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Research Article
Sero-Positivity Rate of Rubella Infection and Associated Risk Factors Among Pregnant Women in Mukalla City, Hadhramaut, Yemen

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Abstract

Background and Objective: Seropositivity rates of rubella virus infection among pregnant women vary worldwide. Yemen is among the developing countries the rubella disease is still present. This study was designed to estimate the seropositivity rate of rubella infection and risk factors associated among pregnant women attending antenatal care clinics in Mukalla city, Hadhramaut, Yemen. **Materials and Methods:** This was a cross-sectional study performed on a total of 190 pregnant women and the serum samples were collected and screened using the enzyme-linked immunosorbent assay (ELISA) anti-rubella virus IgM and IgG test. Qualitative demographic and reproductive data were collected using a standardized questionnaire. **Results:** One hundred-ninety pregnant women tested for rubella antibodies, 136 (71.6%), were positive for anti-rubella IgG, while 17 (8.9%) was positive for IgM. Higher seropositivity rates were found in the age group of the age groups 15-30 years with significantly dependent (COR = 0.749, 95% CI = 0.113-0.557, p = 0.001) and the moderate level income (COR = 0.761, 95% CI = 0.075-0.760, p = 0.015). Anti-IgM positive rubella infection had a significant relationship with the pregnant women miscarriage (COR = 0.925, 95% CI = 0.020-0.283, p = 0.00) and the risk of contracting rubella virus infection was found to increase with history of live births with a statistical significance (COR = 1.942, 95% CI = 1.020-3.695, p = 0.043). **Conclusion:** Seropositivity rates of a rubella infection are high in Mukalla city, Hadhramaut and are significantly associated with an increase in age and being income level. The risk of contracting rubella infection was found to increase with gestational age and associated with miscarriage. Screening of rubella and immunization of women at risk is highly recommended in this area with a high non-immune rate against the rubella virus.

Key words: Sero-positivity, rubella infection, pregnant women, risk factors, ELISA immunoassay

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Competing Interest: The authors have declared that no competing interest exists.

Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Rubella infection is a public healthcare problem determined by the teratogenic effect of the rubella virus during pregnancy[1]. The rubella infection may be subclinical or cause self-limiting illness with clinical features, these areas low-grade fever, lymph nodes atrophy and febrile rash illness in children and adults[2]. However, if the rubella virus is infected during pregnancy, particularly during the first trimester, can result in stillbirths, miscarriages and congenital rubella syndrome (CRS). CRS is a group of birth defects that often includes hearing loss, cataracts, mental retardation and congenital heart defects[3]. The risk of congenital defects varies from 10-90% depending on the gestational age of the fetus at the time of infection and the occurrence of rubella earlier in gestation increases the risk of more severe outcomes[4].

The seropositivity of rubella infection among pregnant women varies widely in countries of the world. In fact, in many developing countries, the seropositivity of rubella infection in pregnant women has been reported[5,6]. Therefore, serological investigation of Rubella infection based on the detection of the antibodies IgG and IgM remains the mainstay for Rubella diagnosis[7]. For Rubella disease, maternal or CRI, there is no specific treatment. The primary means of preventing CRS is Rubella immunization. Rubella vaccines have been utilized effectively in many developed countries to reduce the prevalence of Rubella and prevent the consequences of CRS[8]. Rubella is a vaccine-preventable infectious disease and is considered to be potentially eradicable. Women's vaccination before pregnancy is the only means to prevent congenital infection. In developed countries, rubella infections are indeed protected by active immunization of measles, mumps and rubella (MMR) vaccine[5]. The data of World Health Organization (WHO) revealed that more than 100,000 children are born with CRS each year in developing countries[9] and the estimated number of CRS cases globally decreased from 119000 cases in 1996-105000 cases in 2010 as a result of the vaccination schedule in many high-income and some low-income and middle-income countries[10].

In Yemen, the rubella vaccination is not included in the national immunization program until the year 2010 and there is no clear strategy for rubella infection surveillance in pregnant women. Although rubella Seroprevalence in pregnant women has been studied elsewhere in Yemen, in Hadhramaut governorate no published data is describing the prevalence of the rubella disease. Therefore, the present study was aimed to determine the seroprevalence of rubella virus infection using the Enzyme-Linked Immunosorbent Assay (ELISA) and their associated risk factors among pregnant women attending antenatal care clinics in Mukalla city, Hadhramaut, Yemen.

