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RESEARCH ARTICLE

"STUDY OF SEROPOSITIVITY FOR TORCH INFECTIONS IN WOMEN WITH BAD OBSTETRIC HISTORY"

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Abstract

Background: Pregnancy loss has been attributed to several factors involved in human reproduction. The prenatal and perinatal infections, falling under the designation of TORCH complex is a medical acronym for a set of perinatal infections. Infections caused by TORCH are the major causes of BOH. Identification of positive titer of IgG and IgM during pregnancy in women with previous negative titers of TORCH antibodies suggests a proliferative disease condition dangerous to the fetus and is more likely to cause a miscarriage or serious birth defects.

Aims and Objectives: To evaluate the incidence of TORCH infections in women having history of previous pregnancy loss and women with high delivery risk factors (HDRF) in Ahmedabad city.

Materials and Methods: A prospective study was done from July 2012 to June 2014, in Ahmedabad city of Gujarat state. A total of 150 women with HDRF were included in the study depending on previous unfavorable fetal outcome in terms of two or more consecutive spontaneous abortion, history of IUD, IUGR, preterm labor, still births, early neonatal death and/or congenital anomalies, in the age group of 19-35 years.

Results: Majority of BOH cases [79 (52.7%)] were found in females aged 25-30 years. Out of 150 BOH cases [90(60.0%)] were serologically positive for one of the TORCH infections. Majority of seropositivity cases [49 (32.6%)] were found in females aged 25-30 years. In BOH cases the seropositivity for toxoplasma gondii was 25.3%, CMV 14.6%, HSV 10.6%, and rubella virus 9.3%. In 25-30 years age group, seropositivity rate were 52.7%, 57.1%, 45.5% and 68.7% for toxoplasma, rubella, CMV and HSV respectively.

Conclusion: The present study demonstrates a strong association between the TORCH infectious agents and women having BOH. All the patients with previous history of recurrent pregnancy miscarriage should be subjected to TORCH screening. All antenatal cases with BOH, should be routinely screened for TORCH agents as early diagnosis to reduce adverse fetal outcome, diminishing the morbidity and mortality.

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INTRODUCTION

Bad obstetric history (BOH) implies previous unfavorable fetal outcome in terms of two or more consecutive spontaneous abortions, early neonatal deaths, stillbirths, intrauterine fetal deaths, intrauterine growth retardations

and congenital anomalies.[1]The causes of BOH may be genetic, hormonal, abnormal maternal immune response, and maternal infection.[2]

Pregnancy loss has been attributed to several factors involved in human reproduction. Genetic and uterine abnormalities, endocrine and immunological dysfunctions, infectious agents, environmental pollutants, psychogenetic factors and endometriosis are most important causes of spontaneous abortion.[3]

The prenatal and perinatal infections, falling under the designation of TORCH complex [4] (also known as STORCH, TORCHES, or the TORCH infections), are a medical acronym for a set of perinatal infections [5], i.e., infections that are passed from a pregnant woman to her fetus. Infections caused by TORCH (Toxoplasma gondii, Rubella virus, Cytomegalovirus (CMV), Herpes simplex virus (HSV), and others agents like Chlamydia trachomatis, Treponema pallidum, Neisseria gonorrhea, HIV, etc. are the major causes of BOH.[1,2]

The TORCH infections are a group of viral, bacterial, and protozoan infections that gain access to the fetal bloodstream transplacentally via the chorionic villi. Hematogenous transmission may occur at any time during gestation or occasionally at the time of delivery via maternal-to-fetal transfusion.[6] These pathogens usually cause only asymptomatic or mild infection in mother, but can cause much more serious consequences in fetus.[7]

Many sensitive and specific tests are available for serological diagnosis of TORCH complex. ELISA for IgM antibodies against these infections is highly sensitive and specific.[8] TORCH tests measured the presence of antibodies against a specific group of infectious diseases and their level of concentration in the blood.

