

## Prevalence of toxoplasmosis, rubella, cytomegalovirus, and herpes (TORCH) infections among women attending the antenatal care clinic, maternity hospital in Abha, Southwestern Saudi Arabia

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### ABSTRACT

**Objectives:** To investigate the presence of toxoplasmosis, rubella, cytomegalovirus, and herpes (TORCH) infections in women attending at the antenatal care clinic in Abha, Kingdom of Saudi Arabia (KSA).

**Methods:** A total of 190 blood samples were collected from Abha maternity hospital in Aseer region, KSA, from February 2018 to May 2019 and screened with the TORCH panel (toxoplasma gondii [IgG/IgM], cytomegalovirus [CMV] [IgG/IgM], rubella [IgG/IgM], and herpes simplex type 1 and 2 [IgG/IgM]).

**Results:** The mean age was 31.42±6.514 years and gestational age was 32.48±6.168 weeks. Serum IgG was positive for *Toxoplasma gondii* (*T. gondii*) (27.4%), herpes simplex type 1 (HSV-1) (94.7%), herpes simplex type 2 (HSV-2) (0.5%), CMV (100%), and rubella (88.9%). Serum IgM was positive only for CMV (9.5%). Though, there was an association between abortions from previous pregnancies (26.5%), intrauterine death (5.8%), premature labor (3.2%), microcephaly (1.6%), other congenital diseases (1.6%) and low birth weight (0.5%) with current IgG positivity for TORCH infections, the results were not statistically significant.

**Conclusion:** Seropositivity for IgG antibodies correlate with TORCH-associated pregnancy complications in Abha, KSA; however, IgM positive CMV pregnant cases warrant further systematic investigation to understand the implications of CMV on outcomes during pregnancy.

**Keywords:** toxoplasmosis, rubella virus, cytomegalovirus, herpes simplex virus, TORCH

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Toxoplasmosis, rubella, cytomegalovirus, and herpes (TORCH) represents a group of pathogens, namely *Toxoplasma gondii* (*T. gondii*), rubella virus, *Cytomegalovirus* (CMV), and herpes simplex virus (type 1 [HSV-1] and type 2 [HSV-2]), which are the main causative factors for congenital infection, and anomalies in the fetus and new-born, and for abortion (10-15%).<sup>1</sup> Research shows that TORCH infections cause high mortality and morbidity in developing countries, and the prevalence of these infections varies between countries.<sup>2</sup>

The Middle East, South-East Asia, Latin America, and Africa have reported a high prevalence of *T. gondii* infections.<sup>1,3</sup> Nearly 40,000 women are infected with CMV annually in the United States and Europe, with 20% of infants born to CMV-infected females acquiring neurological deficits and hearing loss.<sup>4,5</sup> Rubella is acquired by 30-40% of fetuses in the first trimester of pregnancy. The maternal symptoms of rubella infection include lymphadenopathy, arthralgia, fever, malaise, conjunctivitis, encephalitis, and hemorrhagic complications. Hearing loss, mental retardation, blindness, and neurological deficits with widespread infection to the brain, lungs, and liver are common manifestations of toxoplasmosis, rubella virus, and CMV among newborns. Infection with either HSV-1 or 2 in an antenatal woman can cause premature labor, abortion, as well as congenital and neonatal herpes. Globally, approximately 3.7 billion people below 50 years of age (67%) are infected with HSV-1, and 417 million people between 15-49 years of age (11%) have HSV-2 infection.<sup>6,7</sup>

Few studies on TORCH infections have been carried out in the Kingdom of Saudi Arabia (KSA). In 2002, one study conducted on pregnant women in Makkah, KSA, reported IgG antibodies of approximately 35.6% *T. gondii*, 92.1% CMV, 93.3% rubella, 90.9% HSV-1 and 27.1% HSV-2.<sup>6</sup> Another study from Hail, KSA, reported an overall seroprevalence of TORCH infections among pregnant women to be 13% with *T. gondii* IgG at 12%, *T. gondii* IgM at 19%, rubella IgG at 14%, rubella IgM at 13.6%, and CMV IgG at 13.65%.<sup>8</sup> Although isolated studies on CMV have been carried out in the Jizan and Aseer regions reporting nearly 93% CMV seropositivity among 89 pregnant women, the overall TORCH infection burden is not available for these

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regions of KSA.<sup>9</sup> Thus, the present study has attempted to investigate the presence of TORCH infections among the antenatal women in the southern part of KSA and the relation between TORCH infections and pregnancy-related complications.

