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Research Article

Prevalence of TORCH Infections during Pregnancy: A Prospective Cohort Study in Tribal Region of Gujarat, India

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Abstract

Introduction: Maternal infections are important causes of poor birth outcomes, child morbidity, and mortality. The most common infections during pregnancy causing adverse birth outcomes are TORCH. Few studies have been done in India to know prevalence of TORCH in general population. The objective of this study is to determine the Prevalence of TORCH infections in a tribal area of the Aravalli district in Gujarat, India.

Methods: Pregnant women in any gestational age residing in tribal area were eligible for this study. The maternal blood sample were collected once during pregnancy to study TORCH infections through molecular detection by nested-PCR and IgG-IgM antibodies detection through ELISA method.

Results: At the time of the study women who were pregnant (n = 901) were included in this research. Prevalence of toxoplasmosis, CMV, and HSV was reported to be 39%, 37%, and 38% respectively. ELISA IgM positivity for toxoplasmosis was 1.22%, CMV was 2.7%, HSV was 4%, and Rubella was 1.55%.

Conclusion: High prevalence of TORCH infections in tribal community by DNA detection indicates higher vulnerability of this population. Regular screening during antenatal period should be done to prevent poor pregnancy outcomes in women.

Keywords: Pregnancy; Prevalence; TORCH; Tribal Women; India; Poor Birth Outcomes; Maternal Infections

Introduction

Infections acquired during any stage of pregnancy often lead to serious adverse outcomes. Poor birth outcomes can be miscarriages, still birth, intrauterine growth retardation, congenital abnormalities, and early neonatal death [1]. TORCH infections (Toxoplasmosis, Others-Hepatitis B/Epson Barr, Rubella, Cytomegalovirus, and Herpes Simplex virus) are known to cause a variety of perinatal complications including congenital anomalies and childhood morbidity/mortality [2,3].

While the placental barrier between mother and fetus protects and chances of adverse effects of infections in fetus are higher in the first trimester of pregnancy [4]. Due to the asymptomatic nature of these infections, identification and diagnosis is largely dependent on serological evidences [5,6]. To more accurately confirm the infections, specific IgG, IgM and various methods of polymerase chain reaction (PCR) have been utilized [7].

The literature shows that the prevalence of TORCH infections varies with geography, socioeconomic status, and poor environmental and hygiene conditions [8,9]. Screening of pregnant women is not possible in low and middle income countries due to high cost and lack of infrastructure [10,11]. Despite established connection between infection and poor birth outcomes, a national level screening program for TORCH infections is still lacking in India [12].

There are few community-based studies done to know prevalence of TORCH in general population. Most of the studies used measurement of antibodies using serological tests that have inherent limitations. This study estimated prevalence of TORCH infections during pregnancy in Aravalli district of Gujarat which is a tribal district, and thereby fulfilling an important gap in the literature.

Materials and Methods

Study design and setting

A prospective cohort study was conducted from September 2018 to March 2020 in the Aravalli district, Gujarat. Two blocks Bhiloda and Modasa with the estimated population of 239, 216 and 67, 648 were selected [13]. The study protocol was approved by the Institutional Ethics Committee, Indian Institute of Public Health Gandhinagar. Written informed consent was obtained from the study participants before the interview and sample collection.

Study participants

Inclusion criteria - All pregnant women in the age group 15 - 49 years and at any gestational age were eligible participants. Universal sampling was used to get the direct information from the study participants.

Exclusion criteria- Pregnant women who were anemic or not willing to participate in the study.

Data collection

Quantitative data on demographic characteristics, household status, antenatal, delivery and post-delivery information was collected using a structured questionnaire. The questionnaire was translated into local language (Gujarati) and information was obtained through personal interviews. Open Data Kit (ODK) was used to collect and manage the data obtained from the field. A team of supervisor and field investigators were trained at the beginning of the study to collect detailed information from the participants. Follow-up visits were made three weeks' post-parturition to collect information on delivery outcomes.