The prevalence of TORCH infections varies from one geographical area to another. However, countries of the Southeast Asia and Sub-Saharan Africa are reported to have the highest figures of stillbirths.[9]

Toxoplasma: Most of the information on toxoplasmosis in India is on pregnancy wastage. Toxoplasma is a parasitic infectious disease caused by a protozoan Toxoplasma Gondii, which is transmitted to humans through the infection of food or water contaminated with cat faces or eating undercooked meat of the infected sheep, goat, cow, or pig and other avian species. The infection is carried to the infant through the mother's placenta, and can cause infections of the eyes or central nervous system. Identification of positive titer of immunoglobulin G (IgG) and immunoglobulin M (IgM) during pregnancy in women with previous negative titers of antitoxoplamsa IgG antibodies suggests a proliferative disease condition dangerous to the fetus and is more likely to cause a miscarriage or serious birth defects.[10]

Rubella: Rubella is caused by RNA virus of paramyxovirus group. It spreads mainly through family. Approximately 30%–50% fetuses of women who contact with Rubella during the first 3 months of pregnancy will be adversely affected by the virus. The Rubella virus readily invades the placenta and fetus during gestation.[11] In the case of Rubella, a woman in the first 2 or 3 months of pregnancy who is exposed may develop the infection and give birth to child with serious congenital defects such as deafness and blindness.[12]

Cytomegalovirus (CMV): This infection is caused by DNA virus of herpes group. The common modes of infection are through saliva (kissing), urine, stool, breast milk, and unscreened blood transmission. Cytomegalovirus is a leading cause of congenital infections and long-term neurodevelopmental disabilities among children. High maternal sero-prevalence rates have been consistently associated with high congenital infection rates. Primary CMV infection in the mother results in a substantially higher risk of congenital CMV infection in the newborn (30%–40% risk) when compared with maternal CMV reactivation infection (1%–3% risk in the newborn).[13] Fetal damage is more likely to be severe when maternal infection occurs early in pregnancy.[14]

Herpes simplex virus (HSV): It is a DNA virus of the same group as CMV. Infection in the neonate is commonly acquired by contact with the mother's infected birth canal. Incubation period for herpes virus is between 4 and 21 days.[15] Primary infection of HSV enters a latent state in the nerve ganglia and may emerge later to cause recurrent active infection.[16] Latency in nervous tissue is caused by HSV-I.[17] Neonatal HSV infection is usually acquired at birth, although a few infants have had findings suggestive of intrauterine infection.

MATERIALS AND METHODS

A prospective study was done from July 2012 to June 2014, on patients who had attended to the private antenatal clinic in Ahmedabad city of Gujarat state. A total of 150 women with high delivery risk factors (HDRF) were included in the study depending on previous unfavorable fetal outcome in terms of two or more consecutive spontaneous abortion, history of intrauterine fetal death, intrauterine growth retardation, preterm labor, still births,

early neonatal death and/or congenital anomalies, in the age group of 19-35 years. Women with known case of hypertension, diabetes mellitus, eclampsia of pregnancy, and Rh incompatibility were excluded from the study.

The approval of the institute's ethical committee was obtained prior to the study. Informed written consent was obtained from all the participants. Detailed clinical history, physical examination, and conventional laboratory investigations were conducted. A preformatted questionnaire, including the socio-economic status, was completed during the antenatal follow-up period from gestation to birth. Delivery outcome was recorded for cases with reference to the gestational age and mode of delivery.

From each woman 3 ml of venous blood was collected in a container with strict aseptic precautions and was allowed to clot and centrifuged at 3000rpm for 5min. The serum was used for serological evaluation for IgM and IgG antibodies for TORCH infections according to manufacturer's instructions using ELISA techniques.[18] The tests were done as per the directions given in the manual supplied along with the kits. The optical density (OD) was read at 450 nm on the ELISA reader [Mindray MR-96A, Microreader].

TORCH index of each determination was calculated by dividing the value of each sample by calibrator values. The sero-titers were interpreted as Non-reactive (<0.9), Equivocal (0.9-1.1) and Reactive (>1.1) as per the literature supplied along with the kits.[19,20,21] Results are presented as positive, equivocal or negative for the antibody titer, indicating the presence or absence of IgG and IgM antibodies for each of the infectious agents tested with the panel. Presence of IgM antibodies indicates either a current or recent infection.

