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Original Research Article

An examination of the seroprevalence of torch infections and their correlation with adverse reproductive outcomes in females exhibiting a bad obstetric history

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ABSTRACT

Background: The term TORCH infections refer to a group of diseases including Toxoplasma, Other (syphilis, varicella-zoster, parvovirus B19), Rubella, Cytomegalovirus (CMV), and Herpes infections. These are a set of pathogens capable of traversing the placental barrier, subsequently causing congenital infections. Often these infections are asymptomatic initially and pose significant diagnostic challenges during gestation, potentially leading to undesirable obstetric outcomes. This research intends to explore the correlation between TORCH infections and perinatal outcomes within pregnancies deemed high-risk.
Methodology: We examined 143 high-risk pregnant patients aged 18-46 from the Obstetrics and Gynecology Department at the Baghdad Gynecology and Obstetrics Hospital. Hundreds of normal pregnancy group were also included. The high-risk group encompassed women with recurring pregnancy loss, fetal congenital anomalies, intrauterine fetal death, and low birth weight intrauterine neonatal death. The presence of IgG and IgM antibodies against TORCH agents in patients' serum control serum were assessed using ELISA kits. We compared perinatal outcomes between TORCH seropositive and seronegative high-risk pregnant women.
Findings: Among the 143 high-risk pregnancies, a significant proportion of young, low-parity women from diverse residences were co-seropositive for Toxoplasma gondii, rubella virus, Cytomegalovirus, and Herpes Simplex infections. Of these, 55 cases (48.4%) were seropositive for all the four TORCH agents compared to 88 cases (38%) were seropositive for antibodies to one to three of the TORCH agents. IgG seropositivity was 74.5%, while IgM seropositivity was 31.8% for Toxoplasma gondii, 3.6% for CMV and 0% for RV infections, respectively. Significantly, high-risk pregnancies with TORCH seropositivities exhibited a clearly strong correlation with Habitual abortions outcomes.
Conclusion: High-risk manifestations demonstrated for Toxoplasma gondii, Rubella virus, Cytomegalovirus and Herpes Simplex infections strongly associated with habitual abortions compare to high but less significant association in those seropositive to one, two or three of the TORCH agents

1. Introduction

The expression 'Bad Obstetric History' (BOH) denotes prior unfavorable fetal results, encompassing two or more sequential spontaneous miscarriages, intrauterine fetal demise, retardation of growth, stillbirth, early neonatal death, and congenital anomalies.[1] Several possible etiologies of BOH may encompass genetic determinants, hormonal fluctuations, abnormal maternal immune reactions, and maternal infections.[2] The term 'high-risk pregnancy' is associated with a pregnancy that augments the mother's, fetus's, or neonate's risk of morbidity or mortality during gestation or delivery. Such pregnancies

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are complicated by factors that adversely affect pregnancy outcomes (either maternal, fetal, or both). Interestingly, while only 10-30% of pregnant women are categorized as high-risk during their antenatal period, they contribute to 70-80% of perinatal mortality and morbidity.[3] The TORCH test is categorized under the Infectious-Disease Antibody Titer blood examinations. It quantifies the presence and concentration of antibodies against a specific cluster of infectious diseases in the bloodstream. The TORCH acronym encapsulates a group of acute and chronic infections that women can potentially acquire during gestation, resulting in profound implications for the newborn. These infections can induce a spectrum of symptomatic congenital disabilities in neonates, collectively called the TORCH syndrome.[2] A positive IgG antibody test generally signifies past exposure to a TORCH agent and does not necessarily imply a currently active infection. In contrast, the detection of IgM antibodies is more intricate and can yield false negative and positive outcomes.[4] Toxoplasmosis is engendered by Toxoplasma gondii, a parasite ubiquitously found in humans. Maternal infection can induce severe eye or central nervous system infections in infants, the later the maternal infection occurs during gestation, the higher the probability of fetal infection. Conversely, toxoplasmosis acquired early in pregnancy can result in a miscarriage or severe birth defects.[2,5,6] Rubella impacts 0.1-2% of neonates. Birth defects are most likely to transpire when infants are infected during the initial eight weeks of gestation.[7,8] Cytomegalovirus (CMV), a member of the herpesvirus group of infections, can induce severe complications in infants, such as hearing loss, mental retardation, pneumonia, hepatitis, or blood disorders.[9] Herpes simplex virus infection can pose a risk if transmitted to an infant during delivery but generally does not affect gestation or fetal health.[10] There is a lack of adequate data on the prevalence and contributing factors among pregnant women co-infected with TORCH in Iraq. This research aims to fill this knowledge void by evaluating the status and factors associated with high-risk pregnancies among women attending antenatal health care about TORCH infections. A thorough look on the possibility of any differences between the 4 major TORCH agents and some of the TORCH agents in respect to BOH manifestations was also put in consideration.

