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Rubella Seroprevalence in Women with Bad Obstetric History

Hala Mohamed Majeed Hassan[1]*, Abdulghani Mohamed Alsamarai[2,3], Ferah Ghali Alsalihi[4], Amina Hamed Alobaidi[5] and Zainab Khalil Mohamed Aljumaili[6]

[1]*Department of Microbiology, Tikrit University College of Veterinary Medicine, Iraq*

[2]*Department of Medicine and Microbiology, Tikrit University College of Medicine, Iraq*

[3]*Asthma Allergy Centre, Tikrit Teaching Hospital, Iraq*

[4]*Department of Biology, College of Science, Iraq*

[5]*Department of Biochemistry, Tikrit University College of Medicine, Iraq*

[6]*Kirkuk Health Authority, Iraq*

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***Corresponding author:** Hala Mohamed Majeed Hassan, Department of Microbiology, Tikrit University College of Veterinary Medicine, Tikrit, Iraq, Email: m.hala17@yahoo.com; galsamarrai@yahoo.com

Abstract

Objective: To determine rubella seroprevalence in women with bad obstetric history (BOH).

Patients and Methods: A case control study was conducted in Kirkuk, Iraq, which included 538 women with age range from 15 to 48 years. Structured questionnaires were used to gather sociodemographic data and ELISA was used to detect rubella infection using IgG and IgM kits.

Results: Out of the 538 women, 435 (80.9%) and 18 (3.3%) were rubella IgG and IgM positive respectively. Women age, occupation, education and family size were significantly associated with serpositive Rubella IgG. Women with BOH were with high Rubella IgG seropositivity than that in women with normal pregnancy. Current infection was higher in women with normal pregnancy outcomes as compared to that with BOH.

Conclusion: This study provides important and highly useful information on baseline seroprevalence data on rubella in Iraq. A 19.1% of our women study population were non rubella immune and were susceptible for rubella infection. In addition, rubella seroprevalence associated with BOH.

Keywords: BOH; Rubella; IgG; IgM; Pregnant women; Socio-demographic variables; Iraq

Introduction

Bad obstetric outcomes was recognized as social and medical problem in Iraqi society [1,2]. Adverse pregnancy outcomes were with multifactorial etiology. Maternal infection was one of the important Etiology for pregnancy adverse outcomes in developing countries [3]. Rubella infection association with fetal death or congenital defects was a documented [4]. Risk of rubella defects is high in infants whose mothers are infected by rubella virus in the first 16 weeks of pregnancy [5]. In a recent report [3], we reviewed a fifty- nine studies characterizing the epidemiology of maternal rubella were identified mostly for low and middle income countries and 19 studies for Arab countries.

Seven studies were with a retrospective (12.1%) study design and of the total 13 (22.4%) studies deals with women with bad obstetric history (BOH). These studies detected the presence of maternal anti-rubella IgG as a marker of past infection or immunization and mothers who did not possess these antibodies were susceptible to rubella infection. Maternal IgM was detected in some studies as a marker of recent or current infection, which is associated with an increased risk of vertical transmission. The range of maternal susceptibility to rubella was 2.1% to 43% in pregnant women and 21.1%-71.04% in women with BOH. Higher susceptibility rates were reported in Nigeria (84.8%), India (71%), Nepal (50%), Brazil (28.4%), Iran (25%), and Sri Lanka (24%) [3].

The higher susceptibility rates for Arab countries excluding Iraq were reported in Morocco (83.4%), Sudan (34.7%), Qatar (25.1%), and Tunisia (20.3%). The lowest susceptibility was reported for Saudi Arabia (6.7%) [3]. Concerning Iraq, the reported studies indicated a high susceptibility rates in Thi Qar (98.05%), Kirkuk (91%), Baghdad (79%), and Waset (45.7%)

[3]. While the lowest susceptibility rates were reported for Diyala (0%) in women with previous abortion, and 3.9% in pregnant women without history of BOH. The same figures were reported later by another research group in Babylon [3].

For Kirkuk, only one prospective study [6] was reported in literature, thus the present study conducted with larger study population. The aim of the present study is to determine the seroprevalence of rubella IgG and IgM and the rate of non rubella immune in women with bad obstetric history compared to that with normal pregnancy outcomes.

