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Status of Torch Infections in Women of Child Bearing Age Group in Uttar Pradesh

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Abstract:

Purpose: *The present study was conducted to estimate the seroprevalence of Toxoplasma, Rubella, Cytomegalovirus, Herpes Simplex Virus (TORCH) infections among the pregnant females of <22 weeks of period of gestation with Bad Obstetric History(BOH) in Uttar Pradesh. Material &*

Method: *Over a period of one year, 100 patients blood samples were collected after screening of 2000 pregnant females of <22 weeks of period of gestation having BOH. Serum was separated from blood by centrifugation. All samples were examined by ELISA for the presence of TORCH antibodies IgM and IgG.*

Results: *Out of the 100 blood samples screened, 75 (75%) cases were seropositive for (TORCH) Toxoplasma, Rubella, CMV and HSV alone or in combination. Out of 75 seropositive cases, 44 (58.66%) were positive for any one of the components (Toxoplasma, Rubella, Cytomegalovirus or Herpes simplex virus), 20 (26.67%) were positive for any two components (Toxoplasma with Rubella, Toxoplasma with Cytomegalovirus, Toxoplasma with Herpes simplex virus, Rubella with Cytomegalovirus, Rubella with Herpes simplex virus or Cytomegalovirus with Herpes simplex virus). 9 (12%) cases were positive for any three components (Toxoplasma with Rubella & Cytomegalovirus, Toxoplasma with Rubella & Herpes simplex virus, Toxoplasma with Cytomegalovirus & Herpes simplex virus, Rubella with Cytomegalovirus & Herpes simplex virus. Whereas 2 (2.67%) cases were positive for all four components of TORCH (Toxoplasma, Rubella, Cytomegalovirus & Herpes simplex virus). Among 44 cases which were positive for any one component of TORCH, there was Toxoplasma in 3 cases (6.81%), Rubella in 2 cases (4.55%), CMV in 20 cases (45.45%) and HSV in 19 cases (43.19%). IgM positivity for Toxoplasma was 16.67%, for Rubella was 7.14%, for CMV was 68.75% and for HSV were 2.22% of their respective values.*

Conclusion: *This study shows that there is a very strong association of TORCH agents as a potential cause of BOH. Hence screening and early diagnosis for TORCH Infections in women can help in proper management of these cases and prevent dreadful outcomes and pregnancy wastage. Rubella cases were 14 in our study, so incorporation of rubella immunization into the national immunization schedule, and to look into proper patient compliance is recommended.*

Keywords: ***Seroprevalence, TORCH infection, BOH***

Introduction

Bad obstetrics history (BOH) implies previous unfavourable foetal outcome in terms of two or more consecutive spontaneous abortions, history of intrauterine growth retardation, stillbirths, early neonatal deaths and/or congenital anomalies.[34] Causes of BOH include genetic causes, hormonal, abnormal, maternal immune response and maternal infections.[20] Maternal infections play a critical role in pregnancy wastage and they occur in patients with bad obstetric history.[22] Infections acquired in utero during gestation period or during the birth process are significant cause of foetal and neonatal mortality. TORCH complex (Toxoplasma, Rubella, Cytomegalovirus, Herpes Simplex Virus) are important contributor of infantile and childhood morbidity & mortality. Infections by TORCH agents in women are usually asymptomatic and chronic. It is well recognized that at least 12-15% of all conceptions end in miscarriage, and pre-clinical pregnancy loss is around 22-30% due to the TORCH infections.[24]

The degree of severity of infection depends upon gestational age of the foetus when infected, the virulence of the organism, the damage to the placenta and the severity of maternal disease. Usually this infections in mothers are inapparent or asymptomatic hence difficult to diagnose clinically.[9] Therefore it is important to screen pregnant

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ladies during first trimester of pregnancy for TORCH infection especially in those who have Bad Obstetric History (BOH) in earlier pregnancy.

By screening we can make early diagnosis & can take appropriate measure to limit the patient's suffering.

