Specific IgM to Toxoplasma gondii, Rubella and Cytomegalovirus Infection in First Trimester Miscarriage with Seasonal Variation

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Abstract

**Objectives**: To assess the prevalence of IgM antibodies against *Toxoplasma gondii*, Rubella and Cytomegalovirus (CMV) from sera of miscarriage women during first trimester. In addition to estimate information about abortion rates by seasonal variation to establish basic information for future diagnostic and prophylactic measures in maternal and child health care.

**Material and Methods**: A total of 639 miscarriage women aged 18 to 30 years old [mean age 24.2±4.5 years] were enrolled in this cross-sectional study. Blood samples were collected and sera were separated for estimation of IgM antibodies against *Toxoplasma gondii*, Rubella and CMV, which were assayed by ELIZA [enzyme linked immune sorbent assay] method using Biocheck, Inc foster city, CA according to manufacturer's instructions.

**Results**: 639 samples were tested in this studies, seropositivity for anti-toxoplasma IgM antibodies was found in 70 [11%]. The seropositivity for anti-rubella IgM and anti-CMV IgM were found in 73 [11.4%] and 341 [53.4%] respectively, while 155 [24.2%] of the subjects tested were negative for IgM antibodies of the screened pathogens. Seasonal pattern was highly significant [p<0.05] for average monthly number of miscarriage women that associated with IgM seropositivity with major peak during spring and summer seasons.

**Conclusion**: Widespread serologic screening before pregnancy is essential and because of the high seropositivity of Toxoplasma, Rubella and CMV association in pregnant women, preventive measures should be taken. Moreover, abortion cases were significantly associated with relatively hot season than that of cold season, so management facilities should be readily available during the high frequency of abortion.

**Key Words**: Miscarriage, IgM antibody, Toxoplasma, Rubella, CMV

Introduction

The first trimester of pregnancy is an important period often fraught with complications like bleeding and pain, leading to severe apprehension in the mother[1]. Recurrent spontaneous abortion (RSA) is one of the important complications in pregnancy, its incidence is 0.5-1%, and the etiology of RSA is varied, and includes maternal or paternal chromosomal aberrations take off, uterine anatomic abnormalities, endocrine disorders, infections and reproductive autoimmune defects[2,3]. TORCH [Toxoplasmosis, Rubella, Cytomegalovirus (CMV) and herpes

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simplex virus [HSV] ,that can cause illnesses in pregnant women and may cause birth defects in their new borne .These entire infectious agents induce a shift of immune response during pregnancy, from Th2 –Th1 and apoptosis which can be observed clinically as an abortion process[4]. Primary infections with Toxoplasma gondii, rubella virus ,and cytomegalovirus [CMV] in pregnant women can lead to serious complications that initially unapparent or asymptomatic[5] .The rate of spontaneous abortion from foetal infection by the infectious agents like TORCH group and others such as Treponema pallidum is believed to range from 10-15%[6] .The risk of miscarriage increases in some maternal infections ,especially during the early gestation , can result in fetal loss or malformations because the ability of the fetus to resist infectious organisms is limited , and the fetal immune system is unable to prevent the dissemination of infectious organism to various tissues[7] . There are also reports saying that most of the infection of the mother will not result in fetal infection[8] . However ,the etiology is undetermined in 40-60% of women with recurrent abortion[3,9].About half of the concepts of recurrent spontaneous abortion have an abnormal Karyotype[10]. Diagnosis of acute Toxoplasmosis, Rubella and CMV infection can be established by demonstration of seroconversion in paired sera or by demonstration of specific IgM antibodies . These maternal infections with adverse outcome are initially in apparent or asymptomatic and are thus difficult to diagnose on clinical grounds[11] a descriptive study investigators observed variation in the frequency of abortion in different months in comparison to other cases. Abortion cases were significantly associated with relatively hot season [March-August ] than that of cold season [September-February , P<0.01 ][12] . The presence of significant seasonal variation in the monthly rate of spontaneous abortion is important for public health ,that research’s should be conducted to determine the etiology of spontaneous abortion with emphasis on the months above average rate, in addition to based as monitoring system which is increasingly important as a public concern about the environment’s role in reproductive health[13] .

The aim of this study was to find out the significance of TORCH infections in first trimester pregnancy loss related to seasonal patterns .

