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Research Article

Role of TORCH infection in recurrent pregnancy loss

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Abstract

Background: Recurrent pregnancy loss (RPL) is defined as loss of two or more pregnancies before 24 weeks by both the European Society of Human Reproduction and Embryology and the American Society for Reproductive Medicine. **Aim:** To conduct a comprehensive evaluation of how cytomegalovirus and toxoplasmosis infections contribute to recurrent pregnancy loss. **Methods:** The present study was carried out at the Clinical Pathology Department, Faculty of Medicine, Minia University, Minia, Egypt, it was conducted on 80 subjects divided into: 20 apparently healthy individuals as a control group (group II) and 60 patients of women with recurrent abortion (group I), they were subdivided into 2 subgroups (Abortion at 1st trimester group Ia) and Abortion at 2nd trimester Ib). Routine laboratory investigations were done to all participants. The Toxoplasma assay and the CMV assay were measured by ELISA. **Results:** Results revealed that patients with recurrent abortion showed no statistically significant cytomegalovirus and toxoplasmosis infection when compared to control group. **Conclusion:** The findings of this study indicate that there is no statistically significant association between cytomegalovirus and toxoplasmosis infections and recurrent pregnancy loss when comparing affected patients to a control group. Despite the established importance of cytomegalovirus and toxoplasmosis infections in various pregnancy complications, our results suggest that these infections may not play a significant role in recurrent abortion in the studied cohort. This highlights the need for further research to explore other potential etiological factors and to better understand the complex interplay of infections and recurrent pregnancy loss. Future studies should aim to include larger sample sizes and consider additional variables to provide a more comprehensive understanding of the causes behind recurrent pregnancy loss.

Key words: TORCH, Toxoplasmosis, cytomegalovirus, recurrent pregnancy loss, ELISA

Introduction

Recurrent pregnancy loss (RPL) is characterized by the loss of two or more pregnancies before 24 weeks of gestation, as defined by the European Society of Human Reproduction and Embryology. The American Society for Reproductive Medicine similarly describes RPL as two or more failed clinical pregnancies [1]. Despite its prevalence, the exact causes of RPL remain unclear. Known factors include abnormal parental karyotype, antiphospholipid syndrome, infectious agents, and uterine anomalies, which account for about 50% of cases; the remaining 50% have unknown causes [2].

TORCH infections comprising toxoplasmosis, other agents, rubella, cytomegalovirus (CMV), and herpes simplex virus (HSV) are known to cause significant pregnancy complications. These infections are often asymptomatic or mild in the mother but can lead to severe fetal outcomes such as congenital anomalies, fetal growth restriction (FGR), intrauterine fetal death (IUFD), recurrent pregnancy loss (RPL), and stillbirth.

Toxoplasmosis, caused by Toxoplasma gondii, is transmitted through contaminated food, water, or undercooked meat. Although typically asymptomatic in pregnant women, it can lead to pregnancy loss or fetal malformations [3]. CMV, spread via contact with infected saliva, urine, or genital secretions, can cause intrauterine growth retardation, microcephaly, and other severe symptoms in neonates, including long-term disabilities like vision and hearing loss [4].

HSV infection during pregnancy can lead to complications such as miscarriage or severe neonatal infections. Early diagnosis and management are crucial to reduce risks to the fetus.

Because TORCH infections are often asymptomatic, diagnosing them based solely on clinical symptoms is challenging. Serological tests are essential for accurate diagnosis, with the TORCH panel testing for IgM antibodies against toxoplasma, rubella, HSV, and CMV proving particularly useful [5].

Early detection through the TORCH panel allows for timely intervention, potentially mitigating the adverse effects of these infections on pregnancy and improving outcomes for both mother and child.

Aim of the work

The aim of this study was to conduct a comprehensive evaluation of how cytomegalovirus and Toxoplasmosis infections contribute to recurrent pregnancy loss

Subjects and Methods

The present study was carried out at the Clinical Pathology Department, Faculty of Medicine, Minia University, Minia, Egypt, during the period from November 2023 to June 2024. The hospital ethics committee approved this study, and written consent was obtained from each case. (Approval number 875:10:2023). it was conducted on 80 subjects divided into: 20 apparently healthy individuals as a control group (group II) and 60 patients (group I) of women with recurrent abortion classified later according to their presentation. They were selected from the Obstetrics and Gynecology Department, Faculty of Medicine, Minia University Hospital, they were subdivided into 2 subgroups (Abortion at 1st trimester group Ia) and Abortion at 2nd trimester Ib). Routine laboratory investigations were done to all participants. Exclusion criteria for participation in the trial were a Chronic disease as diabetes, hypertension, cardiac diseases, endocrinal disturbances. History of any anatomical abnormality, intrauterine adhesions and cervical incompetence, History of oral anticoagulant intake and laboratory testing (including CBC, RBS, renal function test, CRP, PC, INR, APTT, Anticardiolipin, Lupus anticoagulant and TORCH infection) were all performed on patients and controls, respectively.