MATERIALS AND METHODS

Study design and population: A cross-sectional study was conducted from November, 2019 to June, 2020 of 190 pregnant women attending antenatal care clinics in Mukalla city, Hadhramaut, Yemen. The range of age of the population study was 15-45 years. Written informed consent was obtained from all studied participants before commencing the study.

Inclusion and exclusion criteria: Pregnant women confirmed to be in their first, second or third trimester was included in this study. Women excluded when were they are non-pregnant.

Data collection: A standardized, interviewer-administered, structured questionnaire was developed to obtain data regarding rubella infection risk factors. It consisted of systematic questions on socio-demographic and reproductive characteristics. The questionnaire was filled with the aid of an interviewer.

Laboratory procedures: All blood samples were collected in plain tubes, allowed to clot and centrifuged at room temperature. Then the sera were separated and stored at -20°C until transported in dry ice to the National Center of Public Health Central Laboratories in Mukalla city for analysis. ELISA immunoassay technique was used for detection of anti-rubella IgG and IgM using commercial diagnostic kits according to the instructions supplied by PerkinElmer Company, USA. Manufacturer reference values for positive results were rubella IgG index of 1.00 or greater or >15 IU mL^{-1} and Rubella IgG index of 0.90 or less, <13 IU mL^{-1} for negative results, while rubella IgM index of 1.00 or greater was considered as positive and rubella IgM index less than 0.9 as a negative result.

Statistical analysis: Statistical Package for Social Sciences (SPSS) version 25 (SPSS Inc, Chicago, IL, USA) was used for data analysis. The association between different variables and the outcome of rubella virus infection was calculated and compared using Pearson Chi-square (χ^2) test. Binary and multiple regression tests (crude odds ratio/adjusted odds ratio) were used to detect independent predictors of rubella virus positivity in pregnant women. The level of statistical significance was set at a $p<0.05$.

RESULTS

Overall prevalence of rubella IgG and IgM antibodies: Out of the 190 enrolled pregnant women, the seropositivity of Rubella-specific IgG antibody 136 (71.6%) and 17 (8.9%) positive for Rubella-specific IgM antibody were included in the final analysis as given in Table 1.

Prevalence of rubella infection concerning demographic characteristics: High prevalence of anti-rubella IgG94 (49.5%) was observed with significantly association in the age group 21-30 years (COR = 0.749, 95% CI = 0.113-0.557, p = 0.001), while anti-rubella IgM1(0.5%)was observed with significantly association in the age group 15-20 years (COR = 8.750, 95% CI = 1.016-75.374, p = 0.048). There was significantly association of rubella specific IgG antibody 115 (60.5%) with moderate-income level (COR = 0.761, 95% CI = 0.075-0.760, p = 0.015). The Seropositivity rate was slightly higher among pregnant women residing in urban than rural areas for IgG antibody 114 (60.0%) and anti-IgM16 (8.4%) but this difference was insignificant statistically (p>0.05). No statistical difference was observed for sero-positivity rubella specific IgG and IgM antibodies with occupation and educational level (p>0.05). In multivariate logistic regression analysis, the risk of contracting rubella virus infection was found to increase with age groups and income level with a statistical significance as shown in Table 2.

Prevalence of rubella infection concerning reproductive characteristics: High prevalence of rubella antibodies IgG136 (71.6%) and IgM17 (8.9%) was observed with no significantly association in trimester at the time data collection (p>0.05). The risk of contracting rubella was higher in the parity (1-3) for anti-rubella IgG 92 (48.4%) (COR = 1.942, 95% CI = 1.020-3.695, p = 0.043) and for anti-Rubella IgM 6 (3.1%) (COR = 0.668, 95% CI = 0.122-0.902, p = 0.031). Moreover, anti-rubella-IgM

