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ORIGINAL ARTICLE

Seroprevalence and Influence of Torch Infections in High Risk Pregnant Women: A Large Study from South India

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Abstract

Background The increased complications to the mother and fetus during or after pregnancy and birth are often caused by a wide array of pathogenic organisms mostly belonging to the TORCH group [toxoplasmosis, rubella, cytomegalovirus (CMV), and herpes simplex virus (HSV)]. These agents cause asymptomatic or mild infection in the mother while serious consequences in fetus. The present study was aimed to find significant etiological pathogens in the causation of high risk pregnancy (HRP) in South Indian population.

Material and Methods A total of 1,158 HRP women (2010–2013) from Modern Government Maternity Hospital, Hyderabad were considered. Two milliliter of blood was obtained and the serum was analyzed for IgG and IgM antibodies against TORCH agents by ELISA.

Results Twenty-five percent of the study group had fetal congenital malformation in the present pregnancy (Group 1; $N = 291$) while 75 % showed bad obstetric history (BOH) (Group 2; $N = 867$). Maternal age of $\leq$25 years, primi gravida, and consanguinity showed predisposing role for Group 1 while maternal age $\geq$30 years and $\geq$ 3 gravida were contributing risk for Group 2. The seropositvity in

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HRP women for toxoplasma, rubella, CMV, and HSV was 28, 84, 92, and 61 %, respectively for IgG while it was 6, 3, 4, and 3 % for IgG + IgM. Total seropositvity of toxoplasma, rubella, CMV, and HSV in Group 1 was 29, 97, 97, and 62 % while it was 36, 84, 97, and 65 % in Group 2, respectively.

Conclusion Maternal age of ≤25 years, primi gravida, and consanguinity contributed to fetal congenital malformation in the present pregnancy while maternal age of ≥30 years and ≥ 3 gravida towards BOH. Toxoplasma is protective while rubella and CMV are the infectious agents for HRP. Among the groups, toxoplasma and rubella conferred a predisposing risk towards Group 2 and Group 1, respectively. Sixty-one percent seropositvity of HSV in relation to bad obstetric outcome is the highest prevalence reported so far in India.

Keywords Bad obstetric history · Congenital malformations · High-risk pregnancy · IgG · IgM · TORCH infections

Background

High-risk pregnancy (HRP) is a condition where the mother or the developing fetus or both are at an increased risk for complications during or after pregnancy and birth. The TORCH agents—toxoplasmosis, rubella virus, cytomegalovirus (CMV), and herpes simplex virus (HSV)—are the most common infectious agents causing asymptomatic or mild infection in the mother but much more serious consequences in the fetus [1]. The primary infection is likely to have more serious effects on fetus than recurrent infection and may cause spontaneous abortions, intrauterine fetal death, congenital anomalies, intrauterine growth retardation, prematurity, stillbirth, and liveborn infants with the evidence of disease [2]. Infection with these agents can result in significant morbidity and mortality especially in developing countries [3].

Toxoplasmosis in human beings is caused by Toxoplasma gondii, an intracellular protozoan parasite that is transmitted through contaminated food or water and undercooked meat. The incubation period is 5–23 days after ingesting the cysts. The infected women are usually asymptomatic, and during pregnancy, she may undergo pregnancy loss, stillbirth, and intrauterine malformations in the fetus [4, 5].

Rubella infection is transmitted from person to person by tiny droplets in air and mother-to-child is through placental transfer. This disease lasts for 1–5 days and the incubation period is 2–3 weeks [6]. It usually presents mild or asymptomatic infection in children and adults. However, virus may cross the placenta and could result in miscarriage, fetal death, or an infant with serious birth defects including hearing impairment, cataracts, and cardiac defects, collectively known as congenital rubella syndrome (CRS) [7].

CMV is ubiquitous and species-specific. Human beings are the reservoir hosts for this virus, and the viruses are transmitted by direct contact with saliva, urine, and genital secretions. In pregnant women, the transmission is by direct contact with infected urine or saliva from young children or through sexual activity [8]. The incubation period of CMV infection ranges between 4 and 12 weeks. In neonates, the symptoms include intrauterine growth retardation, microcephaly with intracranial calcification, hepatosplenomegaly, jaundice, chorioretinitis, thrombocytopenic purpura, and anemia [9]. The major childhood disabilities like loss of vision, hearing, and cognitive impairment are also due to CMV infection [10].

