

Table.5 Comparative study of seropositivity

S.No	Year of Study	Other studies	*T. gondii*		Rubella		CMV		HSV-2
			IgM%	IgG%	IgM%	IgG%	IgM%	IgG%	IgG%
1	1993	Surinder Kaur *et al*	22	-	-	-	-	-	-
2	2001	Yasodhara *et al*	13.1	-	6.5	-	5.8	-	-
3	2002	Han O Ghazi *et al*	-	35.6	-	93.3	-	92.1	27.1
4	2003	Turbadkar *et al*	10.52	42.1	26.8	61.3	8.42	91.0	33.58
5	2006	Rajendra B Surpam *et al*	14.66	-	4.66	-	5.33	-	-
6	2007	Gumber *et al*	-	-	-	-	4.67	-	3.33
7	2008	Denoj Sebatian *et al*	50.7	-	11.3	-	28.2	-	59.2
8	2009	Zhiyan Li, *et al*	3.9	-	2.2	-	1.8	-	10.6
9	2010	Khurana *et al*	3	15.3	-	-	-	-	-
10	2010	Tatjana *et al*	2.4	29.1	3.2	94.6	2.2	75.3	6.8
11	2010	Marawan *et al*	5.2	35.1	-	-	-	-	-
12	2011-2012	Present study	20	30	5	46.6	6.66	93	6.66

Its importance for humans refers mainly to primary infection during pregnancy. The prevalence of toxoplasmosis in Indian pregnant women is variably reported.

Studies of Yasodhara *et al.,* (2001) showed 13.1%, Rajendra Surpam *et al.,* (2006) 14.66%, Turbadkar *et al.,* (2003) 10.52%, Khurana *et al.,* 3%.In the present study, we found that 20 % of women with BOH were positive for IgM antibodies to *T. gondii*, while only 10% were positive in the control group (Chi-Square=2.88, P=0.090). The higher rate of seropositivity can be attributed to warm and humid environments, change in food habits from home cooked food to fast foods, contaminated water, poor sanitation and lack of hygiene. Also farming is the main occupation around Kakinada which increases the exposure to the soil contaminated with faeces of cats. Primary prevention of toxoplasmosis in pregnant mother can be achieved through education to practice precautionary measure, which include washing hands frequently, washing all the vegetables and fruits and, proper handling of raw meat while preparation of food.

In our study seropostivity for Anti *T. gondii* IgG antibodies was found to be 30% in women with BOH while it was 16.66% in the control group. Turbadkar *et al.,* reported seropostivity of 42.1%, Hani O Ghazi 35.6%, Marawan *et al.,* 35.1% and Tatjana *et al.,* 29.1 % in women with BOH (Tables 1–3).

Women who have specific IgG antibodies are protected and there is no foetal risk unless they are immune-compromised. Women with negative serologic tests are at risk of acquiring primary infection during pregnancy. So, in our study women with BOH showed higher IgG positivity which may be due to previous exposures. Acute infection with *T. gondii* may be the cause of previous pregnancy losses.

About 70% in BOH group and 83.34% in control group were sero-negative and they are at risk of acquiring infection during the pregnancy. This suggests the need for regular antenatal screening and early detection is important because the mother can be treated with Spiramycin to prevent fetal infection.

Rubella is a benign self limited viral illness characterized by exanthem and posterior cervical lymphadenopathy but results in devastating manifestations in the fetus when contracted by pregnant women in early weeks of pregnancy. Although rubella vaccination has reduced the incidence of rubella virus substantially; WHO estimates more than 100,000 children/year born with CRS (congenital Rubella syndrome), most of them in developing countries.

In the present study seropositive rate was 5% which is in line with studies of Yasodhara *et al.,* (2001) and Rajendra Surpam *et al.,* (2006) which showed 6.5% and 4.66% respectively. Turbadkar *et al.,* (2003) and Denoj Sebatian *et al.,* (2008) study showed a higher percentage of 26.8% and 11.3% respectively. Control group on the other hand was negative (0%) for IgM antibodies to rubella. On follow up in our study one patient had abortion and one delivered a child with congenital anamolies.