RESULTS:

Table : 1 : Number of cases having BOH in various age groups.

Sr. No.	Type of BOH	Different Age Groups			Total No. (%)
		19-24 Yrs	25-30 Yrs	31-35 Yrs	
		No. (%)	No. (%)	No. (%)	
1.	Sp. Abortion	29 (19.3)	45 (30.0)	12 (8.0)	86 (57.3)
2.	IUGR	2 (1.3)	4 (2.7)	1 (0.7)	7 (4.7)
3.	IUD	8 (5.3)	14 (9.3)	2 (1.3)	24 (16.0)
4.	Preterm Labor	5 (3.3)	7 (4.7)	2 (1.3)	14 (9.3)
5.	SB/END	4 (2.7)	5 (3.3)	2 (1.3)	11 (7.3)
6.	CM	3 (2.0)	4 (2.7)	1 (0.7)	8 (5.3)
	Total	51 (34.0)	79 (52.7)	20 (13.3)	150 (100)

The history of the 150 BOH cases consisted of spontaneous abortion in 86 (57.3%), intrauterine growth retardation in 7 (4.7%), intrauterine death in 24 (16.0%), premature labor in 14 (9.3%), still birth or early neonatal death in 11 (7.3%), and congenital malformation in 8 (5.3%).

This table shows the age specific distribution and clinical presentation of 150 BOH cases. Majority of BOH cases [79 (52.7%)] were found in females aged 25-30 years followed by [51 (34.0%)] in 19-24 years and [20 (13.3%)] in 31-35 years.

Table : 2 : Different age group wise seropositivity of TORCH agents.

Sr. No.	TORCH Agent	Different Age Groups			Total No. (%)
		19-24 Yrs	25-30 Yrs	31-35 Yrs	
		No. (%)	No. (%)	No. (%)	
1.	Toxoplasma	14 (9.3)	20 (13.3)	4 (2.6)	38 (25.3)
2.	Rubella	5 (3.3)	8 (5.3)	1 (0.7)	14 (9.3)
3.	CMV	9 (6.0)	10 (6.6)	3 (2.0)	22 (14.6)
4.	HSV	5 (3.3)	11 (7.3)	0	16 (10.6)
	Total	33 (22.0)	49 (32.6)	8 (5.3)	90 (60.0)

Out of 150 BOH cases 90(60.0%) were serologically positive for one of the TORCH infections. Majority of seropositivity cases [49 (32.6%)] were found in females aged 25-30 years followed by [33 (22.0%)] in 19-24 years and [8 (5.3%)] in 31-35 years. In BOH cases the seropositivity for toxoplasma gondii was 25.3%, CMV 14.6%, HSV 10.6%, and rubella virus 9.3%.

Table : 3 : IgG and IgM seropositivity and seronegativity of TORCH agents.

Sr. No.	TORCH Agent	Age Group	IgG No. (%)		IgM No. (%)		All +ve
			+ve	-ve	+ve	-ve	
1.	Toxoplasma	19-24	9 (33.3)	42 (34.1)	5 (45.5)	46 (33.1)	14 (36.8)
		25-30	15 (55.6)	64 (52.0)	5 (45.5)	74 (53.2)	20 (52.7)
		31-35	3 (11.1)	17 (13.8)	1 (9.0)	19 (13.7)	4 (10.5)
		Total	27 (18.0)	123 (82.0)	11 (0.7)	139 (99.3)	38 (100)
2.	Rubella	19-24	4 (40.0)	47 (33.6)	1 (25.0)	50 (34.3)	5 (35.7)
		25-30	5 (50.0)	74 (52.8)	3 (75.0)	76 (52.0)	8 (57.1)
		31-35	1 (10.0)	19 (13.6)	0	20 (13.7)	1 (7.2)
		Total	10 (6.7)	140 (93.3)	4 (2.7)	146 (97.3)	14 (100)
		19-24	6 (37.5)	45 (33.6)	3 (50.0)	48 (33.3)	9 (40.9)

