



SUSCEPTIBILITY TO RUBELLA AND ITS RELATED TO VACCINATION STATUS AMONG PREPARATORY YEAR STUDENTS IN ADEN UNIVERSITY, YEMEN

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ABSTRACT

Background: Rubella is a contagious viral infection characterized by mild fever and rashes. Maternal infection early in pregnancy often leads to birth defects known as congenital rubella syndrome (CRS). **Objective:** To determine susceptibility to rubella among preparatory year's students in Aden University and relate it to vaccination status. **Methods:** A cross-sectional study was carried out among 146 preparatory year students in Aden University. Level of rubella IgG was evaluated by Enzyme linked immunosorbent assay (ELISA) technique using a commercially available kits on 146 serum samples. **Results:** The seropositivity rate of anti-rubella IgG was 130 (89 %) with 69 (53.1%), 61 (46.9%), for male and female, respectively. However, the susceptibility rate among respondents was 16 (11.0 %); 5 (31.25 %) were male and 11 (68.75 %) were female. **Conclusion:** This study reveals that alarmingly considerable percentage of susceptibility among students. Hence, there is a great need for a proper health education programmes and community mobilisation to encourage of population toward vaccination.

KEYWORDS: Rubella, Susceptible, Preparatory year.

INTRODUCTION

Rubella, also called German measles or three-day measles which is an acute viral infection caused by a Togavirus of the Rubivirus (Lambert *et al.*, 2015). Rubella is mainly transmitted through the respiratory route and commonly occurs in children and young adults. It can also be transmitted from infected pregnant women to their unborn babies, that cause congenital rubella infection (CRI) has outcomes including miscarriage, stillbirth, and abortion.

Before the development of the rubella vaccine, rubella infection was prevalent worldwide, for instance in the United States an epidemic resulted 20,000 infants with permanent damage due to intra-uterine infection with rubella virus; world health organization (WHO), estimates that more than 100 000 children are born with CRS each year, and most of them in developing countries (Lambert *et al.*, 2015).

Safe and effective rubella vaccines have been available since 1969. However, until the 1990s, developed countries primarily used rubella vaccines, because the disease burden caused by rubella virus had not been

documented sufficiently in the developing world, and because of the additional cost of the rubella vaccine component when combined with Measles and Rubella (MR) or Measles, Mumps and Rubella (MMR) vaccine and concern that the risk for CRS might increase if high vaccination coverage could not be achieved and maintained. Low coverage might result in increased virus circulation which could increase the average age of rubella infection for females from childhood to the childbearing years (Dannetun *et al.*, 2004).

In Yemen, an incidence rate of rubella of 41 and 52 cases per million was registered in 2013 and 2014, respectively. Prior to war, Yemen had a relatively stable vaccination rate reaching 70–80% of the target population (Qirbi & Ismail, 2016). In March 2015, Yemen underwent major political upheaval civil war. Yemen had a fragile health care system prior to the onset of war, did not have the infrastructure to withstand these changes and is currently on the brink of collapse (WHO, 2016).

A national campaign against rubella and measles was launched in 2014 with the participation of representatives

from WHO, United Nations International Children's Emergency Fund (UNICEF) and the World Bank in Yemen. The ten-day campaign, is targeting 11, 637, 887 children aged from 9 months to 15 years with MR vaccine. In addition, polio vaccine is administered to 4, 884, 630 children under five years. The campaign also targets students in schools and high risk groups such as refugees, internally displaced persons and other marginalized communities (Raslan *et al.*, 2017).

In Yemen, a community based study was conducted in 1985 among 476 subjects, they were investigated using haemagglutination test for rubella. The result showed that the prevalence of rubella among children aged 1-6 years was 46.2%, the values obtained for girls aged 15-18, women in the 19-24 and 25-29 years age group being 81%, 86.3% and 89.9%, respectively. The authors have been discussed the comparatively high risks of contracting rubella during pregnancy in four regions of Yemen (Strauss *et al.*, 1989).

Similarly, another study was conducted in Sana'a among schoolgirls aged 11-21 years old, to estimate the prevalence of rubella Immunoglobulin Gamma (IgG) antibodies, and stated that 8.36 % were susceptible to rubella (Sallam *et al.*, 2003). A previous study among 1368 subjects in urban and rural Sana'a, found that 14.6% of respondents had no antibodies to rubella (Sallam *et al.*, 2006).

Interestingly, findings from a recent study in New York State, United States of America (USA) reported the detection of two infants with CRS, both mothers were foreign born and travelled to Yemen during their pregnancy (Robyn *et al.*, 2017). No data was available on the prevalence of CRS in Yemen. In Yemen, though vaccination against rubella was launched in 2014, there were few studies conducted on the susceptibility of peoples to rubella (Strauss *et al.*, 1989; Sallam *et al.*, 2003; Sallam *et al.*, 2006).

More epidemiologic studies are needed to explore immunity along with associated risk factors for rubella infection. It is hoped that the information from this study will provide insight into the current status of rubella susceptibility in student preparatory year, so that preventive measures can be taken.

