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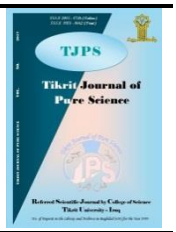

Detection of infection by rubella and cytomegalovirus among women exposed to abortion in Ninavah province

Mahmood Nafi Mahmood[1] , Adeeba Younis Shareef[2]

[1] *Department of Biology , College of Science , Tikrit University , Tikrit , Iraq*
[2] *Department of Biology , College of Science , Mosul University , Mosul, Iraq*

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Corresponding Author:

Name: Mahmood Nafi

E-mail:

mahmoodnafi.mn@gmail.com

Tel:

ABSTRACT

The study aims to correlate infection with rubella, cytomegalovirus and abortion at different age groups.

Blood samples were collected through the period between beginning of February to the end of September 2017, one hundred and twenty-seven women exposed to abortion and thirty apparently health controls. Serum samples were tested for IgM and IgG antibodies for rubella and cytomegalovirus.

The results showed that CMV was the most common infection with high level of IgM antibodies (15.7%) and IgG (12.5%), only 0.7% of the cases gave positive results for rubella IgM, and 6.2% had rubella IgG while the control group only 6.6% had CMV IgM, and 3.3% had CMV IgG antibody. All the age groups did not show infection with rubella except age 25-31 years as 2.1% and 8.5% had IgM and IgG respectively. The highest rate of infection with CMV was at age group 25-31 years (21.2%) then age group 18-24 years (13.7%). Most of the patients experienced two abortions were reported at age group 25-31 years, 1.5% and 4.7% of CMV infected patient experienced 3 and 2 respectively while 1.5% of rubella infected patients had only one abortion, 18.1% of the patients with CMV experienced 2 abortions had cut off >1.25. Hundred % of the patients with rubella had cut off value of > 1.25 experienced one abortions.

Introduction

Rubella virus infection (German measles)

Rubella virus is considered a human pathogen that belongs to the Toga virus family of RNA viruses and is generally a mild disease with nonspecific symptoms[1]. However, it can lead to congenital rubella syndrome (CRS) when infection happens during pregnancy [2]. Rubella virus infection has often been related with adverse pregnancy outcomes in early pregnancy because of its teratogenic effects. It is regarded among the most common reasons of spontaneous abortion aside from causing congenital rubella syndrome [3]. It is a contagious viral infection that in pregnant women leads to the infection of a developing fetus, causing fetal death or congenital rubella syndrome [4].

Infection causes damage in nearly 90% of the surviving infants in the first eight to ten weeks of pregnancy, where multiple defects are common [5]. Congenital rubella happens when the rubella virus in the mother influences the developing fetus at a vital time throughout the first three months of pregnancy. After the 4th month, the mother's rubella infection has a small probability to damage the developing fetus [6].

Cytomegalovirus (CMV) infection

The human cytomegalovirus, (CMV) is regarded as the most widespread congenital viral infection globally and may be asymptomatic forms (90% of cases) to severe fetal harm and, in rare occasions, death because of abortion [7].

Cytomegalovirus is a worldwide pathogen with an estimated 40–70% of the world's population carrying evidence of infection [8].

Normally, CMV is obtained through contact with infected individuals' secretions (any fluid can transmit the virus) in childhood or in early adult life, the disease seldom has serious clinical manifestations in immunocompetent individuals. The virus turns

latent after the preliminary immune response, resting mainly in cells of myeloid lineage [9].

Primary maternal CMV infection essentially leads to mother-child transmission, this infection holds a risk of transmission of around 40 %, in the last weeks of gestation, the rate of transmission increases to about 78%. There have been cases reported of CMV transmission caused by nonprimary infection in just 1 – 2.2 % of cases [10]. Primary maternal infection occurred in the first trimester of pregnancy is often related to the extent of fetal-newborn injury, for example severe brain damage [11].