In the present study seropostivity for Anti Rubella IgG antibodies was 46.6 % in BOH group and 40% in the control group. In this study seropositivity is less compared to the studies of Turbadkar *et al.,* and Gondhoke *et al.,* who reported 61.3% and 87% respectively. The low seropositivity in our area may be due to lack of awareness about rubella vaccination and poor MMR Immunization coverage. So, 53.4% in BOH group and 60% in control group do not have protective immunity and are at high risk contracting infection in pregnancy. Studies from other countries Hani Ghazi *et al.,* (2002) and Tatjana *et al.,* (2010) showed higher rate of seropositivity for IgG antibodies i.e. 93.3% and 94.6% respectively suggesting successful vaccination campaign (Table 5).

The prevention of rubella is dependent upon adequate early immunization, resulting in high prevalence of immunity in women of child bearing age. All the sero-negative women should be immunized against rubella immediately after delivery.

Cytomegalovirus (CMV) is the most important cause of congenital infection and long term neurodevelopment disabilities among children. Populations from low and middle income group have high rate of acquisition of CMV infection with seroprevalence rates ranging from 80-100%. Poor socio-economic conditions that are characterized by overcrowding and a lack of hand hygiene, and placing children in day care centres, promote CMV transmission. Primary CMV infection can result in 30–40% risk to newborn when compared to reactivation which has 1- 3% risk.

Our study showed the seropositivity of 6.66% for IgM antibodies to CMV. Other studies also showed similar incidence. Yasodhara *et al.,* 5.8%, Turbadkar *et al.,* 8.42%, Rajendra B Surpam *et al.,* 5.33%, Gumber *et al.,* 4.67%. Denoj Sebastian *et al.,* study showed a significantly higher percentage 28.2%. Studies from other countries- Zhiyan Li *et al.,* (2009)

and Tatjana *et al.,* (2010) showed very low seropositivity -1.8 and 2.2 % respectively. Such low seropostivity may be due to better standards of living. In our study control group was negative (0%) for Anti CMV IgM antibodies.

In present study seropostivity for Anti CMV IgG antibodies was 93% in women with BOH and 66.66% in control group which is similar to other studies Turbadkar *et al.,* (2003) and Hani Ghazi *et al.,* (2002) which was 91% and 92.1% respectively. Tatjana *et al.,* study showed slightly lower positive rate 75.3%. The prevalence of congenital CMV infection varies widely among different populations.

Neonatal herpes infection is a potentially devastating consequence of common genital infection caused by human herpes simplex virus (HSV)-2. Intrauterine HSV infection during early pregnancy is rare; most neonatal herpes simplex virus infections are perinatally acquired via contact with infected lesions in maternal genital tract. In our study seropositivity for Anti –HSV IgG antibodies was 6.66% in BOH group and 3.33% in control group. In other studies from our country by Turbadkar *et al.,* (2003) it was 33.58%, Denoj Sebastian *et al.,* (2008) showed 59.2 %.

Prevention of neonatal disease consists of timely diagnosis and appropriate management in the mother including acyclovir treatment and delivery by caesarean section in the presence of active lesions. Subclinical infection in the mother is very often seen, as only about 9% of them have genital herpes at the time of delivery. So, serodiagnosis plays an important role in preventing neonatal herpes.

In the present study, control group showed low seropositivity for IgG antibodies to TORCH agents compared to BOH group. Indicating that in control group exposure to TORCH agents was less. So they are at risk for TORCH infections in the present pregnancy and future pregnancies unless protected from exposure during pregnancy.

In conclusion,

1. TORCH infections are associated with recurrent abortions, intrauterine growth retardation, intrauterine death, preterm labour, early neonatal death, and congenital anomalies. Knowledge about previous history of pregnancy wastages and positive serological reactions during the present pregnancy helps management of these patients in order to reduce adverse outcome.

2. Pregnant women should be educated during antenatal visits regarding TORCH infections and on their prevention.

3. Population based studies and prenatal screening programmes for TORCH infections over a period of time could be fruitful in decreasing perinatal morbidity and mortality.

4: Universal vaccination is a powerful tool in eliminating congenital rubella syndrome.

5. A sound knowledge of congenital and perinatal infections is essential for prompt recognition and management of these conditions in order to prevent further disease and disability.