HSV is the most common sexually transmitted viral disease (STD) worldwide. HSV1 is transmitted during childhood by non-sexual contacts, while HSV2 is always transmitted sexually and is the major cause of genital herpes [11, 12]. Incubation period of herpes ranges between 4 and 21 days. In more than 75 % of cases, primary genital HSV infection remains asymptomatic [13]. In newborns, this infection remains a major cause of morbidity and mortality [14–16]. Genital herpes infection during pregnancy may lead to spontaneous abortion, prematurity, congenital, and neonatal herpes [16, 17].

As studies on seroprevalence of TORCH agents in HRP are very meager in South Zone of India, the present study was aimed to evaluate both IgG and IgM levels on a larger sample size to find significant etiological pathogens causing abortions, stillbirths, and congenital anomalies in the causation of HRP in South Indian population.

Material and Methods

In the present study, a total of 1,158 HRP women attending the antenatal clinic of Modern Government Maternity Hospital, Hyderabad, Andhra Pradesh during 3 years (2010–2013) were enrolled. The study was approved by the institutional ethics committee and informed consent was obtained from all pregnant women prior to inclusion. The pregnant women with fetal congenital malformation in present pregnancy and pregnant women with BOH were included in the present study, while the fetal congenital malformations caused due to any injuries during pregnancy were excluded.

The study subjects were personally interviewed, counseled, and information regarding maternal age, gravida, consanguinity, religion, maternal education, maternal occupation, and family income were collected in a specially

designed proforma. Two milliliter of blood was aseptically drawn by venipuncture into a tube containing clot activator. Blood samples were then transported to Institute of Genetics and Hospital for Genetic Diseases, Hyderabad, Andhra Pradesh. They were then centrifuged and serum was separated. The levels of IgG and IgM were measured in all subjects using commercially available ELISA kits (Euroimmun, Germany), and Optical Density (OD) was measured at 450 nm in a microplate ELISA reader (Bio-Rad, USA) according to manufacturer instructions. The results were interpreted on the basis of Immune Status Ratio (ISR) index calculated by dividing the specimen OD value by the cut-off calibrator ratio. The tests were considered seropositive if ISR value is >1.11 and considered seronegative if ISR <0.9. Samples with an ISR value in between 0.9 and 1.10 were considered equivocal. According to the kit insert, the cut-off value for IgG or IgM seropositivity is >1.11 and for the present study, the samples were considered seropositive even if there was a marginal increase. Statistical analysis was performed using openepi software (http://www.openepi.com). The difference in the seropositvity was determined by χ^2 test. The risk analysis was performed by calculating Odds Ratio (OR) at 95 % CI. A two-tailed p value of <0.05 was considered to be significant.

Results

A total of 1,158 HRP women were investigated in a period of three years (2010–2013). Twenty-five percent of the study group had fetal congenital malformation in the present pregnancy while 75 % showed bad obstetric history (BOH). Further, the studied population was categorized into 2 groups:pregnant women with fetal congenital malformation in the present pregnancy (Group 1; $N = 291$) and pregnant women with BOH such as repeated abortions/intrauterine death/fetal congenital malformation/early neonatal deaths/preterm labor (Group 2; $N = 867$).

When demographic characteristics were taken into consideration, maternal age of ≤25 years, primigravida, and consanguinity showed a predisposing role for Group 1, while maternal age ≥30 years and ≥3 gravida were contributing for Group 2 ($p < 0.05$) (Table 1).

The seropositvity for toxoplasma IgG antibody was 28 %, while 6 % of the subjects were positive for both IgG + IgM antibodies. Around 84 % of pregnant women showed seropositvity for anti-rubella IgG, while 3 % were positive for IgG + IgM antibodies. The seropositivity of pregnant women for CMV IgG and IgG + IgM was 92 and 4 %, respectively. With respect to HSV, 61 % were positive for IgG and 3 % for IgG + IgM antibodies. Odds ratio analysis revealed significant protective role of toxoplasma ($OR = 0.21$) and predisposing role of rubella ($OR = 2.06$) and CMV ($OR = 1.46$) infections in HRP women. However, the HSV infections did not show any influence on HRP women in the present study (Table 2).