Study design and settings

The study design is a Descriptive Case Control Study and was performed in Kirkuk General Hospital. The study proposal was approved by Tikrit University College of Science ethical committee and Kirkuk Health Authority Research Committee. Informed consent taken from each woman included in the study.

Study population

The study population is women with childbearing age. Study population was recruited from Kirkuk General Hospital. 838 women with age range from 14 to 48 were included in the study. Of the total, 547 women were with bad obstetric history (BOH) and 291 women with normal previous pregnancy as control group. The demographic information of these groups is shown in (Table 1). For serological analysis, 5-10 mL of venous blood was collected in a sterile container with strict aseptic precautions from each study subject. The serum was separated and stored in numbered aliquots at -20 °C till assayed. All the serum samples collected from the study and control groups were tested for Rubella IgM and IgG antibodies by commercially-available (ELISA) kits. The results read by a Microwell reader and compared in a parallel manner with controls; optical density read at 450 nm on an ELISA reader.

Table 1: Study population.

Group		Number	Mean age ± SD in years
Women with bad obstetric history	Pregnant	292	28.35 ± 7.25
	Non pregnant	255	28.24 ± 6.81
	Total	547	
Women with normal pregnancy	Pregnant	140	27.40 ± 6.24
	Non pregnant	151	28.06 ± 10.51
	Total	291	
Grand total		838	28.42 ± 7.72
P value	ANOVA NS		

Collection of data

All recruited women were subject for clinical examination and laboratory investigations were carried out for the study subjects to exclude other causes of foetal wastage, such as hypertension, diabetes mellitus, syphilis, Rh (Rhesus) incompatibility, physical causes of abortion, and consanguinity. Subjects with known causes of foetal wastage were excluded from the study. All of them were interviewed to ascertain age, medical and obstetric information.

Determination of rubella IgM and IgG

ELISA was used for determination of IgM and IgG for Rubella and the test was performed according to manufacturer instructions. The kit purchased from BioCheck, Inc, 323 Vintage Park Dr, Foster City, CA 94404.

Statistical analysis

The proportion and the mean value were computed in appropriate situations. To find out any association between categorical data, Chi square test was employed using the SPSS (Version 16). If the sample size in BOH group not reach the targeted number Power Analysis were performed to determine the accuracy of findings. The study finding data were presented as frequency ± SD and 95% Confidence Interval. The determinants for Rubella infection is determined by calculation of Odd Ratio. Chi square used to determine the significance of differences between the groups.

Results

Table 2: Rubella seroprevalence in women with bad obstetric history.

Group [Number]		Number positive [Percent]	
		IgM	IgG
Bad obstetric history	Pregnant [292]	4 [1.4]	190 [65.1]
	Non- pregnant [255]	4 [1.6]	222 [87.1]
	X2	0.037	34.77
	P value	NS	0.000
	Total [547]	8 [1.5]	412 [75.3]
Normal pregnancy	Pregnant [140]	13[9.3]	99 [70.7]
	Non- pregnant [151]	0 [0]	115 [76.2]
	X2	14.64	1.107
	P value	0.000	NS
	Total [291]	13 [4.5]	214 [73.5]
Grand total [838]		21 [2.5]	626 [74.7]
X2 BOH versus Normal Pregnancy		7.02	0.32
P value BOH versus Normal Pregnancy		0.008	NS

The overall rubella seroprevalence in our study population women was 74.7%, indicating a 25.3% susceptibility rate to

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rubella infection in women with age of 14 to 48 in Kirkuk community. In addition, rubella IgG seroprevalence was not significantly (X2=0.32, P>0.05) in women with bad obstetric history (BOH) (75.3) as compared to women with normal pregnancy (73.5%) outcomes (Table 2).

Current rubella infection was 2.5% (21/838) in our study population and it was lower (X2=7.02, P=0.008) in women with BOH (1.5%) as compared to those with normal pregnancy outcome (4.5%) (Table2). Unfortunately, the current rubella infection was significantly (X2=7.45, P=0.005) higher in pregnant (3.9%) than in non pregnant (1%) women, indicating high risk of mother-to-child transmission of rubella. Furthermore, rubella IgG seropositivity was more in non-pregnant women (83%) than in pregnant (66.9%), which increased the hazard of exposure to rubella infection in pregnant women (33.1%) (Table3).

