The European Research Journal 2022;8(1):37-43 Original Article

DOI: 10.18621/eurj.827322 *Perinatology*

Rubella immunity in native Turkish and Syrian immigrant pregnant women between 2010-2018

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ABSTRACT

Objectives: The study has aimed to investigate the rubella immunity in native-Turkish and Syrian-immigrant pregnant women in Turkey.

Methods: Between September 2010 and December 2018, the hospital records of pregnant patients were evaluated retrospectively. For each year, for the number of patients who were screened for rubella IgG and/or IgM antibodies, IgG avidity (if any), and PCR tests (if any) were investigated, and subjects were categorized by nationality.

Results: During the study period, a total of 80,302 pregnant were tested with at least one of the rubella IgM or IgG antibodies. Of these, 22,962 pregnant women were screened for both IgG and IgM, 24,684 were screened for IgG, and 78,580 pregnant women were screened for IgM rubella antibodies. The seropositivity rate of IgG rubella antibodies in native and Syrian pregnant groups was 93.8% and 95.9%, respectively. In both groups, the IgM rubella antibodies were found as 0.5%. IgG avidity was investigated in 252 patients, whose test results were positive for IgM and IgG; and a low IgG avidity was detected in 5 native patients, while none was detected in the Syrian group.

Conclusions: In the Syrian immigrant group, the susceptibility to Rubella is low, and it does not differ from the native Turkish population.

Keywords: Rubella, seroprevalence, pregnancy, Syrian immigrant, vaccine

The Rubella disease is also called as German measles, and it is an infection caused by the Rubella virus, which is a single-stranded RNA virus of the Togaviridae family [1]. Rubella virus is transmitted from person to person through the respiratory tract. The disease is generally seen during childhood, and in most cases, it is experienced as a mild, self-limiting disease. In the symptomatic cases, the general symptom of the disease is maculopapular rashes, accompanied by fever, fatigue, and lymphadenopathy [2]. But in some cases, especially in post-pubertal women, it can be more serious, causing arthritis and arthralgia, rarely encephalitis, and thrombocytopenic purpura [1, 3].

Received: ***November 17, 2020;*** *Accepted:* ***July 11, 2021;*** *Published Online:* ***January 4, 2022***

e-ISSN: 2149-3189

How to cite this article: *Yücel Çelik Ö, Aksu G, Obut M, Keleş A, Gültekin M, Dağdeviren G, et al. Rubella immunity in native Turkish and Syrian immigrant pregnant women between 2010-2018. Eur Res J 2022;8(1):37-43. DOI: 10.18621/eurj.827322*

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The disease possesses an extra risk in pregnant woman, because it can be transmitted from an infected mother to the fetus by the transplacental way, which may result in the congenital rubella syndrome (CRS) in the fetus [1, 3]. The CRS is associated with multiple anomalies such as cataracts, glaucoma, chorioretinitis, microphthalmia, and hearing loss; brain anomalies such as microcephaly, pulmonary artery stenosis; heart anomalies such as ventricular septal defects; as well as miscarriages and fetal deaths. In the surviving cases, long-term complications like serious hearing loss, the risk of developmental delay, autism, thyroiditis, and insulin-dependent diabetes (type 1 diabetes) can be seen [1].

Vaccination is considered the most effective method to prevent rubella spread and CRS. The World Health Organization (WHO) in 2014, published the global immunization report that 140 countries have already introduced rubella vaccine into their routine immunization program [4]. In 1970, Rubella vaccination was started, especially in rural areas in Turkey. National Expanded Immunization Program (EIP) started in 1981 with the starting of the Measles and Rubella Elimination and the Prevention of Congenital Rubella Syndrome Program with the rubella infection prevention campaign; and it continued after triple measles, mumps, and rubella (MMR) vaccine applications in 2006 [5]. As a result, almost all the children born in Turkey have received two doses of rubella-containing vaccine. Consequently, the number of rubella cases during pregnancy and CRS cases have decreased over time with childhood vaccinations. The eliminating of the CRS cannot be achieved only by vaccination of children; in addition, susceptible women at childbearing age must be identified, and if possible, must be immunized for rubella at least three months before conception.