The HRP group comprised women showing fetal congenital malformation in the present pregnancy (25 %), while 75 % of women revealed BOH that included H/o repeated abortions (23 %), IUD (22 %), fetal congenital malformation in previous pregnancy (13 %), H/o early neonatal death (9 %), and H/o preterm labor (8 %) (Fig. 1).

The seropositive cases for toxoplasma were further distributed and evaluated in relation to type of BOH. Among the seropositive cases for toxoplasmosis, H/o preterm labor 53 (55 %) showed highest seropositvity followed by H/o intrauterine fetal death 111 (45 %), H/o repeated abortions 85 (32 %), fetal congenital malformation in present pregnancy 83 (28 %), H/o fetal congenital malformation in previous pregnancy 38 (25 %), and H/o neonatal death 24 (22 %). Pregnant women with fetal congenital malformation in the present pregnancy displayed maximum seropositvity (97 %) for rubella followed by H/o preterm labor 91 (95 %), H/o neonatal death 95 (88 %), H/o intrauterine fetal death 215 (87 %), H/o repeated abortions 231 (87 %), and fetal congenital malformation in previous pregnancy 95 (63 %). For CMV seropositivity, H/o repeated abortions 262 (98 %) showed highest seropositvity followed by fetal congenital malformation in present pregnancy 284 (97 %), H/o intrauterine fetal death 240 (96 %), H/o preterm labor 91 (95 %), H/o early neonatal death 102 (94 %), and fetal congenital malformation in previous pregnancy 138 (92 %). The seropositive cases for HSV showed highest frequency of fetal congenital malformation in previous pregnancy 114 (77 %) followed by H/o preterm labor 69 (72 %), H/o repeated abortions 186 (70 %), fetal congenital malformation in present pregnancy 181 (62 %), H/o early neonatal death 62 (58 %), and H/o intrauterine fetal death 136 (55 %) (Fig. 1).

The total seropositvity of toxoplasma, rubella, CMV, and HSV in Group 1 was 29, 97, 97, and 62 % while it was 36, 84, 97, and 65 % in Group 2, respectively. None of the samples were positive for IgM antibody alone. Furthermore, the seropositvity of toxoplasmosis was significantly higher in Group 2 than in Group 1 [OR (95 % CI) 0.71(0.53–0.95); $p = 0.026$] and for rubella, the seropositvity was considerably higher in Group 1 than in Group 2 [5.41 (2.80–10.43); $p = 0.000$]. However, no significant difference was observed with respect to CMV and HSV infections in Group 1 and Group 2 ($p > 0.05$) (Table 3).

Discussion

HRP is often considered as a multifactorial condition involving genetic, hormonal, and immune responses in its

Table 1 Distribution of demographic characteristics in high risk pregnant women (Group 1 and Group 2)

Variable	Group 1[a] *N* (%)	Group 2[b] *N* (%)	OR (95 % CI)	*p*-value
Maternal age				
≤25 years	184 (63)	476 (55)	0.71 (0.54–0.93)	0.01575*
26–29 years	91 (32)	305 (35)	1.19 (0.90–1.59)	0.2533
≥30 years	16 (5)	86 (10)	1.89 (1.09–3.28)	0.02904*
Gravida				
1	112 (38)	121 (14)	0.26 (0.19–0.35)	<0.0000001*
2	99 (34)	302 (35)	1.04 (0.78–1.37)	0.8566
≥3	80 (28)	444 (51)	2.77 (2.07–3.70)	<0.0000001*
Consanguinity				
Yes	73 (25)	167 (19)	1.40 (1.03–1.92)	0.04162*
No	218 (75)	700 (81)		
Religion				
Hindu	200 (69)	567(66)	0.86 (0.65–1.14)	0.3331
Muslim	87 (30)	290(33)	1.18 (0.88–1.57)	0.2969
Others	4 (1)	10(1)	0.84 (0.24–3.69)	0.9673
Maternal education				
Primary and less	101 (35)	310 (36)	1.05 (0.79–1.38)	0.8008
Secondary and above	190 (65)	557 (64)		
Maternal occupation				
House wife's	256 (88)	781 (90)	1.24 (0.82–1.89)	0.3646
Laborers	16 (5)	41 (5)	0.85 (0.47–1.55)	0.7126
Agricultural workers	11 (4)	21 (2)	0.63 (0.30–1.33)	0.3116
Professionals	8 (3)	24 (3)	1.01 (0.45–2.27)	0.8497
Family income				
<5,000	98 (33)	276 (32)	0.92 (0.69–1.22)	0.6105
5000–10,000	174 (60)	542 (62)	1.12 (0.85–1.47)	0.4491
>10,000	19 (7)	49 (6)	0.86 (0.50–1.48)	0.6841