Aim of the work

- To determine the presence of rubella and CMV viruses in patient's serum.
- To evaluate the correlation between the presence of infection with rubella and CMV viruses and abortion at different age groups.

Study Design

In the present study blood was collected from one hundred women at child-bearing age exposed to abortion or had repeated abortion. All blood samples were tested for rubella and CMV. Blood samples were taken from the period between beginning of February 2017 to the end of September 2017.

- Three to five ml of blood samples were drawn aseptically from all enrolled cases and controls for routine investigations.
- All the serum samples collected for the study and control groups were tested for rubella and CMV infection by commercially- available (ELISA) kits. The results were read by a Microwell reader and compared in a parallel manner with controls; optical density was read at 450 nm on an ELISA reader.

Results and Discussion

The results in Table 1 showed that CMV was the most common infecting agents in this study. The number of infected women had high rate of IgM antibodies were 20 (15.7%), which was more than those with high IgG 16 (12.5%). Rubella IgM accounted for the lowest number of females with just one case (0.7%), on the other hand, rubella IgG was recorded in 8 cases (6.2%). The control group showed that out of 30 subjects, 6.6% of the women infected with CMV had IgM, while only 3.3% of them infected with CMV had IgG.

Table 1: Seropositive of rubella and CMV in women exposed to pregnancy loss.

Type of infection	No. of positive cases IgM		Percentage		No. of positive cases IgG		Percentage	
	Test	Control	Test	Control	Test	Control	Test	Control
Rubella	1	0	0.7%	0	8	0	6.2%	0
Cytomegalovirus	20	2	15.7%	6.6%	16	1	12.5%	3.3%

This result was in agreement with Nirmal, *et.al.* [12] in Northern India, who showed that CMV was found to be the most common infecting agent followed by rubella infections. Primary infection in pregnancy has a higher incidence, especially in women of rural population. This infection is usually asymptomatic, thus posing trouble in clinical diagnosis. Kishore, *et.al.* [13] reported that IgM positivity to cytomegalovirus and rubella were 30% and 15% respectively. None of the controls had IgM antibodies to any pathogen.

The relationship between infection with CMV and rubella virus IgM and IgG in different age groups is illustrated in Table 2. As shown in Table 2, out of 47 patients within the age group 25-31 years, IgM to rubella was found in one case (2.1%) and IgG was found in 4 cases (8.5%). Also, IgG to rubella was found in 4 cases (7.8%) of women within the age group 18-24 years. Alshami, *et.al.* [14] concluded that 81.7% of women suffering from previous history of recurrent abortions, 4.48% of them had rubella IgM and IgG. The highest rate of infection was detected in those within the age group varied between 17 and 44 years with both IgG and IgM antibodies. Olajide, *et.al.* [4] also showed a seroprevalence of 38.8% (62 of 160) and 93.1% (149 of 160) for rubella IgM and IgG antibodies respectively among the pregnant women. The highest number of positive cases were found at age group 28–32 years and at age group 23-27 years.

Table 2: The relation between rubella and CMV IgG and IgM abs. and different age groups of the studied patients

Age of years	Total No.	No. of IgM positive	Percentage	No. of IgG positive	Percentage	No. of negative
Rubella						
18-24	51	0	0	4	7.8%	47
25-31	47	1	2.1%	4	8.5%	42
32-40	29	0	0	0	0%	29
Cytomegalovirus						
18-24	51	6	11.7%	8	15.6%	37
25-31	47	10	21.2%	4	8.5%	33
32-40	29	4	13.7%	4	13.7%	21

