Detection of Rubella Antibodies in Women with Repeated Miscarriage During Different Seasons in Mosul City

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ABSTRCT

Background: Rubella or German measles is a viral disease transmitted via aerosol droplets affecting mainly children, Mostly, rubella is a simple and self-limiting disease with no chronic consequences, except in infected pregnant women which may result in devastating outcomes depending on the trimester of pregnancy. **Materials and methods:** the study enrolled 1004 women suffering from spontaneous miscarriage tested for rubella IgM antibodies using ELISA. The sampling was conducted in two different seasons, summer and winter. **Results:** Test reading showed that 15.23% of all tested women were positive for rubella IgM antibodies i.e. 153 out of 1004 women. Seasonal change showed no significant variation in the percentage of the infection, where 15.8% of all participants were positive in summer versus 14.35% seropositive in the winter season (p > 0.05). **Conclusion:** Rubella infection is affecting a relatively high number of women suffering from a spontaneous miscarriage in Mosul city, and there was no seasonal variation in the rate of infection.

Keywords: Pregnancy, Rubella, Seasonal infection, Spontaneous miscarriage.

الكشف عن الأجسام المضادة للحصبة الألمانية لدى النساء المصابات بالإجهاض المتكرر خلال المواسم المختلفة في مدينة الموصل الخلاصة:

مقدمة: الروبيلا او الحصبة الالمانية هي مرض فايروسي ينتقل بواسطة قطيرات في الهواء ويؤثر على الاطفال بالدرجة الاساس, ويكون في الغالب مرض بسيط و يشفى ذاتيا بدون عواقب مزمنة, عدا في حالة اصابة النساء الحوامل والذي قد ينتج عنه عواقب وخيمة تعتمد على فترة الحمل اثناء الاصابة. المواد و طرق العمل: تم فحص 1004 امرأة عانت من الاسقاط التلقائي لمستضدات الروبيلا نوع M, تم جمع عينات الدم في فصلين مختلفين والصيف و الشتاء. النتائج: الفحص اظهر ان 15.23% من جميع النساء المشاركات في الدراسة كانت نتائجهم موجبة لمستضدات الروبيلا نوع M بمعنى 153 امرأة من اصل 1004 امرأة مشاركة . التغييرات الفصلية لم تظهر اي اختلاف معنوي في نسبة الاصابة و حيث كان معدل الاصابة في الصيف 15.8% مقارنة ب 14.35% في الشتاء. الاستئتاج: اصابات الروبيلا تؤثر على عدد كبير نسبيا من النساء اللواتي يعانين من اسقاط تلقائي في الموصل و لا يوجد فرق معنوي في معدل الاصابات بين فصلي الصيف و الشتاء.

الكلمات المفتاحية: الحمل الحصية الالمانية الاصابات الموسمية الاسقاط

INTRODUCTION:

Rubella or German measles is a viral disease transmitted via aerosol droplets from an infected person to another and can be

transmitted to the fetus through the placenta [1]. Rubella virus is an RNA virus (single-stranded positive sense toga virus), most of the cases are presented with mild signs and symptoms or even passed unnoticed,

except when infection is established during pregnancy which will show a more severe impact on the embryo (1st trimester) and to, a lesser extent, on the fetus (2nd and 3rd trimester) [2].

Rubella infection may cause serious and multiple damages to the embryo if happened in the early stage of gestation (i.e. first eight weeks) and usually ends with fetal death. Infection between the 11th and 16th week result in about 20% damage, but still could cause death if it affects vital organs, otherwise, it may result in living born baby with congenital anomalies [3].

Rubella infections are mostly with no chronic consequences on patients, and pass without chronic harm, except to the fetus. Also, there is no treatment for such a problem; consequently, most efforts are counting on fetal protection to provide prophylactic methods like vaccines to prevent the damaging effect rather than treating it [4].

The pathological effect of rubella infection on the fetus is mostly depend on change in the rate of fetal infected cellular multiplication. The virus slows down the cellular growth multiplication, and even causes cell lysis and death of infected cells which will result in congenital damage, which could be fatal, especially in early pregnancy [5]. About 20% of rubellainfected pregnant women suffer from spontaneous abortion in the first 12 weeks of gestation [6].

Epidemiologically, the rubella virus is now less frequent in most populations due to vaccine development, but still affects many people resulting in devastating outcomes. Still, there is a variation from one locality to another due to many factors like economic situation and crowdedness [7].

Regional countries showed various rates of rubella infections among childbearing aged women, and even among women with repeated spontaneous miscarriage. For instance, in Turkey, several studies showed a high rate of infection reaching up to 95% positively infected in tested women as IgG antibodies, but less than 1% are positive as active infection expressed as IgM antibodies [8][9][10]. Other studies conducted in Iran showed that the rate of infection is over 80% as exposure to the virus expressed as IgG. but there were about 7% with active infection expressed as IgM antibodies [11][12].