[a] *Group 1* High risk pregnant women carrying fetuses with congenital malformations in the present pregnancy

[b] *Group 2* High risk pregnant women with H/o repeated abortions, previous congenital malformations, previous intra uterine deaths, previous neonatal deaths, previous preterm births, and other medical and obstetric complications

OR odds ratio, *CI* confidence interval, * $p < 0.05$

Table 2 Serological evaluation of IgG and IgG + IgM antibodies against TORCH agents in high risk pregnant women

Type of pathogen	IgG *N* (%)	IgG + IgM *N* (%)	*OR* (95 % CI)	*p*-value
Toxoplasma gondii	323 (28)	71 (6)	0.21 (0.15–0.29)	<0.0001*
Rubella	971 (84)	37 (3)	2.06 (1.43–2.97)	0.0001*
CMV	1,067 (92)	54 (4)	1.46 (1.06–2.01)	0.020*
HSV	708 (61)	40 (3)	1.21 (0.85–1.73)	0.284
χ^2(p-value)	110.77 (<0.0001)			

OR odds ratio, *CI* confidence interval, * $p < 0.05$

causation. In the present study, it was observed that mothers of ≤25 years and ≥30 years age group were significantly higher in group 1 and group 2, respectively. Similar results were observed in other studies also [18, 19]. Primigravida women were considerably higher in Group 1 and comparable to observations made by Akruti et al (2010) and Kanchan et al (2013) [20, 21]. However, HRP women with ≥3 gravida were significantly higher in Group 2. Consanguinity was significantly associated with group 1 but not with Group 2. Various researchers have established

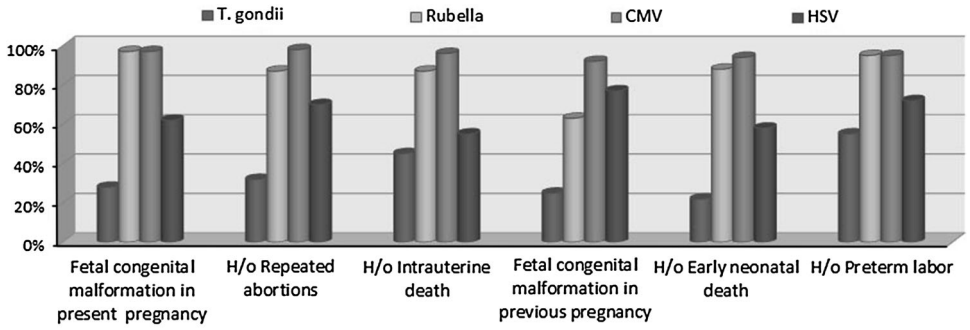

Fig. 1 Total Seropositvity of high risk pregnant women in relation to type of bad obstetric outcome

Table 3 Serological evaluation of IgG and IgG + IgM antibodies against TORCH agents in high risk pregnant women (Group 1 and Group 2)