**Methods.** A cross-sectional study was conducted to investigate the frequency of TORCH infections at the maternity hospital in the Aseer region, KSA, between February 2018 and May 2019. A simple random sampling technique was used to collect a sample size of 190 pregnant females. The inclusion criteria included all the multigravida antenatal patients willing to participate in the research. The exclusion criteria for the study included primi gravida patients, patients with any systemic illness, and pregnant women with a family history of any congenital disease.

**Sample collection.** Blood samples (5-10ml) and clinical data was collected from pregnant females who came for a routine antenatal check-up after informed verbal and written consent and as per inclusion and exclusion criteria. A detailed history of previous pregnancy outcomes, such as premature labor, low birth weight, microcephaly, intrauterine death (IUD), and other congenital anomalies were recorded. Briefly, serum was separated by centrifuging at 2200-2500 RPM for 10 minutes. The separated serum was stored in aliquots and frozen until tested.

**Immunoglobulin G and IgM screening for TORCH infections.** The serum samples were screened for CMV IgG and IgM antibodies, rubella IgM antibodies, *T. gondii* IgG antibodies, HSV-1 and 2 IgG and IgM antibodies using commercially available indirect ELISA kits (Human Diagnostics, Wiesbaden, Germany/ United Diagnostics, KSA/Vircell Microbiologists, Granada, Spain) as per manufacturers' instructions. The serum samples were also screened for rubella IgG and *T. gondii* IgM antibodies using commercially available capture ELISA kits (United Diagnostics, Dammam, KSA/Human Diagnostics, Wiesbaden, Germany) as per manufacturers' instructions.

**Statistical analysis.** In this prospective study, we have gathered the data from purposely constructed questionnaire, coded data was entered in the Statistical Package for Social Sciences (SPSS) Version 22 (IBM Corp., Armonk, NY, USA) for analysis along with the results of TORCH IgG and IgM enzyme-linked immunosorbent assay (ELISA). Descriptive statistics (Mean±SD, frequencies and percentages were computed). While performing Univariate analysis different statistical tests were used to measure the degree

of association between variables of interest. Chi-square and fisher exact test were used to measure the degree of association between the variable of interest. We have further used the linear regression method modeling the relationship between dependent variable and independent variables. Main dependent variables are interpretation of TORCH IgG and TORCH IgM index. While independent variables are: abortions, intrauterine death, premature labor, microcephalus, low birth weight, congenital disease of new born. Level of significance was 5% meaning a  $p$ -value<0.05 was considered significant. We did not take TORCH IgM data due to undetectable results and CMV IgG due to 100% positive titers.

**Ethical considerations.** The study was ethically approved by the Research Ethics Committee, College of Medicine, King Khalid University, Riyadh, KSA (REC# 2017-05-24).

**Results.** The mean age among the 190 antenatal cases was 31.4±6.5 years, and the mean gestational age was 32.4±6.2 weeks. Demographic data has been illustrated in Table 1. The seroprevalence of TORCH infections among pregnant women is illustrated