The highest rate of CMV infection was at the second age group (25-31 years) followed by the first age group (18-24 years) and then the third age group (32-40 years) as 10 (21.2%), 6 (11.7%) and 4 (13.7%) respectively, IgM antibodies for the three age groups, while the patients in the first age group showed IgG antibodies 15.6% followed by age group 3 and 2 in which the result for this immunoglobulin was 13.7% and 8.5% respectively. The results were in agreement with Munro, *et.al.* [15], who found that out of the 600

women tested, 259 (43.2%) had never been infected with CMV and 308 (51.3%) had a past CMV infection. The remaining 33 (5.5%) of women were CMV IgM positive. The CMV infection in the pregnant women in cohort study was found in women less than 20 years of age and between the ages of 20 to 30 years. Tiwari, *et.al.* [16] reported that out of 66.7 % of women infected with TORCH agents, 12.6% were CMV seropositive, and this infection was at highest rate in women within age group 21-25 years.

A number of abortions in relation to the age groups of the female patients included in the study were illustrated in Table 3. The patients in this study were divided in to three groups which were 18-24, 25-31 and 32-40 years all the patients experience abortion for one, two or more.

Table 3: Number of abortion in relation to the age groups in the studied patients

No.	Ages	Total no.	No. of abortions					
			One abortion	%	Two abortions	%	Three abortions	%
1	18-24	51	46	90.1%	4	7.8%	0	0%
2	25-31	47	38	80.8%	8	17%	2	4.2%
3	32-40	29	25	86.2%	4	13.7%	0	0%

The result in Table 3 showed that most of the patients with two abortions were reported in the second age group (25-31years) as eight patients out of the 47 (17%) had two abortion and two 4.2% had three abortions, followed by the third age group as 13.7% had two abortions, then the first age group in which only 7.8% had two abortions, while 90.1% of patients in this age group, and 86.2% of patients in the third group experienced one abortion. The results also corresponded with Alshami, *et.al.* [14], as they showed that the age of the gravidas varied between 17 and 44 years old. Out of 67 cases, the total rate of gravidas with one abortion recorded the highest rate 31(46.27%) patients while the lowest was 7(1.45%) patients recorded by gravidas with ≥4 abortion, 16(23.88%) had two abortions while 13(19.4%) patients had three abortions. Number of abortion times decreased gradually with the increase of gravidas age, in which one abortion recorded 60% and 47.62% among age groups 17-23 and 24-30 years respectively, while 4 times recorded the lowest rates (0% and 9.52%).

Table 4 showed the relationship between the cut off value of infection by CMV with a number of abortions experienced by those patients, the result showed that 18.1% of the patients with cut off (>1.25) experience 2 abortion, 72.7% experience one abortion and one patient experience three abortions, 22.2% experienced two abortions have a cut off value of (1< - 1.25), 66.6% experience one abortion and one patient experienced three abortions.

Table 4: The cut off value of CMV in relation to the number of abortions

No.	Cut off	No. of patients	No. of infected	No. of abortions					
				One abortion	%	Two abortions	%	Three abortions	%
1	1< - 1.25	9	9	6	66.6%	2	22.2%	1	11.1%
2	>1.25	11	11	8	72.7%	2	18.1%	1	9%

This result agreed with Sherkat, *et.al.* [17], who studied samples taken from 43 women with recurrent pregnancy loss (RPL), the study showed that 2.3% of them with (titer of 1) positive IgM of the RPL. Those patients had also positive IgG were considered as having recurrent or reactivated maternal infection. There were 39 (90.6%) of the cases of positive IgG in the RPL. The IgG titer below and above the cut-off (>0.8 or 16 IU/ml as positive). Also agree with Hamdan, *et.al.* [18] who found that out of these 231 pregnant women, 167 (72.2%) and 6 (2.5%) were seropositive CMV IgG and IgM respectively.

Table 5 showed the relationship between the cut off value of infection with rubella virus and the number of abortions experienced by those patients, the result showed that 100% of the patients with cut off value of (> 1.25) experienced one abortion, while no patients with cut off value (1<-1.25) experience abortion. The results of Mohammed [19] that observed the relationship between prevalence of rubella and the number of abortions, showed that the prevalence of rubella substantially escalated with the number of abortions. This indicates that the higher antibody titer, the higher the likelihood of abortions, which implies that those with the higher rate of abortion had the higher antibody titer. While Lulandala, *et.al.* [20], proposed that the prevalence of acute rubella infection as indicated by the existence of specific rubella IgM antibodies was found to be 9/268 with the positive cut off values of (≥1), viral infections throughout pregnancy have been related with poor pregnancy outcome.