Due to the outbreak of the war that took place in Syria, the national health system of the country collapsed, and most people did not have a chance to access the vaccines. After migration due to the war, the vaccination status became too dependent on the migrated countries' vaccination services to the migrants. Turkey has hosted the highest number of Syrian immigrants over time, especially after the year 2011 [6]. There has been great concern about the susceptibility of the Syrian pregnant women because of the reasons mentioned above. The investigation of the rubella susceptibility rates of both native Turkey and immigrant women is essential to preventing rubella and congenital rubella. Nonetheless, there are a few articles on the rates and comparison of rubella immunity among native mothers and Syrian immigrant mothers. Accordingly, the present study has aimed to investigate the rubella immunity among native and immigrant pregnant women in Turkey.

METHODS

Subjects

Between September 2010 and December 2018, a total of 80,302 patients, who were screened for at least one of the IgM or IgG rubella antibodies, were included in this retrospective cohort study. This study was approved by the Medical Specialty Education Board of the Etlik Zübeyde Hanım Women's Health Practices and Research Center, Decision Number: 90057706-799. According to our clinical routine, all pregnant patients who applied to the hospital for prenatal care were screened for rubella disease or seropositivity. For the patients with only the rubella IgG antibody positivity, further tests were not performed because these patients had been immunized to rubella. For the patients with only rubella IgM antibody positivity, the test was repeated after 2 weeks, and if the result of the test was negative, then the first result was accepted as a false positive; but if the result of the test was reported as positive again, then these patients were closely followed up for acute rubella disease. For the patients whose serum rubella IgG and IgM antibodies were both positive, serum IgG avidity was investigated [7]. Patients with low IgG avidity were determined as an acute infection, and further evaluations such as PCR study of chorionic villus sample, amniocentesis, or cordocentesis are performed [8-11]. The patients' nationality, age, test results of IgM and IgG rubella antibodies, IgG avidity (if any), and PCR (if any) was retrieved from the hospital database and patients' files. The patients were evaluated according to the first pregnancy or birth records of the patients in our hospital. Repeated results were excluded from the study.

Serological Tests of Anti-rubella IgG and IgM

Rubella IgG and Rubella IgM tests were studied

from the erum samples using chemiluminescence method on the Liaison brand device of Diasorin Company (DiaSorin, Saluggia, Italy), between 2010 and 2013; and on "Advia Centavur XP (Siemens Diagnostics, Tarrytown, NY) device from Siemens, between 2014-2018, in line with the recommendation of the device manufacturers. Rubella IgG Avidity test was performed with the Microelisa method from serum samples by the manufacturer's recommendations with the Euroimmun brand kit (Euroimmun, Lübeck, Germany).

Statistical Analysis

IBM SPSS Statistics version 21.0 for Windows was used to calculate the variables. Descriptive analysis and categorical variables were defined as numbers and percentages, and numerical variables were defined as median (range minimum-maximum) values. For the comparison of total seropositivity between nationals, a Chi-Square test was performed.

RESULTS

During the study period, rubella antibody tests were performed on a total of 80,302 pregnant women, including IgM for 78,580 patients, IgG for 24,684 patients, and both IgM and IgG for 22,962 patients. The median age of all the tested patients was 32 (16-49). A total of 1,590 Syrian pregnant women were evaluated in the study. The number of Syrian pregnant women who applied to our center for prenatal care was