2. Materials and Methods

This prospective study involved patients attending laboratories in Baghdad. The participant group comprised 243 women, including 143 with high delivery risk factors and 100 clinically normal women with prior normal pregnancies and full-term deliveries. The inclusion criteria were based on a previous history of 2-3 pregnancy losses, specifically habitual abortion (HA), intrauterine fetal deaths (IUFD), neonatal death (NND), congenital malformation (GM), stillbirth (SB), and low birth weight (LBW).

From each participant, 3 ml of venous blood was collected under strict aseptic precautions. The serum was used for serological evaluation of IgM and IgG antibodies for Toxoplasma gondii, Rubella virus, Cytomegalovirus infections, and Herpes simplex virus as per the manufacturer's instructions using ELISA techniques. The following kits were utilized:

1. Rubella IgG ELISA from BIOTEC Laboratories Ltd. (UK).
2. Rubella IgM ELISA from BIOKIT, S.A. SPAIN.
3. CMV IgG ELISA from BIOKIT, S.A. SPAIN.
4. CMV IgM ELISA.
5. Toxoplasma gondii IgG Elisa kit from Biotech Laboratories Ltd. (UK).
6. Toxoplasma gondii IgM from BIOTECH Laboratories Ltd. (UK).
7. HSV-IgG and IgM Elisa kits from Serion Diagnostics (Germany).

3. Results

Table 1 presents the demographic characteristics of the enrolled patients. Occupation, history of contact with cats, and blood transfusion yielded significant data (P = 0.01). Residency, however, did not show any significant variations as demonstrated.

Table 2 displays the age ranges of the recruited patients along with their symptoms of Bad Obstetric History (BOH). The majority of BOH cases were observed in the age groups of 18-27 years for all three selected groups (45.5%, 47.7%, and 37% respectively). Conversely, the lowest seroprevalence rates were found in the age ranges of 38-46 years (23.6%, 17%, and 24% respectively) as shown in Table 2.

Among the 143 cases with BOH manifestations, 55 (38.5%) exhibited TORCH seroprevalence (Table 3). Habitual abortion was observed in 40 cases (72.7%) within the TORCH group, while cases of intrauterine fetal death (IUD) accounted for 3 cases (5.5%), neonatal death (NND) for 6 cases (10.9%), and congenital malformation (CM), stillbirth (SB), and low birth weight (LBW) were present at lower rates (3.6%) respectively. In the group with seroprevalence of 1 to 3 TORCH agents, habitual abortion was significantly lower compared to the TORCH group (25 cases [28.4%] versus 40 cases [72.7%]) with a p-value of 0.05. The rates of other BOH manifestations were higher but not significant compared to those in the TORCH group, except for LBW which was observed in 22 cases (25%) with a p-value of 0.05. Notably, habitual abortion within the TORCH group was significantly higher compared to the normal pregnancy group as shown in Table 3. Furthermore, in Table 3, we present the obstetric outcomes for the TORCH group, where all 55 patients experienced habitual