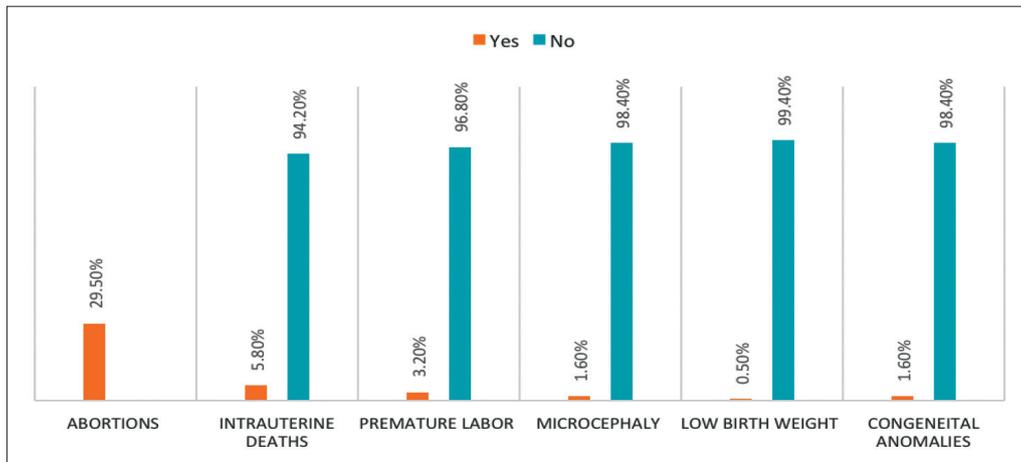
**Table 1** - Demographic information (n=190).

Variables	n (%)
Mean age of women (mean±SD)	31.53 ± 6.190
<b>Gestational age at the time of sample collection</b>	
2 <sup>nd</sup> trimester (13-28 weeks)	44 (23)
3 <sup>rd</sup> trimester (29-40 weeks)	146 (77)
<b>Number of previous pregnancies</b>	
1-2 pregnancies	112 (59)
3 and more pregnancies	78 (41)

**Table 2** - Seroprevalence of toxoplasmosis, rubella, cytomegalovirus, and herpes infections among pregnant women (n=190).

Variables	Immunoglobulin G		Immunoglobulin M	
	Positive	Negative	Positive	Negative
<i>Toxoplasma gondii</i>	52 (27.4)	138 (72.6)	0	190 (100)
HSV-1	180 (94.7)	10 (5.3)	0	190 (100)
HSV-2	1 (0.5)	189 (99.5)	0	190 (100)
CMV	190 (100)	0	18 (9.5)	172 (90.5)
Rubella	169 (88.9)	21 (11.1)	0	190 (100)

Values are presented as number and percentage (%).  
HSV-1: herpes simplex type 1, HSV-2: herpes simplex type 2,  
CMV: cytomegalovirus virus



**Figure 1** - Frequency of previous pregnancy outcomes.

in **Table 2**. Approximately 27.4% were positive for *T. gondii* IgG, 94.7% were positive for HSV-1 IgG, 0.5% were positive for HSV-2 IgG, 100% were positive for CMV IgG, and 88.9% were positive for rubella IgG. We observed 9.5% positivity for CMV IgM, while all other TORCH IgMs were negative or undetectable.

In this study, the relevant clinical associations with TORCH positive antenatal cases included premature labor, low birth weight, IUD abortions, microcephaly, and other congenital malformations observed in babies, as illustrated in **Figure 1**. The highest rate of abortions was found among women with previous pregnancies, followed by women with past IUDs, premature labor, women with microcephalic babies, congenital diseases, and low birth weight; however, these observations were not statically significant.

The association of TORCH IgG positivity with previous pregnancy outcomes were subjected to univariate and multivariate logistic regression as possible predication matrix illustrated in **Table 3**.

*P*-values were not found to be statistically significant at 5% among any of the variables and were not calculated for CMV IgG, and IgM as the former was positive for 100% of cases while the latter did not include any follow-ups to check with birth anomalies.

**Discussion.** The results of our study were in agreement with birth anomalies due to infections outlined in the TORCH panel. The association between infection and clinical condition was first examined in the context of gestational and mean age for all antenatal cases. The results demonstrated a strong impact of TORCH infections on birth anomalies at higher ages,

thus in agreement with previously published studies demonstrating an increase in the incidence of TORCH infections among pregnant women in the age group >30.9. A study conducted in China reported severe pregnancy outcomes in patients infected with TORCH, including congenital malformations (12.9%), abortions (31.8%), premature labor (8.2%), and infant death (9.4%).<sup>10</sup> Although the present study did not report any infant deaths, abortion rates were high and congenital malformations as well as premature labor were low. We also observed microcephaly and low birth weights, in contrast to the above study. All antenatal cases were positive for at least one TORCH organism such as CMV, indicating past infection.