The current study was designed to determine the rubella susceptibility among students of preparatory year and relate it with vaccination status. It is hoped that the results will provide insight into the current status of rubella susceptibility in adolescence, so that preventive measures can be taken.

Study design

A cross-sectional seroepidemiological survey was conducted among the students of preparatory year who study at Aden University, in Yemen. The required sample size was calculated based on the prevalence of

previous study 8.36% (Sallam *et al.*, 2003), with a 95% confidence interval (CI), and degree of precision = 5%. The estimated sample size was 117 participants. This study was approved by Research and Ethics Committee of faculty of medicine, university of Aden, Yemen (Research Code: REC-25-2018). All respondents were fully notified that participation was voluntary and that it was possible to withdraw from the research without notice. Those who wished to participate were required to sign a consent form. Out of 190 students approached, 146 agreed to participate (response rate 76.8%). The students were interviewed face-to-face using a structured data collection sheet that included questions on demographic data (gender, age and residence), past history of rubella vaccination, past history of rubella infection, and past history of contact with person with rubella infection.

Sample collection

5 ml venous blood sample were collected from 146 students by venipuncture, transferred into sterile plane tube, the whole blood was allowed to clot, then centrifuged at 3000 round per minute for 10 min. The clear serum (the supernatant) was transferred into labelled Eppendorf tube using a Pasteur pipette and stored at -20° C until the time of evaluation of rubella-specific IgG antibodies.

Laboratory Methods

The collected serum samples were tested for rubella-specific IgG antibodies by using a commercial enzyme-linked immunosorbent assay (ELISA) kit according to the manufacturer's protocol (chemux bioscience, united states of America, 18-D1-013).

Briefly, 100 µl of diluted serum (1:40) was added to wells of a microtiter plate coated with rubella virus antigen and incubated at room temperature for 30 minutes. The wells were then washed three times with buffer and then 100 µl of peroxidase-labeled rabbit anti-human IgG was added to each well. The wells were then incubated at room temperature for 30 minutes. The wells were then washed again with buffer and then 100 µl TMB/ H₂O₂ chromogen substrate was added to each well. The wells were again incubated at room temperature for 15 minutes. The reaction was then stopped by adding 100 µl 0.5 M sulfuric acid to each well and then gently mixing. The optical density at 450 nm was read using an ELISA reader (Stat fax, Serial no, 303-13467). The experiment was conducted in duplicate; positive and negative control sera were also included. A rubella IgG level of less than 15 IU/mL was taken as a negative test, and the patient was considered susceptible. All results were explained to the students, and those found to be susceptible to rubella infection were advised to take rubella vaccination. The manufacturer's guidelines were used for the interpretation of the results. The test was considered positive if specific anti-rubella IgG ≥15 IU/mL, and negative if below 15 IU/mL.

Statistical Analysis

Data were analyzed using SPSS version 19.0. For categorical data, the Chi-square test was used to study the association between susceptibility to rubella infection and various categorical variables. For categories with number less than 5, Fisher's exact test was used. For continuous

Variables, Student's t test was used for data that were normally distributed, and the Mann-Whitney rank sum test was used for skewed data.. The level of significance was set at 0.05.

RESULTS

General Characteristics of the Participants

A total of 146 students were participated voluntarily in this study. The general socio-demographic characteristics of the respondents in this study are shown in Table 1.

Out of the 146 respondents, 74 (50.7%) were males and 72 (49.3%) were females, with a mean age of 20.29 ± 1.99 years. Of the respondents, 88 (60.3%) were urban residents, while 58 (39.7%) were rural residents. Less than one half of the fathers of the respondents had college education 59(40.5%), while 9(6.2%) of them were uneducated. On the other hand, about 29 (19.9%) of the mothers had college education, while 36 (24.7%) had no formal education.

Table 1: General socio-demographic characteristics of participant (n =146).

Characteristic	Frequency (n = 146)	Percentage (%)
Gender		
Male	74	50.7
Female	72	49.3
Residence		
Urban	88	60.3
Rural	58	39.7
Father's education levels		
Uneducated	9	6.2
Primary	31	21.2
Secondary	35	24
Diploma	12	8.2
College and above	59	40.4
Mother's education levels		
Uneducated	36	24.7
Primary	36	24.7
Secondary	40	27.4
Diploma	5	3.4
College and above	29	19.9

Susceptibility towards rubella among respondents

Overall, the seropositivity rate of anti-rubella IgG was 130 (89%) with 69 (53%), 61 (47%), for male and female, respectively. Thus, the rate of susceptibility to rubella among the students was 16 (11.0%). Of the 16

susceptible students, 5 (31.25%) were male and 11 (68.75%) were female. Highest proportions of individuals with rubella IgG levels were seen in urban residents 78 (60%), while for rural residency was 52 (40%) Table 2.

Table 2: Frequency distribution of susceptible and immune students in relation to socio-demographic factor (n=146).