Several studies conducted in different localities in Iraq showed various rates of infections among tested women. In Mosul city, a study showed that there were 16% of women with recurrent spontaneous miscarriage were positive for rubella IgM antibodies [13], while a study conducted in Baghdad showed that 4.8% of women with recurrent spontaneous abortion tested for rubella were positive for IgM antibodies indicating active infection [14][15]. Another study in Kirkuk showed that there is about 6% of women inspected for rubella (TORCH test) were positive for Rubella [16][17]. On the other hand, Erbil showed a low rate of infectivity of only 2.8% [18], while another study in Basra showed that 8% were positive for rubella using the same test [19].

Many other studies in a wide variety of Iraqi cities and other Arab countries also showed a high prevalence of this infection in low to middle-income countries. Alsamarai epidemiological study, for instance, revealed a high prevalence of this infection in many localities in Iraq, which varied from less than 5% up to 60% or even higher [14].

Seasonal changes may affect the transmission and spreading of many

infectious diseases, concerning the rubella virus, a study conducted in Kenya using mobile phone data to follow the distribution of the disease during the entire months of the year showed that the disease was more transmissible in three different months during the year which was peaked in September, January to March and in June, depending on temperatures and humidity levels [20]. Another study conducted in China showed that there is a higher rate of transmission and infection in low temperature (around 0 ° C) and maximum humidity i.e. winter season [21].

The aim of this study was to estimate the significance of the rubella antibody test among women suffering from repeated miscarriage and to find if there is any seasonal change effect on infections rate.

MATERIALS AND METHOD

The study was designed to collect the referred women who were suffering from spontaneous miscarriage for laboratory investigations according to a specific time frame. The total collected patients were 1004 women enrolled in

this study; all enrolled women were tested for rubella IgM antibodies by enzyme linked immunosorbent assay (ELISA) method using kits from Bioactiva Diagnostica GmbH. following the steps mentioned in the kit's manual [22-27].

The enrolled women in this study were divided into two groups according to the time of the physicians' referral, there were 397 women referred in winter months (December and January), and 607 women referred in summer months (July and August). Their test results were collected and compared. The statistical analysis was conducted using Excel Microsoft and statistical analysis was considered significant at p < 0.05 using Chi-square test (Prism 8.1).

RESULTS

Rubella IgM antibody tests showed that the number of referred women in summer was almost twice the number of women referred in summer, whereas the number of referred women in summer is 605 patients compared to 397 women in winter as shown in figure



Figure 1. Number of participants enrolled in summer and winter. A Higher number of miscarriage cases were referred to have rubella antibody test in summer than in winter season (607 versus 397 cases respectively).

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The net result of rubella tests among all participant women showed that only

153 women (i.e. 15.23%) were positive in both seasons as shown in figure 2.

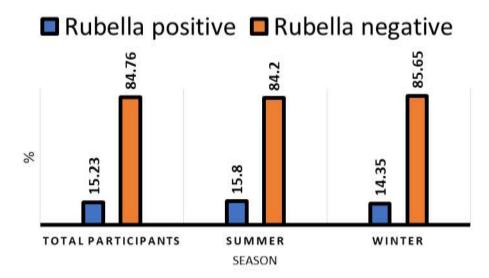


Figure 2. Overall figure of rubella seropositivity differences in total study cases, summer-collected cases, winter-collected cases, and total collected cases.

The seasonal change effect showed no significant change in the rate of infection rate. The percentage of

infected women was 15.8% in summer, while it was 14.35% in winter, as shown in figure 3.

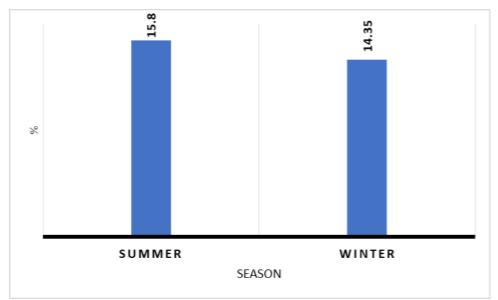


Figure 3. Rubella seropositivity in miscarriage cases collected in summer versus winter seasons. No significant (p > 0.05) difference was encountered between the two groups using the Chi-square test.

The individual values of the participants in the present study were plotted in summer versus winter (Figure 4). The findings confirmed that more

cases with cut-off values greater than 1 were expressed in winter than in summer; the dotted line represented the

cut-off values between positive and negative for the rubella virus.