Table 1: Demographic profile of patients and normal pregnant ladies

Category	Group	Torch Infected Patient	Normal Pregnant Women	Odds Ratio	P-value
Residency	Urban	72.73% (40/55)	80% (80/100)	0.64	0.28
	Rural	27.27% (15/55)	20% (20/100)	1.56	0.28
Occupation	Employee	72.73% (40/55)	37% (37/100)	4.86	<0.001
	Housewife	27.27% (15/55)	63% (63/100)	0.21	<0.001
History of contact with cats during antenatal life	Yes	65.45% (36/55)	45% (45/100)	2.29	0.01
	No	34.55% (19/55)	55% (55/100)	0.44	0.01
History of blood transfusion	Yes	9.09% (5/55)	0% (0/100)	N/A	<0.001
	No	90.91% (50/55)	100% (100/100)	N/A	<0.001

Table 2: Age range in relation to TORCH seropositivity among patients and controls

Group	Age Range	TORCH Seropositivity Rate
TORCH Group	18-27 years	45.5% (n=25/55)
	28-37 years	30.9% (n=17/55)
	38-45 years	23.6% (n=13/55)
Single, Double, or Triple Group	18-27 years	47.7% (n=42/88)
	28-37 years	35.2% (n=31/88)
	38-46 years	17.0% (n=15/88)
Normal Pregnancy Group	18-27 years	37.0% (n=5/100)
	28-37 years	39.0% (n=39/100)
	38-46 years	24.0% (n=24/100)

Table 3: Seroprevalences to TORCH agents and to 1, 2 or 3 of TORCH agents and bad obstetric history BOH) patterns

Group	Total Out of 143 positive Women	HA	IUD	NND	CM	SB	LBW
TORCH Group	38.5% (55/143)	72.7% (40/55)	5.5% (3/55)	16.4% (9/55)	18.2% (10/55)	5.5% (3/55)	21.8% (12/55)
P-value (vs Normal Pregnancy)	-	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Single, Double, or Triple Manifestation	61.5% (88/143)	28.4% (25/88)	11.4% (10/88)	12.5% (11/88)	9.1% (8/88)	13.6% (12/88)	25% (22/88)
P-value (vs Normal Pregnancy)	-	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

abortion during the first trimester.

Table 4 highlights the significance of seropositivity for Toxoplasma gondii IgM in combination with Rubella-IgG, CMV-IgG, and HSV-IgG in the etiology of habitual abortion. In this group, habitual abortion was reported in 10 out of 12 cases (93.3%), which was significantly higher than the rates observed in TORCH-IgG (19 out of 14 cases [46.3%]). Seropositivity for one or two or even three of the TORCH agents' IgG resulted in 30 out of 88 cases (34%), which was significantly lower than the other mentioned groups. Additionally, Table 4 shows that out of the 100 normal pregnancy cases, 12 cases (12%) were seropositive for onlyone, two or three of the TORCH infections.

In Table 5, we conducted an analysis to study the effects of TORCH seroprevalence and seroprevalence of one, two, or three TORCH agents on the type of BOH manifestations. The rate of habitual abortion in the TORCH group was significantly higher (72.7%) compared to the group with

Table 4: TORCH IgG and IGM seroprevalences rates with special emphasis on Habitual abortion (HA) rates

Category	Total	HA	IUFD	NND	CM	SB	LBW
Toxo. IgM+ RubellaIgG+ CMV-IgG+ HSV-IgG	12/55 (21.82%)	10/12 (93.3%)	0	0	0	0	2/12 (16.6%)
CMV IgM Toxo-IgG CMV-IgG HSV-IgG	2/55 (3.64%)	0	0	0	0	0	0
Rubella IgG Toxo-IgG Rubella-IgG CMV-IgG HSV-IgG	41/55 (74.5%)	19/41 (46.3%)	2/41 (4.8%)	3/41 (7.3%)	3/41 (7.3%)	10/41 (24.3%)	4/41 (9.7%)
TORCH -IgG positivity in Single or Double or Triple TORCH Agents	88/88 (100%)	30/88 (34.09%)	7/88 (7.95%)	12/88 (13.64%)	15/88 (17%)	15/88 (17%)	9/88 (10.2%)