Table 1: Distribution of Rubella seropositivity among the pregnant women

			Rubella sero-status (No. =190)			
			Sero-positivity IgG		Sero-positivity IgM	
Characters	Categories	Number of tested	No.	%	No.	%
Age groups	15-20 years	35	25	13.2	1	0.5
	21-30 years	121	94	49.5	9	4.7
	31-45 years	34	17	8.9	7	3.7
Educational level	Illiterate	31	19	10	5	5
	Primary	86	64	33.7	9	9
	High school	59	46	24.2	2	2
	Bachelor	12	6	3.2	1	1
	Postgraduate	2	1	0.5	0	0
Residence	Rural	30	22	11.6	1	0.5
	Urban	160	114	60.0	16	8.4
Income level	High	30	15	7.9	7	3.7
	Moderate	147	115	60.5	9	4.7
	Low	13	6	3.2	1	0.5
Occupation	Student	6	4	2.1	1	0.5
	Employee	12	8	4.2	1	0.5
	Housewife	170	122	64.2	15	7.9
	Others	2	2	1.1	0	0
Gestation age	1st trimester	60	42	22.2	5	2.6
	2nd trimester	57	43	22.6	3	1.6
	3rd trimester	73	51	26.8	9	4.7
Parity	1-3	123	92	48.4	6	3.1
	>3	67	44	23.2	11	5.8
History of miscarriage	1-2	48	32	16.8	15	7.9
	> 2	6	5	2.6	1	0.5
	None	136	99	52.2	1	0.5
Past history of Rubella infection	Yes	7	4	2.1	0	0
	No	183	132	69.5	17	8.9
Immunization against Rubella virus	Yes	0	0	0	0	0
	No	190	136	71.6	17	8.9

Table 2: Seroprevalence of rubella virus infection concerning the demographic characteristics of the pregnant women

		Sero-status IgG					Sero-status IgM				
Characters	Categories	No.	%	COR	CI (95%)	p-value	No.	%	COR	CI (95%)	p-value
Age group	15-20 years	25	13.2	0.584	0.157-1.097	0.076	1	0.5	8.750	1.016-75.374	0.048
	21-30 years	94	49.5	0.749	0.113-0.557	0.001	9	4.7	2.725	0.952-7.98	0.062
	31-45 years	17	8.9	1			7	3.7	1		
	Total	136	71.6				17	8.9			
Educational level	Illiterate	19	10	1			5	2.6	1		
	Primary	64	33.7	0.456	0.228-1.299	0.171	9	4.7	1.645	0.505-5.355	0.408
	High school	46	24.2	0.553	0.173-1.156	0.097	2	1.1	5.481	0.997-30.127	0.050
	Bachelor	6	3.2	1.583	0.413-6.063	0.502	1	0.5	0.038	0.160-5.786	0.966
	Postgraduate	1	0.5	1.583	0.090-27.771	0.753	0	0	310668243.1	0.000	0.999
	Total	136	71.6				17	8.9			
Residence	Rural	22	11.6	1			1	0.5	1		
	Urban	114	60.0	1.110	0.461-2.672	0.816	16	8.4	0.357	0.140-2.953	0.570
	Total	136	71.6				17	8.9			
Income level	High	15	7.9	0.143	0.233-3.159	0.817	7	3.7	1.950	0.369-10.309	0.432
	Moderate	115	60.5	0.761	0.075-0.760	0.015	9	4.7	3.709	0.888-15.484	0.072
	Low	6	3.2	1			1	0.5	1		
	Total	136	71.6				17	8.9			
Occupation	Student	4	2.1	80774441.0	0.000	0.99	1	0.5	1.00	0.000	0.99
	Employee	8	4.2	80774441.0	0.000	0.99	1	0.5	1.00	0.000	0.99
	Housewife	122	64.2	635602183.1	0.000	0.99	15	7.9	1.00	0.000	0.99
	Unemployed	2	1.1	1			0	0	1		
	Total	136	71.6				17	8.9			

Statistically significant at p<0.05, COR: Crude odds ratio and CI: Confidence interval

Table 3: Sero-prevalence of rubella virus infection with the reproductive characteristics of the pregnant women

		Sero-status IgG					Sero-status IgM				
Characters	Categories	No.	%	COR	CI (95%)	p-value	No.	%	COR	CI (95%)	p-value
Gestation age	1st trimester	42	22.2	1			5	2.6	1		
	2nd trimester	43	22.6	0.24	0.335-1.721	0.510	3	1.6	1.205	0.307-4.730	0.790
	3rd trimester	51	26.8	1.007	0.478-2.120	0.986	9	4.7	0.354	0.204-2.044	0.458
	Total	136	71.6				17	8.9			
Parity	1-3	92	48.4	1.942	1.020-3.695	0.043*	6	3.1	0.668	0.122-0.902	0.031
	>3	44	23.2	1			11	5.8	1		
	Total	136	71.6				17	8.9			
History of miscarriage	1-2	32	16.8	1.155	0.555-2.403	0.700	15	7.9	0.925	0.020-0.283	0.00
	> 2	5	2.6	2.178	0.554-8.563	0.265	1	0.5	0.971	0.005-0.164	0.00
	None	99	52.2	1			1	0.5	1		
	Total	136	71.6				17	8.9			
History of Rubella infection	Yes	4	2.1	1.941	0.420-8.978	0.396	0	0	176233621.6	0.000	0.999
	No	132	69.5	1			17	8.9	1		
	Total	136	71.6				17	8.9			
Immunization against rubella	Yes	0	0	-	-	-	0	0	-	-	-
	No	136	71.6	-	-	-	17	8.9	-	-	-
	Total	136	71.6	-	-	-	17	8.9	-	-	-