3.	CMV	25-30	7 (43.7)	72 (53.7)	3 (50.0)	76 (52.8)	10 (45.5)
		31-35	3 (18.8)	17 (12.7)	0	20 (13.9)	3 (13.6)
		Total	16 (10.7)	134 (89.3)	6 (4.0)	144 (96.0)	22 (100)
4.	HSV	19-24	1 (20.0)	50 (34.5)	4 (36.4)	47 (33.8)	5 (31.3)
		25-30	4 (80.0)	75 (51.7)	7 (63.6)	72 (51.8)	11 (68.7)
		31-35	0	20 (13.8)	0	20 (14.4)	0
		Total	5 (3.3)	145 (96.7)	11 (7.3)	139 (92.7)	16 (100)

Most of the seropositive case of both IgG and IgM antibodies are observed in 25-30 years age group followed by 19-24 years age group. In 25-30 years age group, seropositivity rate were 52.7%, 57.1%, 45.5% and 68.7% for toxoplasma, rubella, CMV and HSV respectively. In 19-24 years age group, seropositivity rate were 36.8%, 35.7%, 40.9% and 31.3% for toxoplasma, rubella, CMV and HSV respectively. Out of total 90 seropositive cases, 38 cases were toxoplasma positive, 14 cases were rubella positive, 22 cases were CMV positive and 16 cases were HSV positive.

Table : 4 : TORCH agents seropositivity with different cases having BOH.

Sr. No.	Types of BOH (n=150)	Toxo +ve	Rubella +ve	CMV +ve	HSV +ve	Total
1.	Sp. Abortion (n=86)	22 (43.1)	6 (11.7)	11 (21.5)	12 (23.5)	51 (63.7)
2.	IUGR (n=7)	1 (33.3)	1 (33.3)	0	1 (33.3)	3 (3.7)
3.	IUD (n=24)	6 (42.8)	3 (21.4)	2 (14.3)	3 (21.4)	14 (17.5)
4.	Preterm Labor (n=14)	3 (50.0)	1 (16.7)	1 (16.7)	1 (16.7)	6 (7.5)
5.	SB/END (n=11)	2 (50.0)	0	1 (25.0)	1 (25.0)	4 (5.0)
6.	CM (n=8)	1 (50.0)	0	1 (50.0)	0	2 (2.5)
	Total	35 (43.7)	11 (13.7)	16 (20.0)	18 (22.5)	80 (100)

The highest seropositivity in cases of repeated abortions was seen with Toxoplasmagondii 43.1% followed by HSV 23.5% and CMV 21.5%. In intrauterine growth retardation, toxoplasma, rubella and HSV show equal

seropositivity 33.3% each. In intrauterine death and preterm labor toxoplasma showed highest seropositivity of 42.8% and 50.0% respectively. In still birth or early neonatal death cases, toxoplasma, rubella and HSV showed seropositivity of 50.0%, 25.0% and 25.0% respectively. In congenital malformation seropositivity with toxoplasma and CMV both show equal seropositivity of 50.0% each..

Table : 5 : Obstetric outcome of patients with TORCH infection.

Obstetric Outcome	IgG No. (%)		IgM No. (%)	
	Positive	Negative	Positive	Negative
(A) Toxoplasma				
Full Term (n=78)	14 (9.3)	64 (74.4)	5 (3.33)	73 (48.7)
Preterm (n=22)	6 (4.0)	16 (10.7)	2 (1.33)	20 (13.3)
LSCS (n=34)	4 (2.7)	30 (20.0)	3 (2.0)	31 (20.7)
Still Birth (n=4)	2 (1.33)	2 (1.33)	0	4 (2.7)
Sp. Abortion (n=12)	1 (0.7)	11 (7.33)	1 (0.7)	11 (7.33)
(B) Rubella				
Full Term (n=78)	6 (4.0)	72 (48.0)	2 (1.33)	76 (50.7)
Preterm (n=22)	1 (0.7)	21 (14.0)	1 (0.7)	21 (14.0)
LSCS (n=34)	1 (0.7)	33 (22.0)	0	34 (22.7)
Still Birth (n=4)	1 (0.7)	3 (2.0)	0	4 (2.7)
Sp. Abortion (n=12)	0	12 (8.0)	1 (0.7)	12 (8.0)
(C) CMV				
Full Term (n=78)	9 (6.0)	69 (46.0)	4 (2.7)	74 (49.3)
Preterm (n=22)	2 (1.33)	20 (13.3)	1 (0.7)	21 (14.0)
LSCS (n=34)	3 (2.0)	31 (20.7)	1 (0.7)	33 (22.0)
Still Birth (n=4)	0	4 (2.7)	0	4 (2.7)
Sp. Abortion (n=12)	2 (1.33)	10 (6.7)	0	12 (8.0)
(D) HSV				
Full Term (n=78)	3 (2.0)	75 (50.0)	6 (4.0)	72 (48.0)
Preterm (n=22)	1 (0.7)	21 (14.0)	2 (1.33)	20 (13.3)
LSCS (n=34)	1 (0.7)	33 (22.0)	3 (2.0)	31 (20.7)