Housing was divided into kuccha- mud house with grass roof, kuccha pucca- brick house with grass roof and pucca- brick house with roof. Parity of participants was divided into primi-first time pregnant, multipara-1-2 previous pregnancies and grand multipara-3 or more previous pregnancies. The modified BG Prasad classification was used for determining socioeconomic status based on the per capita income of a family [14].

Laboratory procedure

Plasma samples were collected for the assessment of TORCH infection during pregnancy and mostly at the first contact. The samples were process for molecular detection of organism DNA and antibodies using Nested PCR and ELISA.

Nested PCR

Nested PCR is a modification of regular PCR which uses two amplification rounds with the two pairs of "external" and "internal" primers [15]. The first reaction is performed with primers that cover the target sequence. Amplicons resulting from this reaction are used as template for a second primer and a second amplification step [16,17]. This leads to a significant improvement in sensitivity and specificity.

The detailed methodology and laboratory procedure have been explained in a published methodology paper [18].

Samples were tested for molecular detection of TORCH pathogens using nested PCR approach. Plasma DNA extraction was done to determine β-globin. If DNA and β-globin were found in plasma, the samples were included for further laboratory analysis. However, cases with missing DNA were not included for PCR analysis. The laboratory technicians performed sample preparation, DNA extraction, and PCR amplification.

ELISA test

About 6 - 7 ml of blood was collected in EDTA vacutainer tube from the each participating pregnant women by trained staffs. The blood samples were then transported with proper instructions and cautions to the IIPHG lab. All the samples were tested for IgG and IgM antibodies for TORCH infections by ELISA method. The tests were performed as per instructions provided on manufacturer's commercial kit Diametra.

Data analysis

Collected data were entered to Microsoft Excel and analyzed in STATA MP 14.2.

Results

A total of 1050 pregnant women were registered. After exclusion of anemic and unwilling participants, 901 were included in the analysis. Table 1 shows the general characteristics of the analytic sample including age, education, caste, socioeconomic status, parity, and previous pregnancy adverse outcomes (if any). Age of

the included women ranged from 17 - 40 years and mean age was 24.34 ± 3.52 years. 38.73% of the study participants were primi, 55.49% were multipara and 5.78% were grand multipara category. Further, more than half (59.60%) lived in Kutcha-Pucca house and belonged to a joint family structure (61.71%). As expected more than 60% belonged to Schedule Tribe. More than 30% did not have toilet facilities. Majority earned their living by daily wage activities indicating financial instability. About 7% of the participants had experience adverse obstetric outcome.

Characteristics	Frequency (%)
	(n = 901)
Women's Age in Months Mean (sd)	24.34 (3.52)
Household Head	
Male	805 (89.35)
Female	96 (10.65)
Caste	
SC	71 (7.88)
OBC	249 (27.64)
ST	564 (62.60)
General	17 (1.89)
Type of House	
Kutcha/ No house	160 (17.76)
Kutcha-Pucca	537 (59.60)
Pucca	204 (22.64)
Type of Family	
Joint	556 (61.71)
Nuclear	345 (38.29)
Toilet Facility	
Own Flush toilet	71 (7.88)
Shared/public Flush toilet; own pit toilet	262 (29.08)
Shared/public pit toilet	240 (26.64)
Others (no toilet)	328 (36.40)
Mode of Income	
Daily Wage	667 (74.03)
Salaried (Monthly wage)	80 (8.88)
Food for labour	100 (11.10)
Livestock dependant	54 (5.99)
Mean Monthly Income (sd)	6505.83 (5642.28)
Socioeconomic Status	
Class I	6 (0.67)
Class II	27 (3.00)
Class III	85 (9.43)
Class IV	374 (41.51)
Class V	409 (45.39)
Parity (%)	
Primi	349 (38.73)
Multipara	500 (55.49)
Grand Multipara	52 (5.78)
Previous Pregnancy Outcome	
Still Birth	11 (2.51)
Live Birth	411 (93.84)
Neonatal Death	1 (0.23)
Abortion	15 (3.42)
ANC Checkups (%)	
Yes	793 (88.01)
No	108 (11.99)

Table 1: General characteristics.