The analysis of the data was carried out using the IBM SPSS version 27 statistical package software (IBM; Armonk, New York, USA). Data was tabulated and presented using various tests: frequency, calculation and the mean, standard deviation, IQR, Chi square test for qualitative data between control and study (acute and chronic variables). For parametric data, One-way ANOVA was used for comparisons between two groups. For non-parametric data, Mann-Whitney U test was used for comparisons between two groups. Kruskal-Wallis test followed by Dunn's test was used for comparisons between more than two groups. A p-value less than 0.05 was considered sign.

Results

The age in group Ia ranged from 18 to 42 years with median 27.5, in group Ib ranged from 20 to 39 years with median 30 and in group II ranged from 21 to 35 years with median 28. There was no statistically significant difference between studied groups **(Table I)**

The gravidity in group Ia ranged from 3 to 11 times with median 6, in group Ib ranged from 3 to 10 times with median 7 and in group II ranged from 2 to 6 times with median 3.5. There was statistically significant difference between studied groups **(p =<0.001)** (**Fig. 1) (Table I)**

Regarding frequency of abortion, showed that abortion in group Ia ranged from 2 to 6 times with median 2, in group Ib ranged from 2 to 7 times with median 3 and while there is no abortion in group II. There was statistically significant difference between studied groups **(p =<0.001)** (**Fig. 2) (Table I)**

Table I: Comparison between the studied groups regarding demographic data.

Variables	Group I		Control N=20	P- value	Ia vs Ib	Ia vs control	Ib vs control
	Group Ia N=32	Group Ib N=28					
Age (years) Mean ± SD Range	28.97 ±5.82 (18-42)	30.61 ±4.56 (20-39)	27.65 ±3 (21-35)	0.110	0.391	0.603	0.097
Gravida Range Median IQR	(3-11) 6 (4-7)	(3-10) 7 (6-8)	(2-6) 3.5 (2-5)	**<0.001****	0.077	**<0.001****	**<0.001****
Abortion Mean ± SD Range Median IQR	2.56 ±0.95 (2-6) 2 (2-3)	3.43 ±1.37 (2-7) 3 (2-4)	0 ±0 (0-0) 0 (0-0)	**<0.001****	**<0.001****	**<0.001****	**<0.001****

: *Significant level at p value< 0.05.

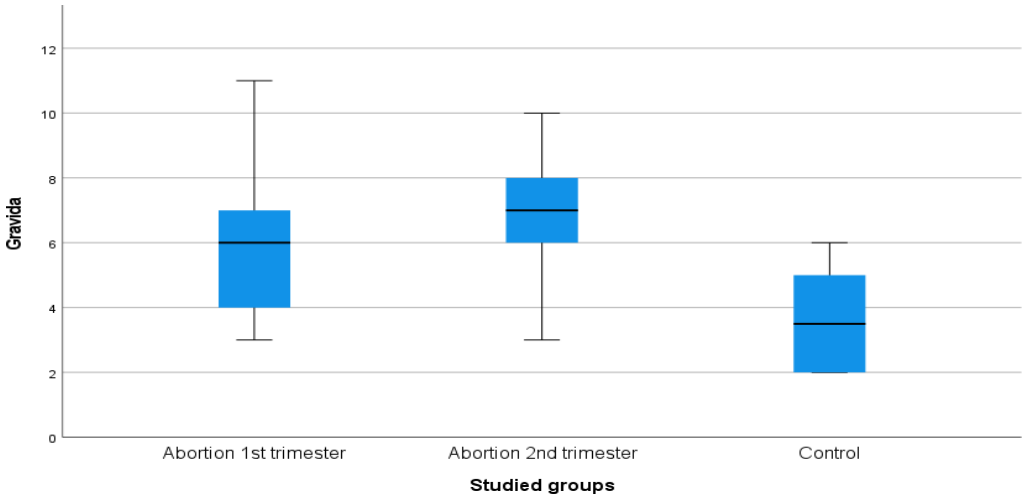


Figure (1): Gravida ranges in the studied groups.