Material and Methods:

Present study is a prospective cross sectional study, which comprises of 100 blood samples taken from females with BOH in OPD and IPD of Obstetrics and Gynecology Department of Era's Lucknow Medical College and Hospital and CSMMU, Lucknow after proper history taking and thorough physical examination, over a period of one year. We screened all 100 blood samples of mothers having BOH with help of ELISA technique using Orgenium laboratories TORCH ELISA kit of Finland. In the inclusion criteria we took all the antenatal cases aged between 18-40 years of less than 22 weeks of gestational age with (BOH) Bad Obstetric History i.e. two or more recurrent spontaneous abortions, still birth, intra uterine death [IUD], Intra Uterine Growth Retardation (IUGR) and Congenital anomalies in new born like (Microcephaly, Hydrocephalus, GIT anomalies, Non Immunogenic Hydrops Fetalis) including dropouts. Exclusion criteria included any structural anomalies of uterus and cervix, pregnancy with history of Diabetes Mellitus, Hypertension, Chronic Liver Disease, history of intake of anticoagulant drugs, anti-epileptics, anticancer, antiretroviral therapy in present pregnancy and patients with reactive VDRL/ RPR titer > 1:8.[12,22,34]

The selected patients were explained the purpose and the relevance of the study. Those willing to volunteer were included in the study after informed and written consent. Five ml whole venous blood sample of the recruited subjects were drawn in syringes and collected in plain vial taking all aseptic precautions. Samples were then sent to Department of Microbiology for estimation of Serum IgM and IgG levels by ELISA test. Samples taken were kept in plain vial at room temperature before sending it to the laboratory. The blood was centrifuged at 3000 rpm for 5 minutes and the serum was separated and stored in 2 different aliquots at -20^{0}C until tested. The serum IgG and IgM was estimated by ELISA technique of Orgenium Laboratories' TORCH Antibody EIA Test Kit Finland. The tests were performed according to manufactures instructions. Optical Density (OD) was read at 450 nm on an ELISA reader. All the samples showing reading above cut off value were considered to have significant antibody titre to Toxoplasma, Rubella, CMV and HSV.[2,4,5,11,15,21,23,25,30,33]

The avidity test was done for those samples which had shown both IgM and IgG positivity for Toxoplasma. This was done to differentiate between recent and past infection as mere presence of IgM antibodies is inconclusive for detection of recent infected cases.

Results

Out of 100 cases of BOH, 25 were found to be non-TORCH, which included hormonal causes in 13 cases, genetic causes in 9 cases & unidentified causes in 3 cases. When segregation of TORCH cases according to age was done, a striking result became evident that BOH cases increased with increasing age as shown here. Only 18.67% cases of TORCH were up to 25 years age group. 73.33 % cases of TORCH were present between >25 to < 36 year age group and only 8% cases of TORCH were present in age group of 36 years or more. Percentage shows less frequency of BOH cases in >36 years; but when compared to the no. of pregnant cases above 36 years age the ratio of BOH/ Pregnant cases is worse than what is present among >25-<36 years age group. It is to be noted that the females participating in present study were between 19-40 years (mean age 29 years 6 months).

In present study out of total of 75 TORCH positive cases 44 cases (58.66%) were suffering from single infection in which CMV or HSV were found to cause most of the Uni-infections whereas Toxoplasma or Rubella were less than 10% in single infection cases. About 20 cases (26.67%) out of 75 were suffering from any two components of TORCH. Again combination of CMV & HSV were found to be present in about 70% cases, whereas Rubella & CMV were present in 20% cases; Toxoplasma & HSV in 10% cases. No other two infection combination was present in the study. About 9 cases (12%) out of 75 cases were found to be suffering from a more complex tri infection, where Rubella + CMV + HSV were present in 45% cases. Toxoplasma + CMV + HSV present in 33.3% cases, Toxoplasma + Rubella + CMV and Toxoplasma + Rubella + HSV present in 11% cases each. Only Two out of 75 cases were found to have even complex illness, when all four TORCH components were compared (Figure 1 & 2).

As far as correlation between Socioeconomic status and TORCH cases are concerned Middle class (72%) are found to be more affected than Lower class (26.67%) and Upper class (1.33%). For the socioeconomic scale we have referred to the Kuppuswamy's scale. As far as the gravida was concerned, about 42.67% cases of TORCH were bigravida; about 25.33% cases were trigravida and 32% cases were multigravida.

Out of total 75 TORCH cases 65.33% were living in urban setup, whereas 34.67% lived in rural areas. But this does not signify that BOH is more common in urban areas. It is found to be more prevalent in non- vegetarians (57.33%), rather than vegetarians (42.67%).