Materials and Methods

A total of [639] first trimester miscarriage women attended the Obstetrics and Gynecology Department of Al-Ramadi Teaching Hospital, Anbar Medical College , Al-Anbar province ,West of Iraq ,were subjected to this cross-sectional descriptive study ,between January 2008 and December 2009 . Women ranged from 18-30 years were enrolled, and the approval of Teaching Hospital ethical Committee with informed written consents were obtained from all considered patients under the study prior to sample collection. Miscarriage was diagnosed by senior Gynecologists ,using medical , clinical and available diagnostic parameters. Serum samples were collected and separated for IgM estimation of Toxoplasma gondii , Rubella and Cytomegalovirus[CMV] , Enzyme Linked Immune Sorbent Assay [ELISA] was used according to the instruction for detection of Toxoplasma/IgM [ Biocheck , Inc Foster City CA], Rubella /IgM [ Biocheck , Inc Foster City ,CA ] ,CMV./ IgM [ Biocheck ,Inc Foster City, CA] and results were registered as mean optical density [OD] readings .The mean gestational age [GA] at the time of abortion was [9.9±0.55]weeks. Statistical analysis is done using the SPSS software for microcomputers, and Chi
Square test is used to assess statistical significance

**Results**

The mean age of participants in this study was (24±4.5) years [minimum 18, maximum 30 y] of the [639 ] aborted women identified in 12 month study period the positivity for anti-toxoplasma IgM antibodies was found in 70 [11%] .The seropositivity for Rubella IgM was observed in 73 [11.4% ], while 341[53.4%] tested women showed seropositive IgM against Cytomegalovirus [CMV ] .There were 155 [24.2%] patients of unknown or (other) causes of miscarriage , as illustrated by table [1 ] .The seasonal pattern for average monthly number of miscarriage women associated with seropositivity of Toxoplasma IgM was significant [p<0.05 ] with a major peak during spring [March to May ] in 33 [47%] and minor peak during winter [December to February ] in 9 [13%] , table [2] .The estimated monthly number of fetal loss that associated with seropositivity of Rubella IgM was significant [p<0.01] which had a major peak during spring 43 [59%] and minor peak during summer in 5[6.7%]. table [3]. Furthermore, table [4] showed a highly significant [p<0.01] average number of miscarriage women associated by months with seropositivity of IgM against CMV .The major peak during spring in 141 [41.4%] , and minor peak during winter in 38 [11%] .

**Table 1.Frequency and percentage of seropositivity of anti - toxoplasma , anti- rubella , and anti - CMV antibodies in miscarriage women**

<table>
<thead>
<tr>
<th>Type of Antibody</th>
<th>Frequency</th>
<th>percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti - Toxoplasma/ IgM</td>
<td>70</td>
<td>11%</td>
</tr>
<tr>
<td>Anti - Rubella / IgM</td>
<td>73</td>
<td>11.4%</td>
</tr>
<tr>
<td>Anti - CMV / IgM</td>
<td>341</td>
<td>53.4%</td>
</tr>
<tr>
<td>Unknown</td>
<td>155</td>
<td>24.2%</td>
</tr>
<tr>
<td>Total</td>
<td>639</td>
<td>100%</td>
</tr>
</tbody>
</table>

**Table 2. Frequency and distribution of seropositivity of anti – toxoplasma IgM according to seasonal variation**

<table>
<thead>
<tr>
<th>Season</th>
<th>Seropositivity of toxoplasma IgM</th>
<th>Seronegative of toxoplasma IgM</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Winter</td>
<td>9(13%)</td>
<td>76(13.4%)</td>
<td>85(13.3%)</td>
</tr>
<tr>
<td>Spring</td>
<td>33(47%)</td>
<td>179(31.5%)</td>
<td>212(33.2%)</td>
</tr>
<tr>
<td>Summer</td>
<td>18(25.7%)</td>
<td>184(32.3%)</td>
<td>202(31.6%)</td>
</tr>
<tr>
<td>Autumn</td>
<td>10(14.3%)</td>
<td>130(22.11%)</td>
<td>140(21.9%)</td>
</tr>
<tr>
<td>Total</td>
<td>70(100%)</td>
<td>569(100%)</td>
<td>639(100%)</td>
</tr>
</tbody>
</table>

X2 = 4.5 , significant ( p < 0.05 )

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Table 3. Frequency and distribution of seropositivity of anti – rubella IgM according to seasonal variation

<table>
<thead>
<tr>
<th>Season</th>
<th>Seropositivity of rubella IgM</th>
<th>Seronegative of rubella IgM</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Winter</td>
<td>8(11%)</td>
<td>77(13.6%)</td>
<td>85(13.3%)</td>
</tr>
<tr>
<td>Spring</td>
<td>43(59%)</td>
<td>169(29.9%)</td>
<td>212(33.2%)</td>
</tr>
<tr>
<td>Summer</td>
<td>5(6.7%)</td>
<td>197(34.8%)</td>
<td>202(31.6%)</td>
</tr>
<tr>
<td>Autumn</td>
<td>17(23.3%)</td>
<td>123(21.7%)</td>
<td>140(21.9%)</td>
</tr>
<tr>
<td>Total</td>
<td>73(100%)</td>
<td>566(100%)</td>
<td>639(100%)</td>
</tr>
</tbody>
</table>

X² = 4.1 , significant ( p < 0.01 )

Table 4. Frequency and distribution of seropositivity of anti – CMV IgM according to seasonal variation