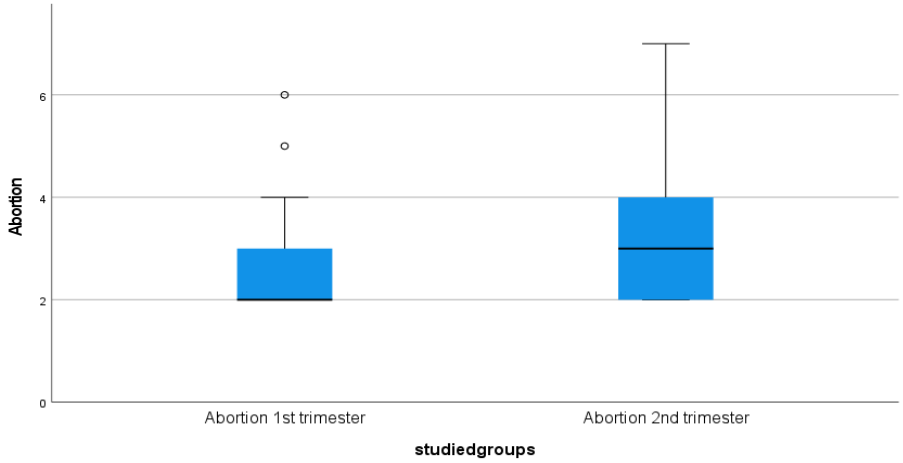


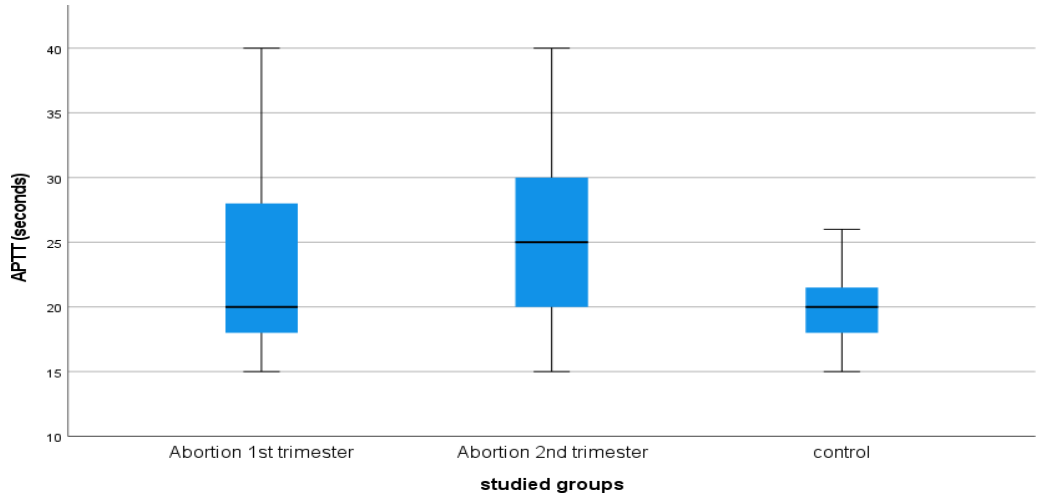
Figure (2): Abortion ranges in the studied groups

Regarding INR, in group Ia the median was 1.02 with IQR (1-1.09), in group Ib the median was 1.035 with IQR (1-1.1) and in group II the median was1 with IQR (1-1.1), there was no statistical significant difference between studied groups (P =0.877) **(Table II)**

Regarding Activated partial thromboplastin time, in group Ia the median was 20 with IQR (18-27), In group Ib it ranged from the median was 25 with IQR (20-30) and group II the median was 20 with IQR (18-20.75), There was statistical difference between the studied groups **(p=0.024*) (Fig. 3) (Table II)**

(Table II): Comparison of coagulation parameters among studied groups:

Variables	Group I		Group II N=20	P-value	Ia vs Ib	Ia vs control	Ib vs control
	Group Ia N=32	Group Ib N=28					
INR							
Mean ± SD	1.06 ±0.09	1.07 ±0.09	1.06 ±0.11				
Range	(1-1.3)	(1-1.3)	(1-1.3)	0.877	0.885	1.000	0.915
Median	1.02	1.035	1				
IQR	(1-1.09)	(1-1.1)	(1-1.055)				
APTT (seconds)							
Mean ± SD	22.63 ±6.69	24.32 ±5.93	19.7 ±3.13	**0.024***	0.490	0.169	0.018
Range	(15-40)	(15-40)	(15-26)				



: *Significant level at p value< 0.05.