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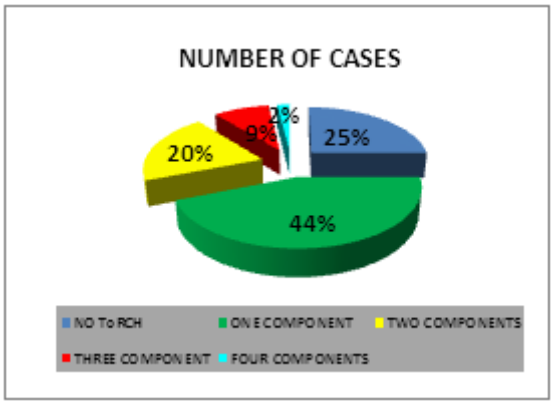

Figure 1: Percentage distribution of BOH cases with or without TORCH infection.

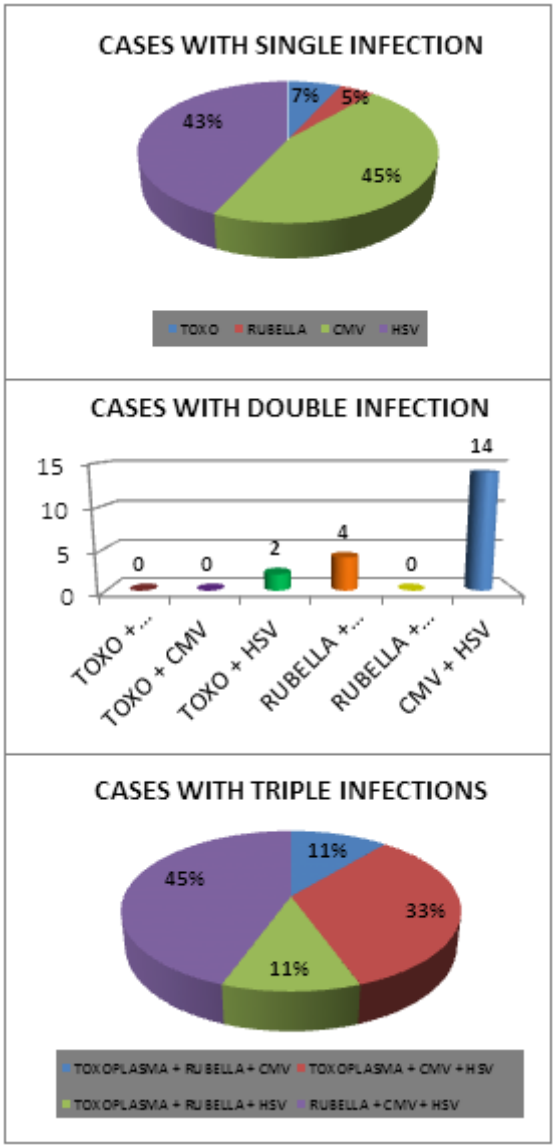

Figure 2: Percentage distribution of TORCH cases with one, two or three components of TORCH in various combinations.

Discussion

Toxoplasma, Rubella, CMV and HSV are known to cause infection in utero and are mostly responsible for abortions, still birth, premature delivery and congenital malformation. There is considerable variation in the prevalence of these agents among the women of child bearing age in different geographical area.

In present study, CMV (48%) is found to be the most prevalent cause for BOH. (Figure 3) The finding of several other studies showed the prevalence of CMV to be 22.66%,[27] 29.5%, [28] 86.0%,[8] 87.4%.[29] (Table 1). Many children died of spontaneous abortion/ intrauterine death. Those who lived had hearing defects, mental retardation and visual disturbances for their whole life.

It was followed by HSV (45%) including both HSV1 & HSV2. (Figure 3) The finding of several other studies showed the prevalence of HSV to be 24.0%,[1] 32.3%,[17] 69.0%,[6] 79-81% (≈ 80%).[31] (Table 1). Infants died of multiple organ involvement, encephalitis and skin involvements.

To a minor extent Rubella (14%) was involved. (Figure 3) The finding of few other studies showed the prevalence of Rubella as 10.38%,[14] 17.9%,[13] 17.5%,[28] and 26.8%[32] (Table 1). Babies were affected having deafness, mental retardation, multi organ involvement and bleeding disorders.

Toxoplasma (12%) also played a role in leading to BOH of females. (Figure 3) The finding of several other studies showed the prevalence of Toxoplasma to be 11.6%,[13] 13.1%,[35] 13-15% (≈14%),[31] and 17%.[10] (Table 1). The babies suffered from neurological and visual disturbances and later some even succumbed to death.