Table 5: The cut off value of rubella virus in relation to the number of abortions

No.	Cut off	No. of patients	No. of infected	No. of abortions					
				One abortion	%	Two abortions	%	Three abortions	%
1	1< - 1.25	0	0	0	0%	0	0%	0	0%
2	>1.25	1	1	1	100%	0	0%	0	0%

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التحري عن الأصابة بفايروس الحصبة الالمانية والفايروس المضخم للخلايا لدى النساء المعرضات للأجهاض في محافظة نينوى

محمود نافع محمود[1] ، أديبة يونس شريف[2]

[1]قسم علوم الحياة ، كلية العلوم ، جامعة تكريت ، تكريت ، العراق

[2]قسم علوم الحياة ، كلية العلوم ، جامعة الموصل ، الموصل ، العراق

الملخص

تهدف هذه الدراسة الى تحديد العلاقة بين الإصابة بفايروس الحصبة الالمانية، الفايروس المضخم للخلايا مع وجود الإجهاض ضمن مجموعات عمرية مختلفة.

تم جمع عينات الدم من بداية شهر شباط ولغاية شهر أيلول عام 2017 من 127 امراة تعرضت سابقا للاجهاض إضافة الى 30 امراة أخرى كعينات سيطرة. تم فحص جميع العينات للكشف عن وجود الكلوبيولين المناعي M و G للاصابات المذكورة.

أظهرت النتائج ان الفايروس المضخم للخلايا كان اكثر الاصابات شيوعا مع نسبة اصابة من الكلوبيولين المناعي M (15.7%) والنوع G (12.5%). بالنسبة لفايروس الحصبة الألمانية، 0.7% فقط من الحالات أعطت نتائج إيجابية للكلوبيولين المناعي M واظهرت 6.2% من العينات نتائج ايجابية للاصابة بفايروس الحصبة الالمانية للنوع G. بينما مجموعة السيطرة، فقط 6.6% من العينات أعطت نتائج إيجابية للفايروس المضخم للخلايا للكلوبيولين المناعي M، وأبدى 3.3% منهم نتائج إيجابية للفايروس المضخم للخلايا للنوع G . لم تُظهر اية فئة عمرية إصابة بفايروس الحصبة الالمانية باستثناء الفئة 25–31 سنة، حيث ابدى 2.1% و 8.5% منهم مستويات عالية من الكلوبيولين المناعي M والنوع G على التوالي.

كانت اكثر مستويات الإصابة بالفايروس المضخم للخلايا ضمن الفئة العمرية 25–31 سنة بنسبة 21.2%، ثم اتبعها الفئة العمرية 18–24 سنة بنسبة 13.7%. عانت معظم المصابات من حالتي اجهاض، تم الكشف عنها في الفئة العمرية 25–31 سنة. سجل العدد الأعلى من الاجهاضات في المرضى المصابين بالفايروس المضخم للخلايا مقارنة مع الاصابات الاخرى، حيث عانت 1.5% ، 4.7% منهن 3 و 2 اجهاضات على التوالي بينما 1.5% فقط من المصابات بفايروس الحصبة الالمانية كنّ قد تعرضن لحالة اجهاض واحدة.

كانت نسبة 18.1% من المصابات بالفايروس المضخم للخلايا قد عانين من حالتي اجهاض وبلغت قيمة ال cut off (>1.25)، و100% من المصابات بالحصبة الالمانية كنّ قد عانين من حالة اجهاض واحدة وبلغت قيمة ال cut off (>1.25).