Table 3: Rubella seroprevalence in pregnant compared to non-pregnant women.

Group [Number]	Number positive [Percent]	
	IgM	IgG
Pregnant [432]	17 [3.9]	289 [66.9]
Non- pregnant [406]	4 [1]	337 [83]
X2	7.45	28.73
P value	0.005	0.000
OR	4.1169	0.4138
P value	0.0115	<0.0001

In addition, pregnancy in women with present infection was a risk factor (OR=4.1169, P=0.0115) for development of BOH, while it was not in women who rubella IgG seropositive (OR=0.4138, P<0.0001) (Table 3). Rubella IgG and IgM were not significantly varied with age. The majority (87.5%, 7/8) of current infection cases was in women win age of 20 -39 years, and IgM not detected in the age groups of 14-19 years. Rubella IgG seropositivity was 80% in women with age of <20 years, then decline to reach 75.8% in the age of 20-29 years, but increased in the subsequent age groups and reach the plateau of 79.2% in women with age of 40-48 years (Table 4). In addition, there was a significant difference in IgM seroprevalence (X2=16.2, P=0.000) between BOH and control group in women with age of 20-29 yr. Furthermore, IgG seroprevalence was significantly different between BOH and control group in women with age of 20 – 29 yr (X2=6.19, P=0.01) and 40-48 yr (X2=7.62, P=0.006).

Comparison between patients and control groups for women with age of 14-20 yr indicated a significant differences for both IgM (X2=13.3, P=0.000) and IgG (X2=6.71, P=0.01). However, only IgG seroprevalence was significantly (X2=6.25, P=0.012) different between women with BOH and control in age of 30-48 yr. But there was none significant differences in IgM and IgG seroprevalence between BOH with <30 yr and BOH with >30 yr (Table 5). OR confirmed the association between rubella IgM seroprevalence and women age of < 30 years (OR= 19.93, P=0.038), but not for IgG (X2=1.828, P>0.05) (Table 6).

Table 4: Comparison of Frequency of Rubella in BOH compared to control agents in regard to age.

Age group in years	IgMNumber positive\total [%]				IgGNumber positive\total [%]			
	Control	Patient	X2	Pvalue	Control	Patient	X2	PValue
14 – 19	0\47 [0]	0\45 [0]	-	-	33\47[70.3]	36\45[80]	1.17	NS
20 – 29	13\126[10.3]	3\240[1.3]	16.2	0.000	80\126[63.5]	182\24075.8]	6.19	0.01
30 – 39	0\86 [0]	4\214 [1.9]	1.63	NS	69\86 [80]	156\214 [75.6]	1.76	NS
40 – 48	0\32 [0]	1\48[2.1]	0.67	NS	32\32[100]	38\48[79.2]	7.62	0.006
X2	17.8	2.68			20.3	1.62		
P value	0.000	NS			0.000	NS		

Table 5: Frequency of Rubella according to age of <30 and above.

Age iyears	Number.			IgMNumber positive [%]					IgGNumber positive [%]				
	Con	Pat	T	Con.	Pat.	X2	P	T	Con.	Pat.	X2	P	T
14 -29	173	285	458	13[7.5]	3[1.1]	13.3	0.000	16[3.5]	113[65.3]	218[76.5]	6.71	0.01	331[72.3]
30-48	118	262	380	0 [0]	5[1.9]	1.66	NS	5[1.3]	101[85.6]	19 [74.1]	6.25	0.012	295[77.1]
X2				9.28	0.694			4.03	14.8	0.439			3.16
P				0.002	NS			0.045	0.000	NS			NS

Table 6: Odd ratio of Rubella in regards to age of women lower than 30 years.

Variable	Odd ratio [95% Confidence interval]	P value
Rubella IgM	19.930 [1.173 – 338.71]	0.038
Rubella IgG	1.828 [0.432 – 7.729]	NS

Rubella IgG seroprevalence was higher in rural (78.7%) than in urban (73.7%), but the difference not statistically significant (X2=1.6, P>0.05). In addition, current rubella infection was not significantly (X2=0.12, P>0.05) different in urban women (1.3%) than in rural (1.7%) living women. OR not confirmed

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the association between residence and rubella IgG (OR=1.41, P>0.05) and IgM (OR=1.29, P>0.05) seroprevalence (Tables 7,8).