Table 1. Prenatal rubella screening results between September 2010-December 2018

Year	Nationality	Number (n) of the Patients	Age	IgM-	IgM+	IgG-	IgG+	Avidity		
			Median (Min-Max)	n	n (%)	n	n (%)	Total	High	Low
2010	Turkish	2.765	34 (23-49)	2.649	13 (0.5)	49	841 (94.5)	8	8	0
	Syria	5	37 (33-41)	5	0 (0)	1	0 (0)	0	0	0
2011	Turkish	8.602	34 (21-47)	8.234	80 (1)	142	2.304 (94.2)	17	17	0
	Syria	19	37 (28-47)	18	0 (0)	0	8 (100)	0	0	0
2012	Turkish	9.026	33 (22-47)	8.779	36 (0.4)	91	1.377 (93.8)	36	35	1
	Syria	21	35 (27-48)	21	0 (0)	0	3 (100)	0	0	0
2013	Turkish	9.010	32 (21-47)	8.683	69 (0.8)	229	2.450 (91.5)	19	19	0
	Syria	16	32 (24-42)	16	0 (0)	0	5 (100)	0	0	0
2014	Turkish	8.756	31 (19-47)	8.567	49 (0.6)	93	1.925 (95.4)	23	23	0
	Syria	19	32 (26-46)	19	0 (0)	0	7 (100)	0	0	0
2015	Turkish	10.166	31 (18-47)	9.976	59 (0.6)	27	2.406 (98.9)	31	31	0
	Syria	155	29 (16-48)	152	1 (0.7)	0	35 (100)	1	1	0
2016	Turkish	10.932	30 (18-49)	10.694	40 (0.4)	58	3.078 (98.2)	53	51	2
	Syria	262	28 (18-44)	259	1 (0.4)	6	105 (94.6)	1	1	0
2017	Turkish	10.408	29 (18-47)	10.203	35 (0.3)	40	3.755 (98.9)	42	40	2
	Syria	469	27 (18-45)	452	1 (0.2)	6	194 (97)	1	1	0
2018	Turkish	9.047	28 (18-47)	8.824	34 (0.4)	73	4.907 (98.5)	20	20	0
	Syria	624	26 (18-46)	607	4 (0.7)	17	352 (95.4)	0	0	0
2010-2018	Turkish	78.712 (98%)	32 (18-49)	76.609	415 (0.5)	802	23.143 (93.8)	249	244	5
	Syria	1.590 (2%)	32 (16-48)	1.549	7 (0.5)	30	709 (95.9)	3	3	0
p value			0.92	0.631			0.292			

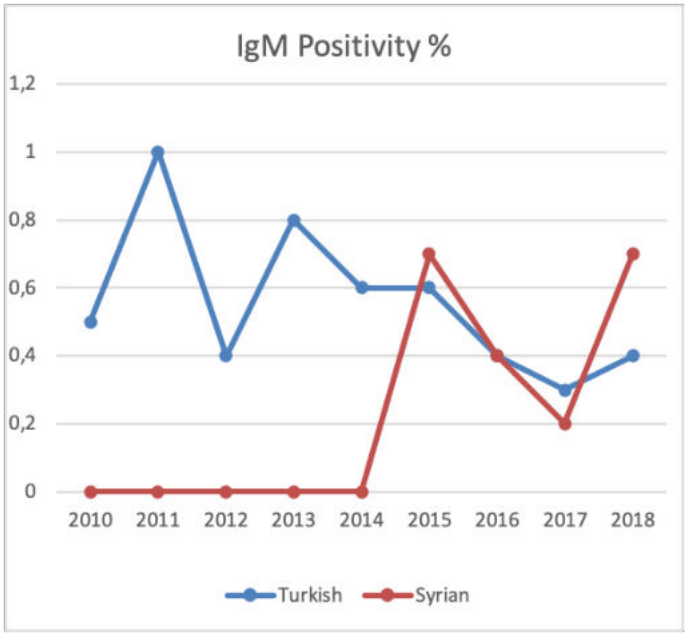

Fig. 1. Graphic of IgM posivity

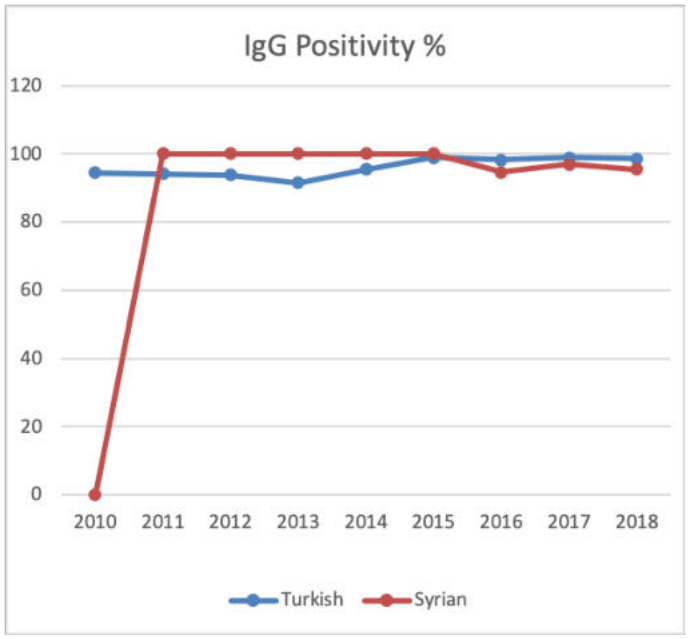

Fig. 2. Graphic of IgG positivity.