Still Birth (n=4)	0	4 (2.7)	0	4 (2.7)
Sp. Abortion (n=12)	0	12 (8.0)	0	12 (8.0)

Table : 6 : Comparative results of TORCH.

TORCH Infection	IgG No. (%)		IgM No. (%)	
	Positive	Negative	Positive	Negative
Toxoplasma	27 (18.0)	123 (82.0)	11 (7.3)	139 (92.7)
Rubella	9 (6.0)	141 (94.0)	3 (2.0)	147 (98.0)
CMV	16 (10.7)	134 (89.3)	6 (4.0)	144 (96.0)
HSV	5 (3.3)	145 (96.7)	11 (7.3)	139 (92.7)

Out of total 150 BOH cases with the TORCH antibody (IgG and IgM) titers showed the following results: In Toxoplasma, 18.0% IgG positive, 7.3% IgM positive, 82.0% IgG negative, and 92.7% IgM negative. In Rubella, 6.0% IgG positive, 2.0% IgM positive, 94.0% IgG negative, and 98.0% IgM negative. In CMV, 10.7% IgG positive, 4.0% IgM positive, 89.3% IgG negative, and 96.0% IgM negative. In HSV, 3.3% IgG positive, 7.3% IgM positive, 96.7% IgG negative, and 92.7% IgM negative.

DISCUSSION :

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 Toxoplasma 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.[22]

In the present study Toxoplasma gondii, which is a known etiological agent in recurrent pregnancy loss was found in 43.1% pregnant women with HDRF , this is similar to what has been reported earlier.[18,23] In our study the seroprevalence of Toxoplasma IgM/IgG among pregnant women with BOH was 7.3%/18.0% respectively. Sadik MS, et al. [24] and Turbadkar D, et al. [2] have also reported an incidence of 18%/6% and 10.5%/42.1% respectively. Janak K, et al. [25] reported overall IgM antibody positivity of 8.3% in 60 cases of BOH.

In our study, the seroprevalence of the BOH cases for Rubella IgM/IgG were 2.0%/6.0% respectively. Surpam RB, et al.[26] and Yasodhara, et al.[19] have also reported overall IgM antibody positivity of 4.66 and 6.5% in cases of BOH while other workers reported seropositivity ranging from 4-17.7%.[27,28]

Cytomegalovirus remains the most common cause of congenital infection in the United States. The present study shows seropositivity rate of 4.0%/10.7% for CMV IgM/IgG in women with BOH.Several studies have reported between 84.5-95% prevalence of CMV IgG among pregnant women in Turkey.[29] In other studies seropositivity ranges from 3 to 12.9%.[9,27]

Seropositivity rate of HSV IgM among the HDRF patients in our study was 10.7% similar to what has been reported in other study. While other workers reported seropositivity ranging from 4 to 17.7%.[9]The seropositivity rate for HSV IgM/IgG among BOH patients in our study was 7.3%/3.3%. Turbakar, et al. [2] and Janak k, et al. [25] reported a seropositivity rate of HSV IgM as 3.6 and 3.3%.

SUMMARY :

The present study demonstrates a strong association between the TORCH infectious agents and BOH in women especially among young aged women. ELISA method is more efficacious than any other methods in demonstrating TORCH elements antibodies .