Table 2 represents the prevalence of TORCH infections in pregnant women in the Aravalli district. DNA was detected in 898 samples hence molecular prevalence was tested in these mothers and seroprevalence was tested in 901 pregnant women. PCR was not performed for rubella. As seen in the table molecular prevalence of Toxoplasmosis was highest (39.20%) while detection of past infection was highest in Herpes Simplex-HSV. Majority of the infections had molecular prevalence of around 30% or more. Active infection in serological testing is low with highest of 4% for HSV.

Infections	PCR	IgG	IgM
	Frequency (%)		
Toxoplasmosis	352 (39.20)	689 (76.47)	11 (1.22)
Cytomegalovirus	329 (36.64)	837 (92.90)	24 (2.66)
HSV	345 (38.42)	846 (93.90)	36 (4.00)
Rubella	-	816 (90.57)	14 (1.55)
EBV	344 (38.31)	-	-
VZV	268 (29.84)	-	-
		HbsAg	
Hepatitis B	244 (27.17)	26 (2.89)	-

Table 2: Prevalence of TORCH in pregnant women.

Discussion

In the present study, prevalence of TORCH infections was estimated in tribal women who were currently pregnant. Use of molec-

ular diagnosis makes the study unique. Literature suggested that pregnant women are at higher risk of TORCH infections and these infections can affect the pregnancy outcome adversely [19]. TORCH infections are considered an important factor to cause abortions, congenital birth defects, disability, and infant morbidity/mortality [20]. Transmission of these infection is generally occurs during prenatal, perinatal and postnatal period through trans placental and contamination of blood or vaginal secretion [10]. Due to difficulty in clinical identification of TORCH, laboratory diagnosis helps in early identification and timely treatment to prevent poor outcomes [21].

Diagnosis of TORCH infection was done through PCR and ELISA method in the current study to improve sensitivity/specificity and to compare both methods. PCR method is considered highly sensitive but only a few laboratories have the capacity to perform molecular testing of infection [10]. Majority of studies conducted have also used serological tests for diagnosis of TORCH.

A large number of seropositive individuals in this study suggests that tribal Indian women are highly susceptible to TORCH infections. Toxoplasmosis is an environmental condition attributed to poor personal hygiene, poor sanitation, eating patterns, low level of education, and socioeconomic status [22-24]. We found prevalence of toxoplasma IgG (76.47%) which is higher than reported by previous literature. Studies conducted in different parts of India found variations from 9.73 - 38.03% for IgG [8,19] and 0.7 - 19.4% for IgM toxoplasmosis [5,8,12]. Toxoplasma sero-prevalence vary among and within the countries and young pregnant women are at higher risk of primary infection of the same [25]. High seroprevalence in current study population may be explained by poor personal hygiene and environmental sanitation as more than 30% do not have access to toilet. Living in inadequate housing may also contribute along with close contact with animals and consumption/handling of raw agriculture produce. Interestingly molecular prevalence of Toxoplasma is highest at more than 39%.

The seroprevalence of IgG for HSV was 93.90%, whereas other studies in India reported a seroprevalence of 10.49 - 61.00% for IgG [19,26]. On the other hand, our findings for IgM HSV (4.00%) are in line with the literature which reports 1.56 - 30.1% seroprevalence [27,28]. Transmission of HSV is considered through sexual contact at early age [29,30]. Our study population is very young with minimum age of 17 years and average of 24 years which indicates early sexual debut. This may be reason for high prevalence of HSV as molecular prevalence was also 38%.

Our study revealed Cytomegalovirus-CMV seroprevalence of IgG 92.90% and IgM 2.66%, similar to the reported range between 22.22 - 92.00% for IgG [19,26] and 0.4 - 34.7% for IgM [3,5,31]. As with toxoplasmosis and HSV, CMV is also known to vary according to demographics, socioeconomic status, and women are more susceptible to sexual transmission of CMV [32]. Evidence reported infection acquired during first trimester have a negative impact on child's central nervous system [32]. Molecular prevalence of CMV is about 37%.