Rubella IgG seroprevalence was lower in housewife women (74.4%) as compared to working (82.2%) women, but the difference was not significant (X2=1.257, P>0.05). In contrast, rubella IgM (current infection) was higher in housewife women (1.6%) than in working (0%) women (X2=0.728, P>0.05). OR not confirmed an association between occupation and both IgG (OR=0.638, P>0.05) and IgM (OR=1.56, P=>0.05). Women education was significantly influenced rubella IgG (X2=5.08, P=0.0241) but not IgM (X2=2.71, P>0.05) seroprevalence. OR confirmed the association between Occupation and IgG seroprevalence (OR=1.71, P=0.04), but not IgM seroprevalence (OR=0.281, P>0.05) (Tables 7,8).

Small size (crowding index<3) families were with higher seroprevalence for Rubella IgM (1.6%), but not reach significant (X2=0.5, P>0.05). However, Rubella IgG was significantly (X2=6.02, P=0.01) lower (66.7%) in families of >3 crowding index. OR confirmed significant association between family size and IgG seropositivity (OR=1.716, P=0.01), but not for IgM (X2=0.327, P>0.05) (Tables 7,8). Rubella IgM seropositivity rate was lower in smoker (0.92%) as compared to non- smoker (2.3%) women with BOH, but the difference was not significant (X2=1.67, P>0.05). However, Rubella IgG seropositivity was significantly (X2=18.55, P=0.000) higher (85%) in smoker than non-smoker (68.8%) women (Table 7). OR confirmed the association between smoking and Rubella IgG seropositivity (X2=2.569, P=0.000), but not for current infection (X2=2.512, P>0.05) (Table 8).

Rubella IgG seroprevalence was about the same in BOH women with haemoglobin of <11 g/dl and with >11 g/dl, for both IgM and IgG. OR not confirmed an association between haemoglobin level in women with BOH and both Rubella IgM (OR=0.873, P>0.05) and IgG (OR=0.987, P>0.05). BOH women exposed to animal was with significantly (X2=72.65, P=0.000) lower (54.1%) IgG seroprevalence than non exposed women (89.8%). In addition, Rubella IgM was significantly (X2=4.46, P=0.02) higher (2.3%) in non exposed BOH women (0%). OR not confirmed association between animal exposure and both Rubella IgG (OR=0.134, P>0.05) and IgM (OR=0.223, P>0.05) in women with BOH (Tables 7,8).

There was a significant (X2=15.31, P<0.0001) differences in Rubella IgG seroprevalence in women with repeated abortion of >3 (71.5%) and those below 3 (89.6%), while IgM did not show a significant difference (X2=0.03, P>0.05). OR confirmed an association between number of abortion and Rubella IgG seropositivity (OR=2.697, P<0.0001). Women with history of congenital anomalies were with higher (95.9%; X2=12.28, P=0.000) Rubella IgG seroprevalence than those without (73.3%). In addition, Rubella IgM seropositivity was 0% in women with history of congenital anomalies and 1.63% in those without (X2=0.799, P>0.05). OR confirmed an association between congenital anomalies and Rubella IgG (OR=8.563, P=0.003), but not Rubella IgM (X2=1.716, P>0.05) (Tables 7,8).

Table 7: Frequency of Rubella IgG and IgM in regard to sociodemographic characteristics.

Variable	[Number]	Number positive [Percent]	
		IgM	IgG
Residence	Rural [174]	3 [1.7]	137 [78.7]
	Urban [373]	5 [1.3]	275 [73.7]
	X 2	0.121	1.602
	P value	NS	NS
Occupation	House wife [502]	8 [1.6]	375 [74.4]
	Working [45]	0 [0]	37 [82.2]
	X 2	0.728	1.257
	P value	NS	NS
Education	Uneducated [142]	5 [3.5]	123 [86.6]
	Educated [405]	16 [4.0]	376 [92.8]
	X 2	2.71	5.081
	P value	NS	0.0241
Crowding Index	≤ 3 [382]	7 [1.8]	302 [69.1]
	3.1 – 8 [165]	1 [0.6]	110 [66.7]
	X 2	0.5	6.02
	P value	NS	0.01
Smoking	Present [327]	3 [0.92]	225 [68.8]
	No smoking [220]	5 [2.3]	187 [85]
	X 2	1.67	18.55
	P value	NS	0.000
Haemoglobin	< 11 [151]	2 [1.3]	114 [75.5]
	11 -19 [396]	6 [1.5]	298 [75.3]
	X 2	0.05	0.003
	P value	NS	NS
Animal exposure	Present [194]	0 [0]	105 [54.1]
	Absent [353]	8 [2.3]	317 [89.8]
	X 2	4.46	72.65
	P value	0.02	0.000
Abortion number	1 – 2 [116]	2 [1.7]	104 [89.6]
	3 – 8 [431]	6 [1.4]	308 [71.5]
	X2	0.03	15.31
	P value	NS	<0.0001
Congenital anomalies	Absent [498]	8 [1.63]	365 [73.3]
	Present [49]	0 [0]	47 [95.9]
	X2	0.799	12.285
	P value	NS	0.000