TORCH infections are associated with recurrent abortion, intrauterine growth retardation, intrauterine death,

preterm labor, still birth, early neonatal death and congenital malformation.
It may not be possible to screen all pregnant women with BOH for TORCH as it is economically not possible, but all the patients with previous history or recurrent pregnancy miscarriage should be subjected to TORCH screening.
In cases where antibodies are positive, the patient should be advised and counseled about the adverse effect of the TORCH infection on the fetus, due to this the complications such as congenital, malformation, abortion, stillbirth, and preterm deliveries may occur, and the affected female should be counseled with her husband regarding continuation of pregnancy and treatment.
TORCH infections play a role on adversefetal outcome in current pregnancy so all antenatal cases with BOH,even if asymptomatic should be routinelyscreened for TORCH agents as early diagnosis to reduce adverse fetal outcome,diminishing the morbidity and mortality.

CONCLUSION :

All pregnant women should have their blood examined for TORCH antibodies. A previous history of pregnancy wastage and the serological reaction for TORCH infections during current pregnancy must be considered while managing BOH cases so as to reduce the adverse fetal outcome.

ABBREVIATIONS:

BOH = Bad obstetric history, HSV = Herpes simplex virus, CMV = Cytomegalo virus, IgG = Immunoglobulin G, IgM = Immunoglobulin M, HDRF = high delivery risk factors, IUGR = intrauterine growth retardation, IUD = intrauterine death, SB = still birth, END = early neonatal death, CM = congenital malformation, LSCS = lower segment cessarian section,

BIBLIOGRAPHY:

(1) Mc Cabe R, Remington JS. Toxoplasmosis: the time has come. N Engl J Med 1988;318(5):313-5.
(2) Turbadkar D, Mathur M, Rele M.Seroprevalence of torch infection in bad obstetric history. Indian Journal of Medical Microbiology 2003;21:108–10.
(3) Dicker D, Goldman JA, Levy T, Feldberg D, Ashkenazi J. Theimpact of long-term gonadotropin-releasing hormone analoguetreatment on preclinical abortion in patients with severe endometriosisundergoing in vitro fertilization-embryo transfer. Fertil. Steril. 1992;57:597-600.
(4) Nickerson, J.P., Richner, B., Santy, K., Lequin, M.H., Poretti, A., Filippi, C.G.,et al. Neuroimaging of pediatric intracranial infection, Part 2: TORCH,viral, fungal, and parasitic infections. J Neuroimaging. 2012;22(2):e42 e51.
(5) Maldonado, Y.A., Nizet, V., Klein, J.O., Remington, J.S., Wilson, C.B.Current concepts of infections of the fetus and newborn infant. In: Remington, J.S., Klein, J.O., Wilson, C.B., Nizet, V., Maldonado, Y.A. (Eds), Infectious Diseases of the Fetus and Newborn Infant, 2011; 7th Edn. Elsevier, Saunders, Philadelphia, PA. Pp. 1-23.
(6) Kumar V, Abbas AK, Fausto N, Aster J. Robbins &Cotran, Pathologic Basis of Disease (8th Edition) 2009. Philadelphia, PA: Elsevier, p. 480.
(7) Kaur, R., Gupta, N., Nair, D., Kakkar, M., Mathur, M.D. Screening for TORCH infections in pregnant women: A report from Delhi. Southeast Asian J. Trop. Med. Public Health. 1999;30(2):284-6.
(8) Malhotra V, Bhardwaj Y. Comparison of enzyme linkedimmunosorbant assay and indirect haemagglutination test inserological diagnosis of toxoplasmosis. J Communicable Dis 1991;23:154-6.
(9) Kapil A, Broor S. Primary cytomegalovirus infection in pregnant and nonpregnant women in India. Indian J Med Microbiol. 1992;10(1):53-5.
(10) Gomella, T.L. Infectious Diseases: TORCH Infections. In Neonatology: Management, Procedures, On-Call Problems, Diseases and Drugs, Norwalk, CT: Appleton &Lange .(1994).
(11) Coulter C, Wood R, Robson J. Rubella infection in pregnancy. Communicable Diseases Intelligence. 1999;23:93–6.
(12) Deorari AK, Broor S, Maitreyi RS, Agarwal D, Kumar H, Paul VK, et al. Incidence, clinical spectrum, and outcome of intrauterine infections in neonates. Journal of Tropical Pediatrics. 2000;46(3):155–9.