Statistically significant at p<0.05, COR: Crude odds ratio and CI: Confidence interval

positive 15 (7.9%) had a significant relationship with pregnant women miscarriage (1-2) (COR = 0.925, 95% = CI = 0.020-0.283, p = 0.00) and (COR = 0.971, 95% CI = 0.005-0.164, p = 0.00), while statistical not significant associated for IgG antibody 32 (16.8%) (p>0.05). No statistical difference was observed for sero-positivity anti-rubella IgG 4 (2.1%) and IgM 0 (0%) with past history of rubella infection (p>0.05). In multivariate logistic regression analysis, the risk of contracting rubella virus infection was found to increase with parity and history of miscarriage with a statistical significance. In this study, all pregnant women were not protected against rubella virus as shown in Table 3.

DISCUSSION

This study revealed the anti-rubella IgG prevalence of 71.6% in Mukalla city is relatively high which indicates prior exposure to the rubella infection i.e., immune as a result of previous wild-type rubella infection. Other studies with high levels of anti-rubella IgG exposure in pregnant women were reported in Turkey 95.0% and 96.1%[10,11], Nigeria 83.3%[12], India 86.8%[13], Ethiopia 79.5%[14], Egypt 88.2%[15], Saudi Arabia 91.6%[16], Sudan 95.1%[17], Kenya and Tanzania 92.9 and 92.6%, respectively[18,19], Zimbabwe 92%[20], Ghana 93%[21]. These findings revealed that a high proportion of the population has acquired immunity which confirms the exposure to previous natural infections of the rubella virus. Our study suggests that rubella disease is highly prevalent in the study area which may be attributed to sustained transmission hence development of the antibodies.

The reported Seroprevalence of rubella IgG antibodies in this study is higher than reported in Sudan 65.3 and 51.6%[22,23], Ethiopia 46.4%[24], Nigeria 68.6%[12], China 16.7%[25], India 39.20%[26] and Libya 44.2%[27]. Other Seroprevalence of anti-rubella IgG was reported in some studies conducted in Southern Italy[28], Nigeria[29,30] and Taiwan[31]. These results suggest that there is a high transmission rate of the rubella virus in Mukalla city, Hadhramout. However, this might not reflect the true picture as women were not investigated during early pregnancy and followed-up. Also, the differences in the rate of past exposure to rubella between these countries may indicate a varying epidemiological status of rubella infection in different localities.

The current study reported anti-rubella IgM Sero-positivity 8.9% among pregnant women that represents acute (recent) rubella infection and which is comparable to 9.5% were positive for rubella-specific IgM antibody among pregnant women in Ethiopia[14], Libya 18.9%[27], Ethiopia 39.4%[32], India 17.5% and 46.5%[33,13].

The Sero-positivity of anti-rubella IgM in this study was higher than that reported in Turkey 0.54% and 2%[10,11], Bangladesh 0.75%[34], India 5.26%[26] and Nigeria 3.9%[12]. The variations in Sero-prevalence could be as a result of the epidemics which go unclear due to the gentle nature of the rubella infection. This IgM Sero-positivity could have been attributed to the lack of introduction of rubella vaccination into routine national immunization programs in some countries.

In the current study, the most pregnant women were within the accepted childbearing age infected with rubella virus 49.5% for the age group of 21-30 years with the statistically significant association of rubella IgG antibody. Other studies showed a high prevalence of rubella IgG antibody among Yemeni school girls of age group 11-21 years[35], in Nigeria 85.7% in the age group of 15-19 years, 86.8% in the age group of 20-24 years, 89.6% in the age group of 25-29 years and 100% in more than 40 years age group[36]. Another study carried out in Nigeria revealed that most infections of rubella were acquired before the age of 35 years[30]. Also, the prevalence of rubella infection was 83.9% among women aged 20-25 years and 93.9% among those aged 25-30 years in Egypt[15]. Age groups showed no significant association with rubella-specific IgM and IgG antibodies among pregnant women in Ethiopia[14]. Some studies showed the proportion of women with the high seropositivity rubella infection was in the age group 20-30 years in Kenya[19], the age group of 14-20 years in Tanzania[18], the age group of 20-29 years in Nigeria[6], the age group of 18-25 years in Southern Iran[37], the mean age 30.9 years in Zimbabwe[20], the mean age 29 years in Colombia[38], the mean age of 25.7 years in Western Sudan[22], the age group of 20-29 years in Brazil[39].