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Table 8: Association of Rubella seropositivity with sociodemographic characteristics using Bivariate analysis.

Variable		Odd ratio [95% Confidenceinterval]	P value
Occupation[Housewife versus Official]	IgM	1.564 [0.089 – 27.542]	NS
	IgG	0.638 [0.289 – 1.407]	NS
Crowding Index[< 3 versus >3]	IgM	0.327 [0.040 – 2.676]	NS
	IgG	1.716 [1.133 – 2.599]	0.01
Education [Educated versus Uneducated]	IgM	0.281 [0.016 – 4.91]	NS
	IgG	1.710 [0.959 – 3.046]	0.04
Residence[Rural versus Urban]	IgM	1.291 [0.305 – 5.465]	NS
	IgG	1.413 [0.922 – 2.167]	NS
Smoking	IgM	2.512 [0.594 – 10.619]	NS
	IgG	2.569 [1.658 – 3.980]	0.000
Haemoglobin	IgM	0.873 [0.174 – 4.371]	NS
	IgG	0.987 [0.638 – 1.526]	NS
Animal exposure	IgM	0.223 [0.028 – 1.800]	NS
	IgG	0.134 [0.086 – 0.209]	NS
Abortion number	IgM	1.243 [0.247 – 6.239]	NS
	IgG	2.697 [1.921 – 3.785]	<0.0001
ongenital anomalies	IgM	1.716 [0.097 – 30.172]	NS
	IgG	8.563 [2.051 – 35.745]	0.003

Discussion

In the present study, the seroprevalence of the rubella virus was found to be 74.7%, thus 25.3% of our women study population were non rubella immune [NRI] and were susceptible for rubella infection. Thus about quarter of Kirkuk women are with risk of development of rubella primary infection. Rubella is transmitted by the respiratory route and the incubation period is 13 to 20 days, during which a viraemia occurs and virus disseminates throughout the body [7], make its transmission from human to others simply. The NRI prevalence rate was higher to that expected in society conducting rubella immunization program. Despite the vaccination program 5-10% of women of child bearing age are susceptible to Rubella infection [8]. The increase of NRI may be due to disruption of the vaccination program during the period from 1992 to date. Statistics from the World Health Organization (WHO) show that this virus is present in Iraq with confirmed 15 cases of congenital anomalies in 2010 year [9]. As known that 10-15% escaped rubella infection in childhood, thus it seems that NRI rate that this study shows was high. In addition, the presence of such low incidence which associated with vaccination program disruption may explain such NRI rising rate. In addition, co-infections of rubella with toxoplasma and cytomegalovirus could increase the rate of pregnancy adverse outcomes [10].

The seroprevalence of rubella IgG reported in 59 reviewed studies was from 57% in Nigeria [11] to 97.9% in Nigeria [12] also in pregnant women, while the range in BOH was from 29.06% in India [13] to 78.9% in India [14]. The present study IgG rubella prevalence was in the upper range of the reported range, and it was higher than prevalence rate reported in 10 of the 59 (11.11%) global studies. In addition, this study IgG seroprevalence was higher to that reported for Sudan [15], Morocco [16], and about the same to that reported for Qatar [17]. However, our seroprevalence rate was lower to that reported for Tunisia [18]. Saudi Arabia, Libya and Syria [19-21]. Furthermore, the present study seroprevalence was higher to that reported for Baghdad [4,22], Waset [23], Thi Qar [24], Kirkuk [25], and Babylon [26], but lower than that reported by other studies for Babylon [3,27], Najaf [28], and Diyala [29].