If we consider only IgM into discussion, then this pattern goes further in favour of CMV (33%). It shows acute infection that is quite dangerous for the foetus intrauterine which is supported by similar pattern of IgM positivity reported by other studies like 18.27% IgM,[26] 22.6% IgM.[27]

Toxoplasma 2% IgM was reported in our study. Similarly another study reported only 2 cases of Toxoplasma IgM.[16] A percentage of 7.8% IgM,[18] IgM 7%[3] was reported by other studies. Such wide difference in numbers is due to large number of population studied in different studies as compared to our study in which 100 patients were screened due to limited resources.

HSV in present study was reported to be 1%. Similarly 32.3% IgM[17] and 24% IgM prevalence[1] was given by other researchers. Rubella was reported to be 1% in our study similar to a study conducted by Ballal M et al 2007 who reported 4.49% IgM positive cases.

A different picture arises in case of IgG seroprevalence depicting chronic infection where HSV (44%) proceeds over CMV (15%), Rubella (13%) and Toxoplasma (10%).

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Overall in the present study, Toxoplasma antibodies were found to be in 12% of cases (IgG 10%; IgM 2%), while other workers have reported it to be 13.1%,[35] 34.5%[19] and 42.5%.[28]

There were 2 cases (2%) of Toxoplasma showing IgM positivity. In both cases IgG was also positive. So Toxoplasma IgG avidity test was performed and it was found to be low IgG avidity (Avidity Index = 0.15) in one case whereas high IgG avidity (Avidity Index = 0.35) in another case. Hence it indicates the need of early detection and treatment of any congenital anomaly in the case of low IgG avidity and sparing the other IgM positive case having high IgG avidity from unnecessary use of antibiotics as well as meticulous foetal screenings for abnormalities.

Detection and timely treatment of such infections can prevent mortality and morbidity of the infants born to such mothers. In the present study, antibodies to rubella was found to be present in 14% cases(IgG 13%; IgM 1%), while in other studies it was reported to be 6.5%,[35] 10.38%,[14] 17.5%,[28] and 26.8%[32] respectively. In case of CMV, antibodies were found in 48% cases (IgG 15%; IgM 33%), whereas in other studies it is reported to be 22.66,[27] 29.5%[28] and 86%[8] respectively. In case of HSV seropositivity was found in 45% cases (IgG 44%; IgM 1%), while other studies showed seroprevalence of 17.6%[1] and 32.3%.[17] Thirty one patients were found to have antibodies to more than one agent indicating ploymicrobial infectious aetiology. Out of these 31 patients, 20 patients were found to be seropositive for any two components of TORCH, 9 patients were found to be seropositive for any three out of four components of TORCH and only 2 patients were found to be seropositive for all four components of TORCH. Similar studies, supporting mixed infectious aetiology has been done.[13,19] The present study shows a close association between BOH and TORCH, as TORCH being the most prevalent cause of BOH. Among TORCH, CMV is the most prevalent cause followed by HSV, Rubella and Toxoplasma.

Hence in all the ante natal cases, a detailed history and examination must be carried out to rule out any indication for BOH and in case of even minor suspicion about BOH, a sero-analysis of TORCH agents is must to help in proper management of such cases and to avoid dreaded pregnancy outcomes. This study also emphasizes upon the need for immunization in prospective mothers and adolescent girls who have not received MMR vaccine in their childhood to prevent rubella infection and its treacherous outcomes and similar emphasis over immunisation was given by other studies as well.[12]

Table 1: Comparison of studies showing seroprevalence of TORCH infections

Studies showing seroprevalence of Toxoplasmosis		**Studies showing seroprevalence of Cytomegalovirus**	
Name of Authors	Result (in percentage)	Name of Authors	Result (in percentage)
Present study	12.0	Present study	48.0
Kaur R et al	11.6	Sharma A et al	22.66
Yashodhara P et al	13.1	Chopra S et al	29.5
Taechowisan et al	14.0	Condorelli F et al	86.0
Eurico C et al	17.0	Sheevani et al	87.4
Studies showing seroprevalence of Rubella		**Studies showing seroprevalence of Herpes simplex Virus**	
Name of Authors	Result (in percentage)	Name of Authors	Result (in percentage)
Present study	14.0	Present study	45.0
Kishore J et al	10.38	MJW Van de Lar et al	32.3
Chopra S et al	17.5	Agarwal A et al	24.0
Gunner H et al	17.9	Canessa A et al	69.0
Turbadkar D et al	26.8	Taechowisan et al	80.0

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