Group	N	Seropositivity for IgG N (%)	Seropositvity for IgG + IgM N (%)	Total seropositvity N (%)	OR (95 % CI)	*p*-value
Toxoplasma						
Group 1[a]	291	66 (23)	17 (6)	83 (29)	Reference	–
Group 2[b]	867	257 (30)	54 (6)	311 (36)	0.71 (0.53–0.95)	0.026*
Rubella						
Group 1[a]	291	270 (93)	11 (4)	281 (97)	Reference	–
Group 2[b]	867	701 (81)	26 (3)	727 (84)	5.41 (2.80–10.43)	0.000*
CMV						
Group 1[a]	291	272 (93)	12 (4)	284 (97)	Reference	–
Group 2[b]	867	795 (92)	42 (5)	837 (97)	1.45 (0.63–3.34)	0.488
HSV						
Group 1[a]	291	176 (60)	5 (2)	181 (62)	Reference	–
Group 2[b]	867	532 (61)	35 (4)	567 (65)	0.87 (0.66–1.14)	0.359

[a] *Group 1* High risk pregnant women carrying fetuses with congenital malformations in the present pregnancy

[b] *Group 2* High risk pregnant women with H/o repeated abortions, previous congenital malformations, previous intra uterine deaths, previous neonatal deaths, previous preterm births, and other medical & obstetric complications

OR odds ratio, *CI* confidence interval, * $p < 0.05$

the fact that consanguinity increases the risk of congenital malformation [22] and bad obstetric outcome [23]. Religious pattern of mother had no effect on Group 1 and Group 2. However, other studies have revealed a higher incidence of congenital malformations in muslim community [19, 22]. Maternal education was not associated with Group 1 and Group 2. However, low maternal education showed a significant association with congenital malformations and BOH [24, 25]. Maternal occupation has been implicated in the incidence of congenital malformations [26]. However, maternal occupation did not confer risk in Group 1 and Group 2 similar to other studies [25, 27]. Family income was not associated with Group 1 and Group 2. Similar results were obtained by Singh and sindhu, (2010) and Sunethri et al. (2011) [18, 28].

Infections play a critical role in pregnancy loss associated with BOH and HRP [1, 3]. Several studies have been conducted in the past to know the extent of problem concerning TORCH infections in women of reproductive age, however, the sample size always remained questionable [29]. Therefore, in the present study. we evaluated both IgG and IgM levels in high risk pregnancies on a larger sample size to derive statistically significant conclusions. Sporadic studies with low sample size ($n < 200$ samples) were excluded, and only the studies with $n > 200$ samples from the year 2000 to 2013 were considered for reviewing the Indian status. Further, these studies were divided into 4 zones namely East, West, North, and South Zones (Supplementary Table 1). However, to the best of our knowledge, there are no studies reported so far from East Zone.

The incidence of toxoplasma seropositvity in women with abnormal pregnancies and abortions ranges from 17.5 to 52.3 % [30]. The factors like nutritional status, sociocultural habits, geographic climatic variations, transmission route, and age will influence the toxoplasmosis seropositivity [31]. One-third of the world's population is affected by the infection caused by this parasite [32, 33]. In the present study, 28 % of HRP women were positive for

IgG only indicating remote infection, while 6 % were positive for both IgG + IgM representing recent infection. A study conducted by Yasodhara et al. (2001) in the same zone on IgM seropositvity alone and on a smaller sample size showed the toxoplasma seropositvity to be 14.6 % [34]. Therefore, the present study is the first study from South Zone of India to evaluate both IgG and IgM seropositvity of toxoplasmosis in high risk pregnancies on a larger sample size. While studies by Mathur et al. (2002), Turbadkar et al. (2003), and Sood et al. (2009) from West Zone showed the seropositvity to be 28.5, 42.10, and 46.7 %, respectively for IgG and 9.6, 10.52, and 41.3 %, respectively for IgM [35–37]. IgM seropositvity of 42.5 and 19.4 % was observed in studies from North Zone [38, 39]. In the present study, the protective role ($OR = 0.21$) of toxoplasmosis towards HRP could be due to prior infection long time ago, and the immunity conferred might have prevented the parasite from crossing the placenta and in turn protected the fetus [40]. In addition, increased seropositvity of toxoplasma was observed in Group 2 suggestive of predisposing role of toxoplasmosis in HRP women with BOH ($p < 0.05$).