Previous studies from KSA showed a varied exposure pattern of one or 2 of the TORCH organisms among pregnant women and the general population. A study carried out in the Jizan province of KSA showed 93.1% positivity of CMV IgG among pregnant women, in similarity with our observations.<sup>9</sup> Another report from Al Khobar, KSA, concerning HSV-1 and HSV-2 reported high seroprevalence of HSV-1 IgG antibodies (93.2%), which is close to our results. However, the prevalence of HSV-2 was much higher (54.7%) than that reported in the present study.<sup>11</sup> However, similar to our results, the Al Khobar study did not report HSV IgM positivity, indicating a current infection. Previous studies have revealed that toxoplasmosis is common in the southern part of KSA, with *T. gondii* IgG antibodies at 29.2% and *T. gondii* IgM antibodies at 3.1%, which are similar to the results of the present study.<sup>12</sup> Recent studies on *T. gondii* from Makkah and Riyadh, KSA, reported *T. gondii* IgM positivity at 1.2% in Makkah

positivity and around 6.4% in Riyadh. *Toxoplasma gondii* IgG positive patients had a history of premature labor, IUDs, and microcephaly, indicating that past infection with *T. gondii* could be a predictor of poor obstetric outcomes and congenital malformations, as

in agreement with our observations.<sup>13</sup> In the present study, results of CMV positivity (IgG and IgM)-related complications, including abortions, congenital malformations, IUDs, preterm labor, microcephaly, and early neonatal mortality, were very similar to studies

**Table 3** - Association of toxoplasmosis, rubella, cytomegalovirus, and herpes infections (TORCH) immunoglobulin G (IgG) positivity with previous pregnancy outcomes.

Variables	Abortion		Intrauterine death		Premature labor		Microcephaly		Low birth weight		Congenital disease	
	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	Yes
<i>Toxoplasma gondii</i>												
Positive	33 (63.5)	19 (36.5)	51 (98.1)	1 (1.9)	50 (96.2)	2 (3.8)	50 (96.2)	2 (3.8)	52 (100)	0	51 (98.1)	1 (1.9)
Negative	101 (73.2)	37 (26.8)	128 (92.8)	10 (7.2)	134 (97.1)	4 (2.9)	137 (99.3)	1 (0.7)	137 (99.3)	1 (0.7)	136 (98.6)	2 (1.4)
P-value*	0.190		0.161		0.739		0.124		0.538		0.815	
Univariate p-value†	0.603		0.270		0.969		0.401		0.588		ND	
Multivariate p-value‡	0.446		0.106		0.693		0.682		0.581		0.961	
<i>Herpes simplex type 1</i>												
Positive	127 (70.6)	53 (29.4)	169 (93.9)	11 (6.1)	174 (96.7)	6 (3.3)	177 (98.3)	3 (1.7)	179 (99.4)	1 (0.6)	177 (98.3)	3 (1.7)
Negative	7 (70.0)	3 (30.0)	10 (100)	0	10 (100)	0	10 (100)	0	10 (100)	0	10 (100)	0
P-value*	0.970		0.421		0.557		0.681		0.813		0.681	
Univariate p-value†	0.983		0.929		0.870		0.983		0.838		ND	
Multivariate p-value‡	0.615		0.660		0.608		0.733		0.830		0.806	
<i>Herpes simplex type 2</i>												
Positive	1 (100)	0	1 (100)	0	1 (100)	0	1 (100)	0	1 (100)	0	1 (100)	0
Negative	133 (70.4)	56 (29.6)	178 (94.2)	11 (5.8)	183 (96.8)	6 (3.2)	186 (98.4)	3 (1.6)	188 (99.5)	1 (0.5)	186 (98.4)	3 (1.6)
P-value*	0.517		0.804		0.856		0.899		0.942		0.899	
Univariate p-value†	1.000		0.996		0.930		0.995		0.913		ND	
Multivariate p-value‡	0.622		0.637		0.967		0.981		0.965		0.955	
<i>Cytomegalovirus</i>												
Positive	134 (70.5)	56 (29.5)	179 (94.4)	11 (5.8)	184 (96.8)	6 (3.2)	187 (98.4)	3 (1.6)	189 (99.5)	1 (0.5)	187 (98.4)	3 (1.6)
Negative												
P-value*	0		0		0		0		0		0	
Univariate p-value†	-		-		-		-		-		-	
Multivariate p-value‡	-		-		-		-		-		-	
Multivariate p-value‡	-		-		-		-		-		-	
<i>Rubella</i>												
Positive	116 (68.6)	53 (31.4)	159 (94.1)	10 (5.9)	164 (97.0)	5 (3.0)	166 (98.2)	3 (1.8)	168 (99.4)	1 (0.6)	167 (98.8)	2 (1.2)
Negative	18 (85.7)	3 (14.3)	20 (95.2)	1 (4.8)	20 (95.2)	1 (4.8)	21 (100)	0	21 (100)	0	20 (95.2)	1 (4.8)
P-value*	0.106		0.831		0.656		0.538		0.724		0.215	
Univariate p-value†	0.822		0.244		0.375		0.985		0.851		ND	
Multivariate p-value‡	0.264		0.904		0.912		0.501		0.833		0.199	