Table 5: Comparison between the "TORCH Group" and the "single, double, or triple manifestation" group and their odds ratios

Outcome Variable	TORCH Group	Single, Double, or Triple Manifestation	Odds Ratio	P-value
HA	72.7%	28.4%	4.6	<0.001
IUD	5.5%	11.4%	0.45	0.10
NND	16.4%	12.5%	1.38	0.45
CM	18.2%	9.1%	2.26	0.02
SB	5.5%	13.6%	0.37	0.07
LBW	21.8%	25%	0.84	0.61

seroprevalence of one, two, or three TORCH agents (28.4%) with a p-value of 0.001. The calculated non- adjusted odds ratio was found considerably high at 4.6."

4. Discussion

The widespread utilization of TORCH screening among clinicians investigating congenital and perinatal infections is noteworthy. However, questions have been raised regarding the suitability and specificity of the current screening methodologies.[1] In patients with bad obstetric history (BOH), maternal infections are a significant factor in miscarriage. T. gondii encysted forms can cause fetal infection in the first trimester and frequently result in recurrent miscarriages due to their presence in the uterus with persistent infections and subsequent rupture during placentation.[7] In accordance with preceding studies, our current research data identified TORCH infections as etiological agents in recurrent pregnancy loss, in 55 out of 143 pregnant women exhibiting BOH symptoms.[9–11] Assessing IgM antibodies in maternal sera can signal the acute phase of maternal infection and the probability of congenital transmission of T. gondii.[12] In our research, IgM antibodies were detected in 10 out of 12 (93.3%) patients with HA manifestation, which concurs with other studies reporting approximately 66.3% of T. gondii-infected women demonstrating an IgM response.[13] It is recommended that pregnant women undergo testing for TORCH antibodies, those who experience unfavorable outcomes should take precautions to avoid infection, such as staying away from cat litter, ensuring the meat is thoroughly cooked, and washing their hands after handling raw meat.[14] The pathophysiology of TORCH infections is different and can lead to severe clinical symptoms and drastic consequences. Although it is still a common cause of blindness, congenital toxoplasmosis can be prevented by taking precautions, including avoiding contact with cats and raw meat (15). Cytomegalovirus (CMV) is the most frequent cause of congenital infection in the United States and numerous other regions.[15,16]

Rubella is preventable by vaccination and linked with significant morbidity and adverse pregnancy outcomes, mainly when contracted during the first trimester, leading to severe fetal consequences.[17] In our research, all serum samples underwent testing for Rubella-specific IgG and

IgM antibodies, demonstrating a seropositivity rate of 28.5% among cases with a bad obstetric history. Elevated seropositivity (93.3%) was noted in women experiencing recurrent abortions, followed by low-birth-weight cases (21.8%).[18] Implementing routine screening for rubella in all antenatal cases can enable early detection and appropriate management to enhance fetal outcomes.