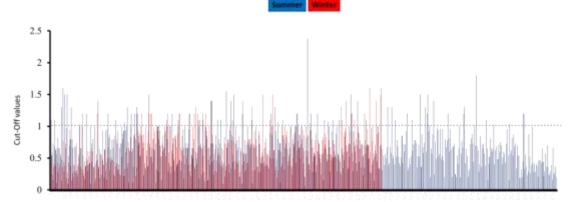


Figure 4. Rubella expression cut-off values in summer versus winter. Data expressed in terms of individual values. The dotted line is the difference between positive and negative values.

DISCUSSION:

Rubella is considered as an easily transmissible viral disease. Although it has been shown to be with no devastating or chronic harm to most individuals, it has been shown to be a true damaging disease in pregnant women, especially in the early stage of pregnancy [2][3].

This study aimed to evaluate the incidence of this infection in Mosul city during two seasons in one year and to evaluate the effect of the seasonal changes on the rate of infection.

The results showed that there is a relatively high incidence of rubella infection in Mosul city which is 15.23% in comparison to other localities in Iraq, like Baghdad which was only 4.8% [14][15], and also in Kirkuk city which showed a 6% rate of infection among the same selected groups [16][17], and also higher than Basra which showed only 8% [19] and far much higher than Erbil which showed only 2.8% [18].

In comparison to other regional countries, the rate of infection is still to be considered high, the rate in Mosul was 15.23%, were was in Turkey less

than 1% [8][9][10], and in Iran about 7% [11][12], this could be attributed to the low economic level for many people in Mosul, and also to the post-occupation conditions that made many people less considerate about many health and vaccination issues.

Seasonal changes in this study showed variance only in the patients' number referred to the laboratory for testing for rubella infection. The number of women referred to the laboratory in summer is much higher than in winter, this could be attributed to many factors including travel difficulties especially patients from rural areas obligations with children and family during school time. The rate of infection among women referred to the laboratory was almost identical in both seasons (summer and winter) which is in conflict with other study conducted in China which showed a positive relationship between cold / humidity and the rate of infection with rubella; this could be attributed to variation in climate between Mosul city and the location of this study in China [21]. But still in relative agreement with another study in India which shows a relative similarity in the rate of infection in winter and summer months [20].

CONCLUSION:

The rate of rubella infection in Mosul city is relatively higher than in other localities in Iraq and other regional countries which require further care about vaccination and maternal care. Moreover, this study showed no significant change in rubella spread among the population in winter versus summer months.

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REFERENCES:

- 1- Verma Ramesh, Khanna Pardeep, Chawla Suraj. Rubella vaccine: New horizon in prevention of congenital rubella syndrome in the India. Hum Vaccines Immuno ther. 2012;8(6):831–3.
- 2- Kaushik A, Verma S, Kumar P. Congenital rubella syndrome: A brief review of public health perspectives. Indian J Public Health. 2018;62(1):52-54. doi:10.4103/ijph.IJPH_275_16.
- 3- Miller E, Cradock-Watson JE, Pollack TM: Consequences of confirmed maternal rubella at successive stages of pregnancy. Lancet. 1982;2:781–4

- 4- Zimmerman LA, Reef SE, Orenstein WA. Rubella Vaccine-A Tale of Appropriate Caution and Remarkable Success. JAMA Pediatr. 2018 Jan 1;172(1):95-96. doi: 10.1001/jamapediatrics.2017.4178. PMID: 29159364; PMCID: PMC5872148.
- 5- Parkman PD. Togaviruses: Rubella Virus. In: Baron S, editor. Medical Microbiology. 4th edition. Galveston (TX): University of Texas Medical Branch at Galveston; 1996. Chapter 55.
- 6- Regan L, Rai R. Epidemiology and the medical causes of miscarriage. Best practice and research Clinical obstetrics and gynaecology. 2000;14(5):839–54.
- 7- Sathanandan D, Gupta L, Liu B, Rutherford A, Lane J. Factors associated with low immunity to rubella infection on antenatal screening. Aust N Z J Obstet Gynaecol. 2005;45(5):435-438. doi:10.1111/j.1479-828X.2005.00467.x
- 8- Koksaldi –Motor V, Evirgen O, Azaroglu I, Inci M, Ozer B, Arica S: Prevalence of Toxoplasmosis, Cytomegalovirus and Rubella IgGAntibodies in Hatay Women and Children. West Indian Med J. 2012:61:154-7.
- 9- Tamer GS, Dundar D, Caliskan E: Seroprevalence of Toxoplasma gondii, rubella and cytomegalovirus among pregnant women in western region of Turkey. Clin Invest Med. 2007;32:E43–7.
- 10- Ocak S, Zeteroglu S, Ozer C, Dolapcioglu K, Gungoren A: Seroprevalence of Toxoplasma gondii, rubella and cytomegalovirus among pregnant women in southern Turkey. Scand J Infect Dis. 2007;39:231–4.
- 11- Majlessi F, Batebi A, Shariat M, Rahimi A, Azad TM: Rubella serology