in an increasing trend each year (Table 1). The results of the native Turkish and Syrian immigrant pregnant woman were similar in respect to having serum rubella IgG antibodies and rubella IgM antibodies. Hence, the rate of rubella IgG antibodies positivity were 93.8% and 95.9%; and the rate of rubella IgM antibodies positivity were 0.5% and 0.5%, respectively (p = 0.292, p = 0.631) (Table 1). Rubella IgM ve IgG positivity results have been presented for the years of 2010-2018, in Fig. 1 and 2. IgG avidity was investigated in 252 patients, whose test results were positive for both rubella IgM and IgG antibodies. A low IgG avidity was detected in 5 patients, and all of them were in the native pregnant group. The results of the two pregnant women, who were negative for amniocentesis and the PCR, is shown in Table 2.

DISCUSSION

Due to the migration wave in 2011, which took place from Syria to other countries (especially to Turkey), there has been an increase in the incidence of vaccine-preventable diseases [12, 13]. One of these diseases, which is the subject of this study, has been thought to be rubella disease. Overall, we observed that the rubella susceptibility and seropositivity rates between native Turkish pregnant women and Syrian immigrant pregnant women were similar. In this study, the rubella susceptibility rates in Syrian groups were found to be in the range from 0% to 5.4%, and in native groups, it was 1.1% to 8.5%, according to years. Rubella IgG seroprevalence can vary even in different regions in the same country [4, 8, 14, 15]. The studies

Table 2. Characteristics of patients with low IgG avidity

Age	Gravidity	Parity	Test week	Nationality	Ultrasound finding	Pregnancy result	PCR result	Birth week
43	7	2	9	Turkish	Normal	Abort	-	-
36	3	2	8	Turkish	Normal	Birth	Negative[a]	39
20	1	0	5	Turkish	Normal	Birth	-	40
27	2	1	14	Turkish	Echogenic focus in the liver and intestine	Birth	Negative[a]	38
34	7	3	8	Turkish	Normal	Birth	-	39

[a] Amniocentesis result

from different areas of Turkey showed that the rate of susceptibility to rubella in native pregnant women ranged from 2.5% to 17%, and IgG seropositivity ranged from 83.69 to 97.5% [16-18]. There is a limited number of studies conducted on Syrian refugees in Turkey for the susceptibility of rubella, and according to one of these studies, which had results that were similar to this study, 1333 Syrian pregnant woman were evaluated, and the IgG seropositivity was found to be 92.8% [19]. The current study evaluated the data of groups between September 2011 and December 2018. In the first years of the migration, the population of Syrian immigrants in Ankara was low. The reason for including the data between 2011 and 2014 was to see the progress of the Syrian immigration application over the years, which we saw increasing from year to year.

Despite all efforts to eradicate rubella, in some areas, the disease is still prevalent, and it is a significant, preventable cause of fetal death, abortion, congenital anomaly, and birth defects [20, 21]. The American College of Obstetricians and Gynecologists suggests a routine screening for rubella in pregnant women [22]. Similar to Turkey, many countries such as The United Kingdom, Japan, and Canada have implemented this strategy into regular obstetrics care, and good performance has been achieved [23, 24]. Via this strategy, necessary measures can be taken during pregnancy, and postpartum vaccination can be completed to reduce the risk of congenital rubella for a subsequent pregnancy [22].

Although the studies for the attenuated rubella vaccine started in 1965, its effective use started in 1978 with the incentive of the Federal Childhood Immunization Program and Measles Elimination Initiative [25]. As of 2018, the rubella vaccine has entered the vaccination programs in 168 countries around the world, and rubella transmission has not been observed in 81 of these countries since that time[24]. Congenital rubella syndrome and rubella infection were prevented in 3 out of 6 WHO regions, and the Global Vaccine Action Plan and WHO plans to increase this to 5 WHO regions by 2020 [26, 27]. The Centers for Disease Control and Prevention suggests two doses as the first dose applied in the 12th-15th month and the second dose applied in the 4-6th year after birth [28]. Two doses of triple MMR vaccine are administered in Turkey. According to WHO data, MMR is applied at 12 and 18 months after birth in the Syrian vaccination program [29].