<table>
<thead>
<tr>
<th>Season</th>
<th>Seropositivity of CMV IgM</th>
<th>Seronegative of CMV IgM</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Winter</td>
<td>38(11%)</td>
<td>47(15.8%)</td>
<td>85(13.3%)</td>
</tr>
<tr>
<td>Spring</td>
<td>141(41.4%)</td>
<td>71(23.8%)</td>
<td>212(33.2%)</td>
</tr>
<tr>
<td>Summer</td>
<td>110(32.3%)</td>
<td>92(30.9%)</td>
<td>202(31.6%)</td>
</tr>
<tr>
<td>Autumn</td>
<td>52(15.2%)</td>
<td>88(25.5%)</td>
<td>140(21.9%)</td>
</tr>
<tr>
<td>Total</td>
<td>341(100%)</td>
<td>298(100%)</td>
<td>639(100%)</td>
</tr>
</tbody>
</table>

X² = 5.5 , significant ( p < 0.01 )

Discussion

Toxoplasma, Rubella and CMV are known to cause infection in utero, and are often responsible for abortion and other complications .There is considerable variation in the prevalence of these agents among the women of child bearing age in different geographical areas[14] . In this study , IgM against Toxoplasma was observed in 70 [11%] of miscarriage women . This rate is consistent with the 11.6% and 13.1% observed rates by Kaur et al,1999 in Delhi[15],and Yasodhara et al ,2001[16], while the overall Toxoplasma gondii IgM seroprevalence observed by this study was higher to cross-sectional studies from Sudia Arabia [5%][17],United Arab Emirates [3%][18] and Qatar [5.2%][19] .

The present study showed that Toxoplasma gondii infection was highly prevalent in subjected women associated with adverse outcome of pregnancy. Takeoff A recent study shows a rising seropositivity to Toxoplasma in women with bad obstetric history [BOH][20] .In our region ,the climate is hot ,and water supplies are unhygienic . People also frequently eat undercooked meat[21] .These factors may be the most likely causes for the elevated Toxoplasmosis rate found in this study In addition , the study was conducted on high risk group , and the reference hospital surrounded by rural areas where they close contact with contaminated soil with sporulated oocysts during gardening.

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Moreover, the low education level concerning Toxoplasma epidemiology may play an important role in the high rate of infection\textsuperscript{[22]}. However the present study demonstrated that, IgM antibodies to Rubella were found in 11.4% miscarriage women which is agree with other studies of Sharma et al\textsuperscript{[23]} and Sebastian et al\textsuperscript{[24]}, whereas Yasodhara D et al\textsuperscript{[25]}, Kishere J et al\textsuperscript{[26]} and Turbad Kar et al\textsuperscript{[27]} reported that Rubella IgM positivity as 6.5%, 10.3% and 26.8% respectively. The risk of intra-uterine Rubella infection is maximal in the first few weeks of pregnancy and affects fetal development\textsuperscript{[28]}. A positive IgM antibodies were observed in 53.45% of the miscarriage women associated with CMV infection. This rate is higher than the incidence of 29.5% reported by Shash et al\textsuperscript{[14]}, Yasodhara et al\textsuperscript{[25]} and Kapil et al\textsuperscript{[29]}. Cytomegalovirus [CMV] infection is transmitted directly from person to person in urine, saliva and genital secretions\textsuperscript{[30]}. Poor socioeconomic conditions that are characterized by overcrowding and a lack of hand hygiene, provide CMV transmission\textsuperscript{[31]}. Seasonal variation in the distribution of miscarriage seasons had been observed in this study. The data related to abortion showed a significant increase in take-off incidence in spring 47% and summer 25.7% for Toxoplasma, table[2], and spring 59% , autumn 23.3% for Rubella, table [3], while 41.4% in spring and 32.3% in summer for CMV, table [4]. Our data analysis indicates that there is significant seasonal variation in the monthly rate of miscarriage [p<0.05]. Seasonal variation, particularly spring and summer. Seasonal pattern of miscarriage peak is more likely to be associated with environmental, behavioral, social stimuli, and physiological response as well. Various theories have been advanced to explain seasonal variation in outcomes of pregnancy\textsuperscript{[32,33]}. Intensified social activity provides greater opportunities for sexual encounters.

The case for behavioural vacation\textsuperscript{[34,35]} and the calendar year associated with festivities\textsuperscript{[36]} Abortion cases were significantly associated with relatively hot season [March to August] than that of cold season [September to February, p<0.01]\textsuperscript{[37]}.

In conclusion, serologic screening before pregnancy is important, and because of high seropositivity of Toxoplasma, Rubella and CMV, the country's health authorities should be alerted and preventive measures should be taken. It is therefore recommended the antenatal measures should be routinely screened for these agents, because early diagnosis will help in proper management. The seasonal variation in the monthly number of aborts are more likely to be explained when the seasonal variation of biological and environmental determinant's are understood.

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