The prevalence rate of NRI demonstrated in this study (25.3%) was higher to that reported for Taiwan [30,31], Turkey [32-39], Malaysia [40,41], Iran [41-45], Mozambique [46], South Africa [47,48], Haiti [49], Bangladesh [50-52], Nigeria[12,53], Cameroon [54], Italy [55,56], Colombia [57], Canada [58], USA [59], Switzerland [60], Nepal [61], Croatia [62], Sri Lanka [63,64], Singapore [65], India [14], Kenya [66] and Brazil [67]. However, our finding was lower to that reported for India [13,68-70], Iran [45], Nigeria [11,71,72], Brazil [73,74], Russia [75], Burkia Faso [76], Nepal [77]. The susceptibility rate to rubella infection in Kirkuk women was about similar to a study reported for Iran [78].

In Arab Countries, 19 studies reviewed, [3] which revealed that NRI of this study was about similar to that reported for Qatar [17]. In addition, NRI prevalence rate was higher to that reported for Babylon, Iraq [27], Diyala, Iraq [29], Kirkuk [6], Tunisia [18], Saudi Arabia [19], Libya [20], and Syria [21], but lower than that reported for Baghdad [4,22], Waset [23], Thi Qar [24], Kirkuk [25], Babylon [26], Najaf [28], Morocco [16], and Sudan [15].

The present study showed that women in the younger age group were more likely to be seronegative (127/458, 27.7%) than the older women (85/380, 22.4%). Women who were 29 years age and younger had the lowest serological protection, as assessed by rubella serology (27.7% seronegative), while only 22.4% of the older women were seronegative. OR in bivariate analysis confirmed that women with age lower than 30 years were 19 times more susceptible to rubella primary infection than older women (OR=19.93, p=0.038). These finding was in agreement to that recently reported study for Kirkuk [6]. However, when the women classified in to those with BOH and those with normal pregnancy outcomes, the pattern was different. The susceptibility (34.7%) for rubella infection was more in women with normal pregnancy outcomes of <30 yrs age. While in women with BOH there was no significant difference in susceptibility between women with age of <30 and >30 yrs. These findings accepted since the women with BOH do get the infection and thus were with high seropositivity rate.

Rubella IgG seroprevalence was not significantly varied

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between the age group, the lowest rate (71.6%) was in women 20 to 29 years of age, while the highest rate (87.5%) was in women 40 to 48 years of age. This trend is not consistent with that reported for other geographical areas in Iraq [26,27,29] and Morocco [16]. In a study performed in Diyala [29], the highest rate of seropositivity was in the age of >40 years, while the lowest rate was in the age of <20 and 30 to 39 years. In Babylon, two study reported [26,27], in the 1st one [26], the highest seroprevalence was in age of <20 years, while in the 2nd one the highest rate was in 20 to 29 years age. Unexpectedly, the seroprevalence in the two studies reduced with advancing age and the rate is low (2.4% - 45.4%). In Morocco [16], the highest seroprevalence in age of 25 to 29, while the lowest was in age 35 to 39 years.

The higher seroprevalence among older women as this study shows may be a result of more durable IgG titers from natural disease combined with boosting from circulating virus than the titers resulting from immunization [79]. It is also possible that older women were more likely to have received postpartum immunization. One of the important findings of this study is the reduction of rubella IgG seroprevalence from 85.2% as determined for 3 years (2010-2012) [80] to 74.7 in this study (X2=48.4,P=0.000). Given that rubella titers wane over time in the absence of circulating wild virus, there will be a cohort effect representing the waning of vaccine induced immunity among women who had received only one dose of vaccine [81]. Another possibility for the high seronegativity in the prospective study as compared to retrospective may be a high incidence of immigrants from other governorates to Kirkuk without rubella immunization.

The prevalence rate of NRI was more in urban (26.3%) as compared to rural (21.3%) indicating that urban women are more at risk of rubella infection. However, OR calculation in bivariate analysis not indicated that residence was with a significant correlate (X2=1.413, P>0.05) for seroreactivity. This finding consolidated that reported recently for Kirkuk population [6]. The proportion of immigrants was more in urban areas than in rural, which may influence such seroreactivity. The trend of high seropositivity in rural area was reported for study performed in Babylon, Iraq [26]. However, our finding was not agreed with study reported for Diyala, Iraq [29] and Morocco [16] which indicated that seropositivity was more in urban area.