\*Chi-square test used to compare between seropositivity and clinical conditions. †Fisher exact test used for univariate comparisons.

‡Linear logistic regression for multivariate comparisons. ND - not done.

reporting a high incidence of abortion, premature delivery and stillbirths associated with high rates of CMV seropositivity.<sup>5</sup>

Little has changed regarding the TORCH status and has remained unaltered for more than a decade, as evidenced from a study conducted in Makkah, KSA, in 2002. The present study shows IgG antibodies to *T. gondii* at 27.4%, compared to 35.6% in the Makkah study. Furthermore, the antibody prevalence of CMV IgG (92.1%), rubella IgG (93.3%), HSV-1 IgG (90.9%) and HSV-2 IgG (27.1%) were slightly low compared with the present study, with the exception of HSV-2.<sup>14</sup>

Our results showing high IgG rubella positivity are corroborated by the results of premature labor, IUDs, low birth weight and congenital malformations (wherever information was available), and were in good agreement with previously published studies.<sup>14</sup> Immunoglobulin G levels for rubella clearly indicate the success of the 1982 combined vaccination policy against rubella in KSA. However, the increase in poor obstetric outcomes and congenital anomalies (not specific for rubella) needs further investigation.<sup>15</sup>

These results clearly suggest that the prevalence of TORCH agents remains high in KSA and can contribute to various congenital infections and other complications. Periodic screening for antenatal mothers thus becomes necessary to avoid TORCH complications, which results in pregnancy-related and neonatal morbidity.

**Study limitations.** Our study demonstrated an association between IgG antibody positivity of the TORCH panel with previous pregnancy outcomes such as IUDs, abortions, premature labor, congenital malformations, microcephaly, and low birth weights; however, the lack of a higher sample size limited us in obtaining a statistically significant correlation. Further, very few studies are available from this part of KSA, and we, as authors, believe that our results are only part of the larger picture of TORCH infections and their complications, which warrant further investigation.

In conclusion, it is evident that there is an association between TORCH infections and pregnancy-related complications from our observations in the Abha region, KSA. Past infections, as reported here, warrant an independent study in female populations post-puberty. We were also able to link pregnancy outcomes with the TORCH panel results of the study group, indicating

the sustained presence of TORCH infections that are prevalent in these regions. Additionally, these results clearly highlight the need for additional multicenter studies as well as therapeutic and management plans to address the burden of TORCH infections, especially CMV in our case.

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