The course and complications of rubella infection during pregnancy may differ depending on the gestational week. Before the 10th week, it can cause fetal defects, including pregnancy loss, in 85-90% of the infected patients, and rare fetal adverse effects are seen from the 16th week of gestation [30]. Rubella antibody screening at the first obstetric visit provides the chance for early diagnosis and early information about the course of the pregnancy. In the current study, a low IgG avidity was observed in 5 (%1.9) out of 252 patients with positive rubella IgG and IgM antibodies. Only 2 patients were accepted for the amniocentesis and PCR test, which both gave negative results for rubella infection. Two patients who refused both the amniocentesis and PCR test had healthy newborns without any complications. Over-demanding of the IgM antibody test by physicians over the IgG antibody test is due to the non-standardized prenatal screening routine among physicians.

The strength of the study is that the changes in the susceptibility of native and Syrian immigrant pregnant women were evaluated continuously for 8 years.

Limitations

There have been some limitations in our study. First, we collected the data of patients in a single regional center, which might not reflect the susceptibility of the rest of Turkey and Syrian immigrants who live in the other cities of Turkey. Secondly, immunization records of the immigrant women were not present, hence we could not explain how they became seropositive for rubella.

CONCLUSION

The outbreak of the war that took place in Syria, which resulted in the migration of 3.5 million people from Syrian to Turkey, caused great concern for outbreaks of infectious diseases such as rubella. This study showed that vaccination for rubella was successful for both the Syrian migrants and native pregnant women. It is thought that this success will continue in future generations with the vaccination policy implemented by Turkey for immigrants.

Authors' Contribution

Study Conception: ÖYÇ, AY; Study Design: ÖYÇ, AY, DŞ; Supervision: ÖYÇ, AY, DŞ; Funding: ÖYÇ; Materials: ÖYÇ; Data Collection and/or Processing: GA, MO, AK, MGÇ; Statistical Analysis and/or Data Interpretation: ÖYÇ, GD, AY, DŞ; Literature Review: ÖYÇ, AY, DŞ; Manuscript Preparation: ÖYÇ, MO, GD, AK, AY and Critical Review: ÖYÇ, AY, DŞ.

Conflict of interest

The authors disclosed no conflict of interest during the preparation or publication of this manuscript.

Financing

The authors disclosed that they did not receive any grant during conduction or writing of this study.