The seroprevalence was less predominant in housewife women (74.4%), while it was 82.2% in working women. This finding was in consistent with previously reported for Kirkuk [25] and Babylon [27], however, the seroprevalence was very low for housewife (7.28%) and officials (2.01%) in the study reported for Kirkuk [25] and not agreed with recent report for Kirkuk [6]. In a bivariate analysis, OR not confirmed a significant association between seroprevalence of rubella IgG and housewife occupation (OR=0.638, P>0.05).Thus occupation seems not to play significant role in rubella IgG seroprevalence determination as this study indicated.

This high seropositivity in working women could be attributed due to that rubella mostly transmitted through droplet and working women may exposed more to natural infection than house wife. Small size families were more prone for rubella infection (69.1%) and with significant difference from that in large size families (X2=6.02, P=0.01) and this association confirmed by OR calculation. Education was with significant relationship with rubella IgG seropositivity (X2=5.08, P=0.0241), the seroprevalence was more in educated (92.8%) as compared to uneducated (86.6%). This finding was consistent to previously reposted studies for Iraq [6,29]. OR confirm a significant association of rubella IgG seropositivity with education (OR=1.71, P<0.04).

The present study indicated that rubella IgG seroprevalence was significantly (X2=28.73, P=0.000) higher in non-pregnant (83%) as compared to pregnant (66.9%) women. This finding was consistent with that reported for other area in Iraq [6,29] and in contrast to that reported for Babylon [27], which reported higher rate in pregnant women. Rubella acute infection as indicated by presence of specific rubella IgM in serum was demonstrated in 1.5% of women with BOH and the incidence rate was lower in pregnant BOH (1.4%) as compared to non-pregnant BOH (1.6%), but the difference not reach significant level. This finding was 3.21 times lower than minimum reported global figure [2]. Rubella IgM seropositivity range globally was from 4.49% in India [2] to 31.58% in India also [14] in women with BOH.

When the finding of the present study compared to 19 studies performed for Arabian countries in women with BOH, still the incidence rate (1.5%) was lower than the range reported. The lower rubella IgM seropositivity rate was 4.8% in Baghdad, Iraq [22] to 62.3% in Waset, Iraq [23]. Our study and the previously reported [6] figures indicated a low incidence rate of rubella in Kirkuk for the year 2012 and 2013, respectively, a findings that goes with retrospective study for Kirkuk, which indicated a significant reduction (X2=189, P=0.000) of rubella incidence from 20.25% in 2010 to 3.86% in 2012. However, the present study finding was not agreed with that reported for Kirkuk [25], who reported >3 times higher incidence rate for the year 2006-2007.

This study shows that rubella IgM seropositivity in women with normal previous pregnancy was 4.5% with a significant differences (X2=14.64, P=0.000) between pregnant (9.3%) and non-pregnant (0%) women. This finding confirms the pattern reported recently for Kirkuk [6], however, with lower rate. Reported studies in Arabian countries indicated a range of 3.4% for Sudan [15] to 53.9% for Babylon, Iraq [26] in pregnant women with previous normal pregnancy. Globally, the range of rubella IgM seropositivity was with a range from 0% for Turkey [39] in

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pregnant women and Croatia [62] in pregnant and non-pregnant women to 91.3% for Nigeria [11] in pregnant women. Thus the present study shows that current infection was significantly higher (X2=7.02, P=0.008) in women with normal previous pregnancy, indicating a hazard of congenital rubella syndrome development in such hidden cases. This finding agreed to that reported recently by Aljumaili [6] for Kirkuk governorate.

In addition, IgM seropositivity was significantly (X2=7.45, P=0.005) higher in pregnant as compared to non-pregnant women. This association confirmed by OR calculation which indicated that pregnancy was a significant risk factor for development of rubella congenital infection for recent infection (OR=4.1169, P=0.0115) using a bivariate analysis. However, rubella IgG seropositivity was with protective pattern for development of BOH in pregnant women (OR=0.4138, P<0.0001). Multiple regression analyses not indicated pregnancy as risk factor for BOH.