Likewise, a high prevalence of rubella IgG (90.57%) was observed in the present study and other published studies have reported prevalence ranged from 38.88 - 84.00% [19,26]. Rubella IgM (1.55%) shows the similar seroprevalence with other studies (0.5% - 17.8%) carried out in different regions of India [8,27]. Furthermore, rubella was found to be associated with poor birth outcomes such as miscarriage, fetal death, or congenital birth defects [33]. About 30 - 40% of women are known to be susceptible to rubella infection in India [30].

Hepatitis B virus antigen was found in about 3% of study participants but molecular prevalence is more than 27%. Literature suggests 1.3 to 2.9% seroprevalence in blood donors of India [34-37]. Globally, mother to fetus HBV transmission accounts for about 21% of total HBV-related deaths. In India not many studies are available but studies in Africa indicate the relatively high HBsAg seroprevalence in pregnant women, irrespective of age, parity, gestational age, residence, high risk factors such as blood transfusion history. In Ghana the HBsAg prevalence is 16% while in Nigeria HBsAg prevalence among pregnant women is about 8% [38,39].

Unfortunately, screening of all pregnant women for TORCH is not feasible for many developing countries in the current situation but present study suggests the need to establish national level screening program for TORCH for pregnant women to prevent adverse birth outcomes to improve child health indicators. It has been indicated that understanding the epidemiology of TORCH infections is essential to develop strategies for the prevention of poor birth outcomes [23]. Therefore, it is recommended that primary prevention could be achieved through proper educational counselling of pregnant women in terms of maintaining and following WASH practices during and post-pregnancy. Secondly, to ensure the vaccination for all, especially in marginalized population such as tribal women is need of the hour.

Interesting finding of the current study is high molecular prevalence and low active infection-low IgM positivity in the context of more than 74 to 93% of study participants having evidence of past infection of TORCH. This indicates presence of viral DNA-latent infection in majority of pregnant women despite antibodies development. This finding also indicates possibility of reinfection as pregnancy is immunosuppressive condition. There is a need for further research including measuring viral load in mothers that show presence of viral DNA, to predict possibility of reinfection and/or adverse birth outcomes including congenital anomalies.

Current study addresses important research gaps in understanding of epidemiology of TORCH in India and suggests use of molecular prevalence for better diagnosis and prediction of adverse birth outcomes for TORCH infections in pregnant mothers.

Strength and Limitation

The strength of the study lies in the prospective nature of this study as the study participants from the tribal area were followed throughout the study period. Lack of information on the PCR results in previous studies, makes it difficult to compare the findings of our study. Limitation of the study is collection of sample only once in the pregnancy and majority of our participants were in 2nd trimester when enrolled in the study. However, use of PCR helped us to overcome this limitation as detection of DNA of the organism indicates latent or active infection. Study findings demonstrate TORCH infection as a public health problem and should be included as a part of routine ANC checkup to increase women's awareness along with proper management of positive cases. This study provides evidence base for future policy and program reforms in improving maternal and child health practices.

Conclusion

Maternal TORCH infections have been known to cause adverse birth outcomes including abortions, preterm, low birth weight, congenital malformation and future morbidity in the child. Despite established connection with poor birth outcomes, India does not have universal screening for TORCH infections in pregnant mothers. High molecular and seroprevalence indicative of past infection of TORCH among study participants in the present study highlights the need to take measures to diagnose these infections early and prevent/treat them. Inclusion of molecular diagnostic methods for TORCH would improve management of these infections and enhance prediction of adverse birth outcomes in the positive mothers. India has been striving to improve child outcomes for decades, inclusion of modern diagnostic techniques such as PCR in routine maternal health care is need of the hour to achieve child health improvement goals.

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Conflict of Interest

None.

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