(13) Stagno S, Pass RF, Dworsky ME, Henderson RE, Moore EG, Walton PD, et al. Congenital cytomegalovirus infection: the relative importance of primary and recurrent maternal infection. The New England Journal of Medicine. 1982;306(16):945–9.
(14) Boppana SB, Pass RF, Britt WJ. Virus-specific antibody responses in mothers and their newborn infants with asymptomatic congenital cytomegalovirus infections. The Journal of Infectious Diseases. 1993;167(1):72–7.
(15) Fleming DT, McQuillan GM, Johnson RE, Nahmias AJ, Aral SO, Lee FK, et al. Herpes simplex virus type 2 in the Unites States, 1976–1994. The New England Journal of Medicine. 1997;337(16):1105–11.
(16) Corey L, Spear PG. Infections with herpes simplex viruses (1). The New England Journal of Medicine. 1986;314(11):686–91.
(17) Hutto C, Arvin A, Jacobs R, Steele R, Stagno S, Lyrene R, et al. Intrauterine herpes simplex virus infections. The Journal of Pediatrics. 1987;110(1):97–101.
(18) Zargar, AH.,Wani, AI. andMasoodi, SR, Laway, BA., Kakroo, DK.Seroprevalence of toxoplasmosis in women with recurrent abortion and neonatal deaths, and its treatment outcome.Ind J PatholMicrobiol. 1999;42(4):482-3
(19) Yashodhara, P., Ramlaxmi, B.A., Naidu, A.N. and Raman, L. Prevalence of specific IgM due to Toxoplasma, Rubella, Cytomegalovirus and C. trachomoatis infection during pregnancy. Indian J Med Microbiol. 2001;19(2):79-82.
(20) Sharma, P., Gupta, T., Ganguly, N.K., Mahajan, R.C. and Malla, N. Increasing Toxoplasma seropositivity in women with bad obstetric history and in new borns. Natl Med J. 1997;10:65-66.
(21) Mookherjee, N., Gogate, A. and Shah,P.K. Microbiology evaluation of women with bad obstetric history. Indian J Med Res. 1995;102:103-7.
(22) Langer H. Repeated congenital infections with toxoplasma gondii. Am J ObstetGynecol 1963;21:318-29.
(23) Yelikar, K. and Bhat, S. Maternal toxoplasmosis in repeated pregnancy loss. J ObstetGynecol India. 1996;46:29-31.
(24) Sadik MS, Fatima H, Jamil K, Patil C. Study of TORCH profile in patients with bad obstetric history. Biology and Medicine. 2012;4(2):95-101.
(25) Janak K, Richa M, Abhiruchi P, Yashodhra P. Adverse reproductive outcome induced by parvovirus B19 and TORCH infections in women with high risk pregnancy. J Infect Dev Ctries 2011;5(12):868-73.
(26) Surpam RB, Kamlakar UP, Khadse RK, Qazi MS, Jalgaonkar SV. Serological study for TORCH infections in women with bad obstetric history. J ObstetGynecol India 2006;56:41-3.
(27) Sood S, Pillai P, Raghunath C. Infection as a cause of spontaneous abortion with special reference to Toxoplasma gondii, rubella virus, CMV and Treponema pallidum. Indian J Med Microbiol 1994;12:204-07.
(28) Sharma P, Gupta T, Ganguly NK, Mahajan RC, Malla N. Increasing toxoplasma seropositivity in women with bad obstetric history and in new borns. The National Medical Journal of India 1997;10(2):65-6.
(29) Gulden ST, Devrim D, Eray C. Seroprevalence of Toxoplasma gondii, Rubella and Cytomegalovirus among pregnant women in western region of Turkey. Clin Invest Med 2009;32(1):43-7.