Current rubella infection was more predominant in rural women population, but the difference not significant. This finding was not agreed to a recent study for Kirkuk [6], which demonstrates a higher significant current infection in urban women. In addition, all positive cases were housewife women; however, the difference was not significant. This finding agreed to that reported by Aljumaili [6]. Furthermore, current rubella infection was with non significant variation between the education level groups. Current infection was higher in educated women, but the difference was not significant. This could be attributed to the compliance of educated women with the recommendation of giving rubella vaccine booster dose at the first visit physician contact in antenatal program for pregnant women who had waning immunity been recognized in a previous pregnancy. Thus strategies that offer immunizations to women with childbearing age are to compulsory when women access the health care system for other reasons (such as hospitalization or postpartum visit) would be applied to improve the level of rubella immunity. However, the best effective approach for the prevention of congenital rubella syndrome was the use the WHO that called combined strategy [82].

Rubella vaccine was incorporated into the national immunization program in Iraq through MMR vaccine, however; still there were a 2.5% of current rubella infection and 25.3% susceptibility rate for infection. Unfortunately, these rates were higher to that reported recently for Kirkuk [6]. These findings indicated that there was a need for better follow up of the immunization program for women in childbearing age. In the last decade the health system disrupted due to violation and thus the current rubella infection was > twice (3.5%) in age of <30 years as compared to 1.3% in the age of >30 years. OR confirmed (OR=19.93, P=0.038) such association and about 3/4 of the seropositive samples were in women with < 30 years of age.

Unfortunately, rubella screening of pregnant women is not routinely carried out in Iraq. The vaccine failure cases and improper access of targeted group to vaccine receiving or decreasing of the protective level of antibodies may occur in the next few years. Therefore, future screening for rubella antibodies will be more important in childbearing age. In addition, in Iraq, there was no community based rubella seroepidemiological study reported, and this type of study is warranted since it gave the sound data basis of rubella epidemiology. These are of importance since rubella vaccination has been reported to be very efficient and cost effective in preventing CRS [83].

The present study shows a highly significant seroprevalence of rubella in women with congenital anomalies and this illustrates a problem of CRS in studied population OR confirmed such association. A key strategy for preventing rubella and CRS is ensuring sufficient population immunity through natural disease or through vaccination programs that achieve high coverage [84]. But the vaccination coverage cannot be kept high in the last decade, there is a risk of the resurgence of CRS as was expected in Turkey [84] and experienced in Greece after subsequent years of low coverage scores in infant immunization [85]. The universal rubella immunization coverage provided for 12-months-old and 6 year old children should be therefore is kept high to minimize this risk [84]. Also, vaccination policy should be implemented for women at risk, which may be carried out either through the vaccination of the whole cohort (e.g. 14-44 years) or cohorts of particular groups of women such as health care workers, school girls, government workers, college students, postpartum women, premarital couples [86] or rubella susceptible women. However, re-infection can occur which is generally asymptomatic and in pregnancy it poses minimal risk to the fetus [87]. It is important that women are vaccinated prior to their first pregnancy [7]. The vaccine is contraindicated for pregnant women, but when unwittingly used, no problems have been seen [54]. If the patient is pregnant and seronegative, the pregnancy should be monitored carefully and the patient vaccinated postpartum [88].

Rubella IgG seroprevalence was significantly lower in smoking women with BOH as compared to non-smoker. Cigarette smoke was shown to augment the production of numerous proinflammatory cytokines and to decrease the levels of anti-inflammatory cytokines [89]. However, results of studies on paternal smoking and abortions have been inconsistent [90]. The paradox of this study finding may be influenced by secondhand smoke exposure [91], amount of daily smoking, current and previous smoking [92] or direct effect of smoking on men's sperm. The limitation of this study should be considered in the interpretation of the present study finding.

Rubella seroprevalence was significantly more in women with abortion number of 1-2 than those with 3-8 abortions. This association confirmed by OR. This could be attributed

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to that the primary infection was with high magnitude of immunological response, while the immunoglobulin may wane with time. Anaemia and animal exposure seem not influence the rate of current and remote infections in women with BOH. In conclusion, this study provides important and highly useful information on baseline seroprevalence data on rubella in Iraq. A 25.3% of our women study population were non rubella immune and were susceptible for rubella infection. In addition, rubella seroprevalence associated with BOH.

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