In this study, primary and high school levels were at higher risk for rubella infection with no statistically significant association between the level of education of the pregnant women and rubella infection Seroprevalence, similar results of studies conducted in Iran and Zimbabwe showed a relationship between rubella infection and secondary level of pregnant women education[37,20]. There was a significant relationship between rubella infection and illiteracy in Western Sudan[22]. Other studies showed the incidence of anti-rubella IgG and IgM was not associated with the education of pregnant women in Nigeria[36], Egypt[15], Ethiopia[14] and also other previous studies[19,40].

The majority of seropositivity rubella infections of IgG and IgM of pregnant women in the present study were from urban areas with insignificantly associated differences. Another study reported the prevalence in rural areas was 51.5% and in urban areas was 44.7% in Ethiopia[25]. Another study showed residence was not significantly associated with the prevalence of rubella antibodies[14,15]. A study carried out in Ethiopia showed a significant association between residence site and IgG sero-positivity, where the urban residents had higher past rubella exposure compared with rural residents[41]. Likewise, moderate socioeconomic status has been found as a risk factor for acquired rubella infection in the current study and there was a significant relationship between pregnant women's income level and rubella infection Sero-positivity. Lower social-economic status puts people at higher risk of having poor health due to poor housing conditions which are overcrowded[14].

In this study, the majority of pregnant women infected with rubella were housewives with a percentage of 64.2 and 7.9% of anti-rubella IgG and IgM, respectively with an

insignificant statistical association. Mothers who were in small business enterprises had the highest IgG positivity 31.5% followed by farmers 29.5% found in Tanzania[18] and South Africa[42]. Also, most of the participants were farmers 49.4% followed by housewives 45.2% observed in Western Sudan[25], while in Southern Sudan, 94.2% of women were unemployed[43]. Anti-rubella IgG prevalence was not associated with the occupation of pregnant women in Nigeria[36], while occupation showed no significant association with rubella-specific IgG and IgM antibodies among pregnant women in Ethiopia[14]. These findings could have been attributed to the interactions or contact with infected persons in populations. Current study findings revealed no significant association between the prevalence of anti-rubella IgG and IgM with the gestation age of the pregnant women and the seropositivity in various trimesters is still higher than that from other countries with no immunization program in Sudan[22], Nigeria[29] and Kenya[19,40]. Another study revealed that the risk of contracting rubella virus infection was found to increase with gestational age[18]. Rubella IgM and IgG antibodies prevalence concerning gestation age showed no significant association in Ethiopia[14], Nigeria[36], while pregnant women at first trimester were risk factor found to be significantly associated with anti-rubella IgG in Northwest Ethiopia[24].

In this study, the risk of contracting rubella virus infection was found to increase with history of live births 48.4% with statistical significance relationship of rubella IgM antibody, whereas, rubella IgM and IgG antibodies prevalence concerning the history of live births showed no significant association in Ethiopia[14]. In this study, the Sero-positive rubella IgM had a significant relationship with the pregnant women miscarriage 16.8%, whereas other results of rubella IgG and IgM antibodies prevalence about the history of abortion and stillbirth showed no significant association in Ethiopia[14]. In this study, the very small proportion of pregnant women who had a history of rubella infection was positive for rubella IgG antibody compared with those has no history 69.5%. A similar study showed 86.6% of women who reported no history of rubella were positive for rubella antibody[15]. In the present study, all the pregnant women participants were not protected against rubella disease. Another study showed none of the women ever had previous rubella virus vaccination[30], another study revealed the prevalence of rubella IgG was not associated with vaccination in pregnant women in Nigeria[36].

CONCLUSION

The study determined a high rate of seropositive rubella infection among pregnant women in Mukalla city, Hadhramaut and this rate was significantly associated with age and income level. The risk of Rubella infection contracting was found to increase with gestational age and associated with miscarriage. Screening for the rubella virus and immunization of childbearing age women are highly recommended.

SIGNIFICANCE STATEMENT

This study discovers the correlation between rubella virus infection and the importance of immunization with MMR vaccine that can be beneficial for the preventing of Rubella disease among childbearing age women. The study will help the researchers to uncover and study the relationship between the role of risk factors and the occurrence of Rubella infection in the communities.

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