REFERENCES

1. Lambert N, Strebel P, Icenogle J, Poland GA. Rubella. Lancet 2015;385:2297-307.
2. Al-rubaii B, Aboud M, Hamza W. Evaluation of Anti-rubella antibodies among childbearing age women in Babylon Governorate. Med J Babylon 2010;7:233-49.
3. White SJ, Boldt KL, Holditch SJ, Poland GA, Jacobson RM. Measles, mumps, and rubella. Clin Obstet Gynecol 2012;55:550-9.
4. Lane S, MacDonald NE, Marti M, Dumolard L. Vaccine hesitancy around the globe: Analysis of three years of WHO/UNICEF Joint Reporting Form data-2015-2017. Vaccine 2018;36:3861-7.
5. Çalışkan D, Piyal B, Akdur R, Ocaktan ME, Yozgatligil C. An analysis of the incidence of measles in Turkey since 1960. Turk J Med Sci 2016;46:1101-6.
6. United Nations High Commissioner for Refugees. Syria Refugee Crisis Explained 2020. [Available from: https://www.unrefugees.org/news/syria-refugee-crisis-explained/.
7. Wandinger K-P, Saschenbrecker S, Steinhagen K, Scheper T, Meyer W, Bartelt U, et al. Diagnosis of recent primary rubella virus infections: significance of glycoprotein-based IgM serology, IgG avidity and immunoblot analysis. J Virol Methods 2011;174:85-93.
8. Ho-Terry L, Terry GM, Londesborough P. Diagnosis of foetal rubella virus infection by polymerase chain reaction. J Gen Virol 1990;71:1607-11.
9. Tang JW, Aarons E, Hesketh LM, Strobel S, Schalasta G, Jauniaux E, et al. Prenatal diagnosis of congenital rubella infection in the second trimester of pregnancy. Prenat Diagn 2003;23:509-12.
10. Abernathy E, Cabezas C, Sun H, Zheng Q, Chen M-h, Castillo-Solorzano C, et al. Confirmation of rubella within 4 days of rash onset: comparison of rubella virus RNA detection in oral fluid with immunoglobulin M detection in serum or oral fluid. J Clin Microbiol 2009;47:182-8.
11. Bellini WJ, Icenogle JP. Measles and rubella viruses. Manual of Clinical Microbiology, 10th Edition: American Society of Microbiology; 2011: p.1372-87.
12. Terkawi AS, Bakri B, Alsadek AS, Al-Hasan AH, Alrahhal MS, Alsaleh FM, et al. Child and adolescent health in northwestern Syria: findings from Healthy-Syria 2017 study. Avicenna J Med 2019;9:61-74.
13. Ekmekci PE. Syrian refugees, health and migration legislation in Turkey. J Immigr Minor Health 2017;19:1434-41.
14. Adam O, Musa A, Kamer A, Sausy A, Tisserand E, Hübschen JM. Seroprevalence of measles, mumps, and rubella and genetic characterization of mumps virus in Khartoum, Sudan. Int J Infect Dis 2020;91:87-93.
15. Tushabe P, Bwogi J, Abernathy E, Birungi M, Eliku JP, Seguya R, et al. Descriptive epidemiology of rubella disease and associated virus strains in Uganda. J Med Virol 2020;92:279-87.
16. Çetinkaya RA, Yenilmez E. The seroprevalence of Rubella in pregnant women in Turkey: a meta-analysis research of 90988 Rubella IgM, 84398 Rubella IgG, and 522 avidity results. Turk J Obstet Gynecol 2019;16:63-71.
17. Başkesen T, Ecemiş T, Şanlıdağ T. Evaluation of Rubella immunity in pregnants. Med J Kocatepe 2010;11:19-22.
18. Mehmet O, Doğan Y, Bademkıran MH, Akgöl S, Kahveci B, Peker N, et al. [Toxoplasma, rubella and cytomegalovirus seroprevalence in pregnant women in Diyarbakir]. Dicle Med J 2019;46:189-94. [Article in Turkish]
19. Çoşkun B, Gülümser Ç, Çoşkun B, Artuk C, Karaşahin KE. Impact of Syrian refugees on congenital TORCH infections screening in Turkey. J Obstet Gynaecol Res 2020;46:1017-24.
20. Orenstein W, Hinman A, Nkowane B, Olive J, Reingold A. Measles and rubella global strategic plan 2012-2020 midterm review. Vaccine 2018;36:A1-A34.
21. Reef SE, Plotkin S, Cordero JF, Katz M, Cooper L, Schwartz B, et al. Preparing for elimination of congenital rubella syndrome (CRS): summary of a workshop on CRS elimination in the United States. Clin Infect Dis 2000;31:85-95.
22. American College of Obstetricians and Gynecologists. Routine Tests During Pregnancy: American College of Obstetricians and Gynecologists; 2019. [Available from: https://www.acog.org/patient-resources/faqs/pregnancy/routine-tests-during-pregnancy
23. Matthews LA, Lawrance LM, Gray D, Gray S. An audit of rubella IgG antibody status in antenatal women in a NHS Trust over 5 years (2005-2009). Epidemiol Infect 2011;139:1720-6.
24. Grant GB, Desai S, Dumolard L, Kretsinger K, Reef SE. Progress toward rubella and congenital rubella syndrome control and elimination - Worldwide, 2000-2018. MMWR Morb Mortal Wkly Rep 2019;68:855-9.
25. Cooper LZ. The history and medical consequences of rubella. Clin Infect Dis. 1985;7(Suppl 1):S2-S10.
26. Reef SE, Strebel P, Dabbagh A, Gacic-Dobo M, Cochi S. Progress toward control of rubella and prevention of congenital rubella syndrome—worldwide, 2009. J Infect Dis 2011;204(suppl 1):S24-S7.

27. Plan GVA. Decade of vaccine collaboration. Vaccine 2013;31(Suppl 2):B5-31.
28. Rubella Vaccination Centres for Disease Control and Prevention. [05 May 2020]. Available from: https://www.cdc.gov/rubella/vaccination.html
29. WHO vaccine-preventable diseases: monitoring system. 2020 global summary.[05 May 2020] [Available from: ttps://apps.who.int/immunization_monitoring/globalsummary/countries?countrycriteria%5Bcountry%5D%5B%5D=SYR.
30. Morgan-Capner P, Miller E, Vurdien JE, Ramsay ME. Outcome of pregnancy after maternal reinfection with rubella. CDR (London, Engl Rev) 1991;1:R57-9.