Toxoplasma seropositvity in relation to type of bad obstetric outcome demonstrated the highest seropositvity in women with H/o preterm labor, followed by H/o intrauterine fetal death, H/o repeated abortions, fetal congenital malformation in present pregnancy, H/o congenital malformation in previous pregnancy, and the least was in relation to past H/o neonatal death. However, a study by Shashi et al. (2004) from North Zone showed maximum seropositivity for abortions (71.8 %), followed by premature delivery, stillbirths (22.2 %), congenital anomalies (4.8 %), and neonatal death (1.2 %) in pregnant women with BOH [38].

The IgM seropositvity of rubella in India and other countries ranged between 4.66 and 28.6 % in women of reproductive age group [41]. In the present study, 84 % of HRP women were positive for IgG, indicating remote infection while 3 % were positive for both IgG + IgM representing recent infection. Studies by Yasodhara et al. (2001) and Ballal et al. (2007) from the same zone with a lower sample size than the present study evaluated only IgM seropositvity and found it to be 3.8 % [34] and 4.49 % [42] with respect to women with bad obstetric outcome. However, studies from West Zone by Mathur et al. (2002) and Turbadkar et al. (2003) showed a seropositvity of 47.98 and 61.3 % for IgG and 13.8 and 26.8 % for IgM antibodies [35, 36]. Studies from North Zone showed IgM seropositvity to be 17.5 % [38], 26.12 % [43], 86.90 % [29], 3.6 % [4], 3.4 % [44], and 30.4 % [39] with respect to women with bad obstetric outcome. An OR value of 2.06 in our study demonstrated predisposing role of rubella towards HRP and could be due to conception between 3 months to 1 year after infection as reported by Chernesky (1995) [45]. According to Eftyxia (2011), an increased IgG seropositvity indicates acute rubella infection and the rubella IgM antibodies persist only for a short duration of about 20–30 days after acute infection or vaccination [46]. Further, increased seropositvity of rubella was also observed in Group 1 suggestive of the contribution of rubella in HRP women with fetal congenital malformation in the present pregnancy ($p < 0.05$).

Rubella seropositivity analysis in women with bad obstetric outcome showed the highest seropositvity for fetal congenital malformation in present pregnancy followed by H/o preterm labor, H/o neonatal death, H/o intrauterine fetal death, H/o repeated abortions, and fetal congenital malformation in previous pregnancy. However, a study by Ballal et al. (2007) in the South Zone of India with a sample size 3.4 times lower than the present study measured only IgM levels and indicated the highest seropositvity in mothers with previous IUGR fetuses (9.52 %) followed by previous birth with congenitally malformed babies (6.97 %), H/o intrauterine deaths (6.89 %), H/o stillbirth/abortions (3.6 %), and mothers with no significant past clinical history (1.31 %) [42]. A study by Fomda et al. (2004) from North Zone showed maximum IgM seropositvity in women with previous H/o intrauterine death (IUD) (58.38 %) followed by stillbirth (57.14 %), premature delivery (50 %), abortion (21.8 %), and recurrent abortion (17.55 %) [43]. In addition, another study by Shashi et al. (2004) from North Zone showed the highest seropositvity for abortions (59.9 %) followed by premature delivery, stillbirths (23.0 %), congenital anomalies (11.4 %), and neonatal death (5.7 %) [38].

Global prevalence of CMV infection is reported to be approximately between 40 and 80 %, but may vary in developed (45 %) and in developing countries (100 %) [47]. Serological surveys in different parts of India have shown 80–90 % prevalence of CMV IgG antibodies in women of childbearing age [48]. In the present study, 92 % of HRP women were positive for IgG only, indicating remote infection while 5 % were positive for both IgG + IgM representing recent infection. In the same zone, Yasodhara et al. (2001) reported 0.8 % seropositivity of IgM [34] which is extremely lower than our study and it could be due to smaller sample size in their study. Studies by Mathur et al. (2002) and Turbadkar et al. (2003) from West Zone demonstrated IgG seropositvity to be 63.36 and 91.05 %, while IgM seropositvity to be 4.4 and 8.42 % [35, 36]. Studies from North Zone showed IgM seropositvity to be 29.5 % [38], 11 % [3] and 34.7 % [39] with respect to women with bad obstetric outcome. An OR value of 1.46 in our study suggests the predisposing role of CMV in HRP and it could be due to recent infection or reactivation of latent infection that might have significantly raised the IgG antibodies [48]. However,

there was no significant difference in CMV seropositivity between Group 1 and Group 2 ($p > 0.05$).