Selective employment of cesarean delivery and antiviral treatment can assist in reducing the incidence and enhancing outcomes in neonatal herpes cases.[19] CMV and HSV possess intrauterine transmission routes and can instigate significant mortality and morbidity.[20] Our research reported a seropositivity rate of 3.6% for CMV-specific IgM among women with BOH. Other investigations conducted in Iraq have reported seropositivity rates ranging from 6.8% to 8.3% among Iraqi women.[21] A primary CMV infection during gestation increases the risk of manifesting symptomatic congenital infection, leading to the loss of the fetus.[22] Numerous researchers have recommended the serological evaluation of CMV-specific IgM during pregnancy.[15] Patients with a confirmed HIV diagnosis should undergo a check for their toxoplasma antibody titers. If results are positive with a CD4 count below 100, it is advisable to administer prophylactic antibiotics along with antiretroviral therapy until the CD4 cell count elevates.[23] In neonates, a significant portion, about half, of the morbidity and mortality from HSV II originates from a primary infection that women acquire during gestation or from the reactivation of a previous infection.[24] In our research, the seropositivity rate for HSV IgM among BOH patients was null, while a prior study reported a 2% seropositivity rate in asymptomatic women with recurrent infections during pregnancy.[25] The seropositivity rate for HSV IgG among BOH patients in our research was 11%, analogous to findings reported in another study.[25] Mixed TORCH infections were observed in 55 out of 143 patients (28.5%), typically associated with Toxoplasma IgM antibodies. Similar reports of mixed infection have been previously noted.[20] Rubella typically presents as a mild viral disease in children but occasionally infects adults. A primary viral infection during pregnancy may lead to harm to the fetus. In our study, the rubella seropositivity rate was 28.5%, whereas other investigations have reported seropositivity rates varying from 4% to 17.7%, with a surge in incidence noted every 3-4 years.[25] Considering that 10-20% of women within the childbearing age bracket are vulnerable to rubella, a rise in the incidence of rubella is likely to increase the number of pregnant women infected with rubella.[26] Pregnant women who test positive for rubella IgG may indicate a past infection with one of these infectious agents. Testing a second blood sample drawn two weeks later can compare the antibody level. Increased IgG antibody levels would suggest a recent infection.[27] It is crucial to highlight that IgM antibodies are not always specific and may cross-react with other IgMs and proteins. Reference ranges provided by private laboratories should be adhered to.[28] Active infection does not directly correlate with ultrasound growth changes; therefore, ultrasound alone cannot serve as a diagnostic criterion for confirming or refuting the diagnosis of rubella.[29]

It is worth noting that TORCH screening can yield both false-positive and false-negative results.[30] IgM antibodies against TORCH organisms typically persist for about three months, while IgG antibodies remain detectable for a lifetime, providing immunity and preventing or reducing the severity of reinfection. Thus, the presence of IgM antibodies indicates current or recent infection, while the absence of IgM antibodies but presence of IgG antibodies without an increase on serial testing suggests previous infection or vaccination-induced immunity. Individuals lacking evidence of either IgM or IgG antibodies specific to the organism are at risk of infection due to the absence of demonstrable immunity.

Regarding mixed seropositivity among enrolled women, we noted that out of the 55 cases positive for TORCH agents in our study, a significant number exhibited habitual abortion (HA) manifestations (93.3%). Other manifestations did not significantly differ between cases with mixed seropositivity's. These findings are consistent with previous reports.[31] Our study clearly demonstrates the significant role-played by TORCH agents in habitual abortion, as all 55 women with BOH symptoms experienced HA during the first trimester (Table 3). These results align with data presented by previous studies.[32] In our study, we observed that vaginal bleeding in early pregnancy emerged as a prevalent complication and the primary reason for hospitalization during the first and second trimesters. The underlying mechanisms of habitual abortion (HA) and its detrimental impact on pregnancy outcomes are not comprehensively elucidated. Aberrant TORCH infections may contribute to complications in the first trimester, which, if left unresolved, can escalate to spontaneous abortion. Molecular investigations have demonstrated a notable elevation in placental indicators of oxidative stress in pregnancies among women with a history of bad obstetric outcomes (BOH).[33]

5. Conclusions

Currently, accurately predicting the outcome of pregnancies affected by TORCH infections and identifying those that will result in miscarriage remains challenging. The lack of accurate prediction for pregnancies with threatened miscarriage, leading to either survival or spontaneous miscarriage, may result in unnecessary and potentially harmful interventions or wasteful procedures. Therefore, we propose that women diagnosed with TORCH pathology should be provided with the option of hospital bed rest or, if declined, should receive counseling on modified bed

rest at home. Additionally, psychological counseling and fetal surveillance should be offered to improve outcomes. It is crucial to engage patients in discussions regarding the increased likelihood of operative delivery.

6. Author Contributions

Each author that worked on this project significantly influenced the research's design, conduct, and analysis, as well as the interpretation and analysis of the data. They all contributed to the original manuscript's creation or its thorough intellectual content review. They agreed to be accountable for every part of the work and accepted its submission to the current journal.

7. Source of Funding

None.

8. Conflict of Interest

None.

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