(Fig. 3): APTT (seconds) ranges in the studied groups

As regard Cytomegalovirus and Toxoplasma screening, it was found that there was no statistical significant difference between the studied groups **(Table III)**.

Table (III): Comparison of cytomegalovirus and toxoplasmosis parameters among studied groups:

Variables	Group I		Group II N=20	P-value	Ia vs Ib	Ia vs control	Ib vs control
	Group Ia N=32	Group Ib N=28					
Cytomegalovirus IgM (u/ml)							
Mean ± SD	3.92 ±1.26	4.18 ±1.45	3.27 ±1.24	0.089	0.283	0.688	0.085
Range	(2.01-6.29)	(2.08-7.26)	(2.14-6.25)				
Median	3.62	4.24	3.12				
IQR	(3.18-5.21)	.2075-5.21)	(2.2-4.3)				
Cytomegalovirus IgG (u/ml)							
Mean ± SD	44.67 ±34.53	49.55 ±26.76	39.13±51.8	0.635	0.869	0.862	0.608
Range	(4-126)	(5-107)	(3.24-198)				
Median	35.5	50	9				
IQR	(21.35-68.45)	(29.9-61.5)	(4.275-66.4)				
Toxoplasma IgM (u/ml)							
Mean ± SD	2.74 ±1.15	3.27 ±0.87	2.75 ±1.26	0.120	0.144	0.999	0.231
Range	(1.07-5.24)	(1.93-5.24)	(1.05-5.23)				
Median	2.81	3.185	2.515				
IQR	(1.875-3.55)	(2.89-3.6)	(1.99-3.36)				
Toxoplasma IgG (Iu/ml)							
Mean ± SD	0.95 ±0.88	0.57 ±0.68	0.63 ±0.83	0.426	0.476	0.999	0.528
Range	(0.11-2.44)	(0.09-2.87)	(0.01-2.31)				
Median	0.39	0.2545	0.2				
IQR	(0.21-1.9)	(0.18-0.54)	(0.16-0.53)				

: *Significant level at p value< 0.05.

Discussion

Pregnancy loss (PL) is a common complication, affecting about 15% of couples. Recurrent pregnancy loss (RPL) is typically defined as three or more consecutive losses before 24 weeks, though some guidelines require only two. RPL affects approximately 1–3% of couples [6]. The causes of RPL are often multifactorial and not always identifiable, making evidence-based treatment strategies challenging. Known risk factors include chromosomal abnormalities, endocrine issues, thrombophilia, autoimmune disorders, and uterine abnormalities [7].

Pathogenic mechanisms suggested for RPL include insufficient trophoblast invasion, vilitis, and microthrombi in placental vessels [6]. Patients with RPL are at higher risk for complications in subsequent pregnancies compared to the general population [8]. Identifying biomarkers that predict future pregnancy loss could enhance our understanding of RPL.

This study aimed to assess the role of Toxoplasma and cytomegalovirus CMV in RPL. It found no significant differences in maternal or gestational age between RPL and control groups. However, RPL patients had higher rates of previous abortions and greater gravidity. Notably, those who experienced first-trimester abortions had a higher rate of previous abortions compared to those with second-trimester losses.

Coagulation parameters revealed no significant differences in Prothrombin concentration (PC) and INR. However, activated partial thromboplastin time APTT was significantly

increased in second-trimester abortion patients compared to controls. [9] and [10] found similar associations, while [11] reported shortened APTT values, highlighting variability in findings.

TORCH infection screening showed no significant differences between RPL and control groups. [12] and [13] noted that TORCH co-infections are linked to higher abortion risk, with significant findings for Toxoplasma and CMV infections in some cases, aligning with the current study's results. There was a significant difference between patients with RPL and control in acute infection of T.gondii and in the primary infection of CMV but other infections showed no significant difference which agree with other findings.

Conclusions

Maternal infections are a significant contributor to fetal morbidity and loss, with early identification and effective treatment being crucial for preventing these adverse outcomes. Screening and early diagnosis of TORCH infections in high-risk women are essential for timely intervention and management, which can substantially reduce perinatal morbidity and mortality. This study demonstrates that infections caused by Toxoplasma and Cytomegalovirus are prevalent among women and are particularly associated with early pregnancy loss, notably in the first trimester.

Conflict of interest: None.

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