6. Understanding the epidemiology of TORCH is an important element in the development of new strategies for the prevention of congenital infections. Entirely new approaches to prevention and treatment of congenital TORCH infection are necessary, including antiviral interventions and the development of a vaccine strategy.

7. Finally, the importance of good hygiene cannot be overemphasized in contributing towards overall improved perinatal health and protection from infections.

References

Canessa, A., Pantaratto, F. 1987. Antibody prevalence to TORCH agents in pregnant women and relative risk of congenital

infections in Italy (Liguria). *Biol. Res. Pregnancy Perinatol.,* 8: 84-8.

Gumber, S., *et al.* 2007. Department of Microbiology, Government Medical college, Amritsar, Punjab. Occurance of Cytomegalovirus and Herpes simplex virus infections in Pregnancy. *IJMM,* (April-June2008, Pp. 204-205).

Hani, O., Ghazi, *et al.* 2002. Umm Al –Qura University, Makkah, Kingdom of Saudi Arabia. TORCH agents in Pregnant Saudi women. *Med. Principles Pract.,* 11: 180-182.

Khurana, S., *et al.* 2010. Serological screening for antenatal *Toxoplasma* infection in India. Department of Parasitology, PGIMER, Chandigarh, *IJMM,* 28(2): 143-6.

Marawan, A., Abu Madi, *et al.* 2010. Department of health sciences, Qatar. *T. gondii* seropostivity and co-infection with TORCH pathogens in high risk patients from, Qatar. *Am. J. Trop Med Hyg.,*82(4): 626-633.

Nahmias, A.J., Walls, K.W., Stewart, J.A., Flynt, W.J. 1971. The TORCH complex – perinatal infections associated with *Toxoplasma* and rubella, Cytomegalo- and herpes simplex viruses. *Pediatr. Res.,* 5: 405-6.

Rajendra, B., Surpam, *et al.* 2006. Department of Microbiology, Indira Gandhi Govt. Medical College, Nagpur. Serological study for TORCH infections in women with BOH. *J. Obstet. Gynecol. India,* 6(1): 41-43. Ed. Philadelphia: WB Saunders; p. 947-1091.

Stagno, S., Pass, R.F., Coud, G. 1986. Primary CMV infection in pregnancy, incidence, transmission to fetus and clinical syndrome. *JAMM,* 256: 1904-8.(85)

Sue, G., Boyer, *et al.* 2004. Department of maternal and child health, Rush University, Chicago, Illnois. *Update on TORCH Infections in the Newborn Infant,* (89).

Surinder Kaur Sandhu, Jaspal Singh, Harpreet Mann and Harleen Kaur. 1993. Toxoplasmosis and pregnancy wastage. *J. Obstet. Gynec. India*, p. 194-198.

Tatjana Vilibie-Cavlek, *et al.* 2010. Crotian National Institute of Public health, Zagreb, Croatia. Seroprevalence of TORCH infection in women of child bearing age in Croatia. *The J. Maternal-Fetal and Neonatal Med.,* 24(2): 280-283.

Tatjana Vilibie-Cavlek, *et al.* 2010. Crotian National Institute of Public health, Zagreb, Croatia. Seroprevalence of TORCH infection in women of child bearing age in Croatia. *The J. Maternal-Fetal and Neonatal Med.,* 24(2): 280-283.

Thapliyal, N., Shukla, P.K., Kumar, B., Upadhyay, S., Jain, G. 2005. TORCH infection in women with bad obstetric history- a pilot study in Kumaon region. *Indian J. Pathol. Mcrobiol.,* 48: 551-3.

Yasodhara, P., *et al.* 2001. at NIN, ICMR, Jamai Osmania, Hyderabad. Prevalence of specific IgM due to *Toxoplasma*, Rubella, Cytomegalo virus and Chlamydia trachomatis infections during pregnancy. *IJMM,* 19(2): 52-56.

Zhiyan Li, *et al.* 2009. Department of Clinical Laboratory, Peking, University, Beijing, China. Prevalence of serum antibodies to TORCH among women before pregnancy or in the early period of pregnancy in Beijing. *Clinica Chimica Acta*, 403: 12-215.