- in pregnant women attending health centres of Tehran University of Medical Sciences. East Mediterran Health J. 2008;14:590–4.
- 12- Jahromi AS, Kazemi A, Manshoori G, Madani A, Moosavy SH, Seddigh B: Seroprevalence of rubella virus in women with spontaneous abortion. Am J Infect Dis. 2011;7:16-9.
- 13- AL—Taie AAD: Serological Study For TORCH Infections In Women With High Delivery Risk Factors In Mosul. Tikrit J Pure Sci. 2010;15:193-8.
- 14- Alsamarai, Abdulghani Mohamed, Aljumaili, Zainab Khalil Mohamed. Seroepidemiology Of Toxoplasma, Rubella, Cytomegalovirus And Herpes Simplex Virus -2 In Women With Bad Obstetric History. Part I: Toxoplasma And Rubella Infections. Our Dermatol Online. 2013; 4(4): 522-535.
- 15- Abdul Mohymen N, Hussien A, Hassan FK: Association between TORCH agents and recurrent spontaneous abortion. Iraqi J Med Sci. 2009; 7:40-6.
- 16- Hiro M. Obaid, Shawbow A. Juma. TORCH Screening Test in Pregnant Women of Kirkuk City. Al-Mustansiriyah Journal of Science. 2016. 27(5). p-ISSN: 1814-635X.
- 17- Salman YG: Serological Cross Reaction among Some Causative Agents of Women Abortions (Toxoplasma gondii & Cytomegalovirus & Rubella Virus), with the Incidence of Hepatitis Virus (B &C). Tik J Pharm Sci. 2007; 3:102-11.
- 18- Ahmad, Avesta Seerwan, Kareem, Yasin. Frequency of Cytomegalovirus, Rubella, And Herpes Simplex Virus In embryonic tissues of women with missed abortion. Mosul Journal of Nursing. 2020, 8(1):68-88.

- 19- Ali. F. Hussein, Ahmed. H. Dawood, Nada. J. Dawood, Raaid. K. Hussein. Seroprevalence of Torch Infection in Pregnant Women in Basra City Southern of Iraq. Journal of Global Pharma Technology. 2019. 11(01). (Suppl.) 292-295.
- 20- Amy Wesolowskia,b,c, C. J. E. Metcalfd,e,f,, Nathan Eaglea,g, Janeth Kombichh, Bryan T. Grenfelld,e, Ottar N. Bjørnstadi, Justin Lesslerj, Andrew J. Tatemc,f,k, and Caroline O. Buckeea. Quantifying seasonal population fluxes driving rubella transmission dynamics using mobile phone data. PNAS.2015. 112(35): 11114-11119.
- 21- Ma Y, Liu K, Hu W, Song S, Zhang Epidemiological Shao Z. Characteristics, Seasonal Dynamic Patterns. and Associations with Meteorological Factors of Rubella in Shaanxi Province, China, 2005-2018. The American Journal of Tropical Medicine and Hygiene. 2021;104(1):166-174. doi:10.4269/ajtmh.20-0585.
- 22- de Souza VA; Sumita LM; Otsubo ME; Takei K; Pannuti CS. Enzyme linked fenmunosorbentassayformbella antibodies; a simple method of antigen production. A preliminary report Rev Inst Med Trap Sao Paulo 1995; 37(4):357-9.
- 23- Matter L; Germann D; Bally F; Schopfer K. Age-stratified seroprevalence of Rubella, mumps and rubella (MMR) virus infections in Switzerland after the introduction of MMR mass vaccination. Eur J Epidemiol 1997;13(1):61-6.
- 24- M"uhlebach-Sponer M; Zbinden R; da Silva VA; Gnehm HE. Intrathecal rubella antibodies in an adolescent with Guillain-Barr'e syndrome after mumps-Rubella-rubella vaccination [letter]. Eur JPediatr 1995; 154(2):166.

25- Johnson CE; Kumar ML; Whitwe H JK; Staehle BO; Rome LP; Dinakar C; Humi W; Nalin DR. Antibody persistence after primary Rubellamumps-rubella vaccine and response to asecond dose given at four to six vs. eleven to thirteen years. Pediatr Infect Ois J; 1996;15(8):687-92.

- 26- Matter L; Kogelschatz K; Germann D. Serum levels of rubella virus antibodies indicating immunity: response to vaccination of subjects with low or undetectable antibody concentrations. J Infect Dis 1997; 175{4):749-55.
- 27- Bos P; Steele D; Alexander J. Prevalence of antibodies to rubella, herpes simplex 2 and cytomegalovirus in pregnant women and in neonates at Ga-Rankuwa. Cent. Afr. J Med 1995;41(1):14-7.