Women with H/o repeated abortions showed the highest seropositvity for CMV followed by fetal congenital malformation in present pregnancy, H/o intrauterine fetal death, H/o preterm labor, H/o early neonatal death, and fetal congenital malformation in previous pregnancy. However, a study by Shashi et al. (2004) from North Zone showed the highest seropositvity for abortions (61 %) followed by abortion, premature delivery and stillbirths (33.9 %), neonatal death (5.1 %), and congenital anomalies (0 %) [38].

Highest prevalence of HSV has been found in Africa and America and the lowest in Western and Southern Europe, and in Asia [49–51]. The incidence of neonatal infection ranges from 1 in 2,500 to 1 in 20,000 live births and two-thirds of cases are caused by HSV-2 [52]. A study by Sgaier et al. (2011) from India showed HSV2 prevalence among the general population to be around 10 % [53]. In the present study, 61 % of HRP women were positive for IgG only which is considered to be the highest seropositvity reported so far in India in relation to bad obstetric outcome while 3 % were positive for both IgG + IgM representing recent infection. Studies by Mathur et al. (2002) and Turbadkar et al. (2003) from West Zone showed IgG seropositvity to be 32.05 and 33.58 % and IgM seropositvity to be 4 and 3.6 % [35, 36]. Studies by Haider et al. (2011) and Shashi et al. (2004) from North Zone reported IgM seropositvity to be 16.8 % [52] and 33.5 % [39]. HSV did not show any association with HRP in the studied population compared to others, and also the women in Group 1 and Group 2 were not influenced by HSV seropositvity ($p > 0.05$).

Among the seropositive cases for HSV, fetal congenital malformation in previous pregnancy showed the highest seropositvity followed by H/o preterm labor, H/o repeated abortions, fetal congenital malformation in present pregnancy, H/o early neonatal death, and H/o intrauterine fetal death. Since there are no studies pertaining to HSV seropositvity with respect to type of bad obstetric outcome, a comparative analysis could not be performed. Therefore, the present study is considered to be the first in this regard.

It is known that approximately 50 % of all congenital malformations cannot be linked to a specific cause. There are some known causes or risk factors like socio-economic factors, genetic factors, infections, maternal nutritional status, and environmental factors causing congenital malformations [54]. In the present study, all the subjects belonged to the same socio-economic status, specific genetic factors could not be elucidated, and there was no history of exposure to any teratogenic or toxic agents during first three months of pregnancy. Therefore, the present study showed rubella seropositivity, ≤25 years maternal age, primigravida, and consanguinity as predisposing factors in HRP leading to congenital malformation in the fetus. Though causes like genetic, hormonal, abnormal maternal immune response, and maternal infection may be responsible for BOH [55] the present study showed a significant association of toxoplasma seropositivity, ≥30 years maternal age, and ≥3 gravida as risk factors in HRP women leading to bad obstetric outcome.

Conclusion

We conclude that variables like maternal age of ≤25 years, primigravida, and consanguinity contributed to congenital malformation in present pregnancy, while maternal age of ≥30 years and ≥3 gravida towards BOH. In HRP women, toxoplasma is protective while rubella and CMV are the infectious agents. Among the groups, toxoplasma conferred a predisposing role towards high risk pregnant women with BOH, while rubella infection predisposed high risk pregnant women with fetal congenital malformation in the present pregnancy. With respect to bad obstetric outcome, sixty-one percent seropositvity of HSV is the highest reported so far in India. Hence, screening and early diagnosis of these infections in high risk pregnant women may help in early detection and appropriate management. In addition, the present study was the first to evaluate both IgG and IgM seropositvity in high risk pregnant women on a larger sample size from South India.

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Compliance with ethical requirements and Conflict of interest The study was approved by the institutional ethics committee and informed consent was obtained from all pregnant women prior to inclusion. None of the authors declare any conflict of interest.

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