Sociodemographic data	Immune		Susceptible		Total		χ^2	P-value
	No	%	No	%	No	%		
Gender							2.7	.99
Male	69	93.2	5	6.8	74	(100.0)		
Female	61	84.7	11	15.3	72	(100.0)	1.2	.847
Residence Rural	52	89.7	6	10.3	58	(100.0)		
Urban	78	88.6	10	11.4	88	(100.0)		

Approximately 89 (61.0%) of the respondents had been received the vaccine, and about one-third 48 (32.9%) of them were not received it, and 9 (6.2%) individuals were not sure whether they were received it or not. Nearly 14 (9.6%) of students stated they had past history of rubella, while 132 (90.4%) mentioned that they were not had

rubella before. However only a small minority of students stated that they knew someone from his/her family or his/her colleagues in school who had rubella 35 (24.0%), whereas majority of them stated that they didn't know anyone who had rubella 111 (76.0%) as shown in Table 3. It noticed that there were nonsignificant

difference between the immune status and past history of suspected rubella, and infection of relatives or colleagues ($p > 0.05$), whereas there was a significant differences

between immune status and vaccination history ($p < 0.05$).

Table 3: Frequency distribution of the studied group according to past history infection, vaccination and infection of relative or colleagues in relation to immune status.

	Responses	Total N (%)		χ^2	P-value
	Immune N (%)	Susceptible N(%)			
History of rubella infection					
Yes	14 (100)	0 (0)	14 (100)	1.90	.181
No	116 (87.9)	16(12.1)	132(100)		
Vaccination history					
Yes	89 (100)	0 (0)	89 (100)	3.6	.00
No	32 (66.7)	16(33.3)	48 (100)		
History of rubella infection of relatives or friends					
Yes	32(91.4)	3(8.6)	35 (100)	2.7	.435
No	98(88.3)	13(11.7)	110(100)		

DISCUSSION

Despite the efforts that made worldwide for elimination rubella, it is still cause a substantial disease burden globally (Hagstam *et al.*, 2018). The current study was designed to assess rubella seroprevalence among 146 students of Aden University, Yemen. Current information about the immunity status of adolescence against rubella is lacking in our country, no available data on the seroprevalence studies for rubella have been performed over the 10 last years among population. However, there were three previous studies have been conducted to assess rubella seroprevalence among school girls, children, and adult (Strauss *et al.*, 1989; Sallam *et al.*, 2003; Sallam *et al.*, 2006). Despite the recent inclusion of rubella vaccine in the current vaccination program in Yemen; our finding indicated high seroepidemiological in urban and rural area, this is appear to be similar to the previous reports in Yemen (Sallam *et al.*, 2003; Sallam *et al.*, 2006).

The seroprevalence rate of rubella antibodies among study group was 130 (89%), and this means that, they were immune for rubella infection and about 16 (11%) of them were susceptible to rubella. The 89% seroprevalence obtained in this study is similar to several studies have been conducted in various countries (Dominguez *et al.*, 2006; Fokunang *et al.*, 2010; Gadallah *et al.*, 2014; Zahraei *et al.*, 2018). Several studies in Arab countries were in accordance with our finding; in Sudan (Gaber & Osman, 2017), In Egypt (Gadallah *et al.*, 2014), In Kuwait and Saudi Arabia (Makhseed *et al.*, 2001; Almuneef *et al.*, 2006).

The variability of the prevalence rate of rubella virus infections observed by different investigators could be attributed to several factors including, the study population, the diagnostic techniques used, the incidence rate of the virus in different environments, the living conditions and standards of the study group, the season

during which the study was conducted and the different subgroups and serotypes of rubella virus prevalent in the area of the study (Dominguez *et al.*, 2006).

The current study showed that there was no significant difference between the proportion of seropositivity in urban and rural areas indicating that virus circulation is similar in urban and rural zones and that the resident of both areas are at similar risk of infection to rubella virus. Most of studies were in agreement with our finding (Almuneef *et al.*, 2006; Jarour *et al.*, 2007; Hassan *et al.*, 2016).

Moreover, our finding indicated that there were no association between immune status of respondent with gender, age, residence, mother education, and father education of studied students. The variation of the immune status of different populations varies in different countries regarding rubella the association of seropositivity rate with age, residency, and levels of education have yielded controversial results (Ferrer *et al.*, 1999; Bamgboye *et al.*, 2004; Almuneef *et al.*, 2006; Barreto *et al.*, 2006; Majlessi *et al.*, 2008; Caidi *et al.*, 2009; Hassan *et al.*, 2016).

The majority of respondents 90.4%, in this study insisted they did not get rubella infection, and only 32.9% had been vaccinated previously although about 89% of them were seropositive for rubella antibodies. This reflects the heavy circulation of wild rubella virus in Yemen, and most of rubella cases are mild or not clinically recognized. It also implies previous subclinical or clinical infections with the rubella virus as previously stated in other countries such as Egypt and Sudan (Gadallah *et al.*, 2014; Gaber & Osman, 2017).

It is clearly noticed that all the vaccinated students had immunity against Rubella, it in accordance with the previous report that had been stated the vaccination is

the most efficient and effective in preventing rubella and CRS. A key strategy for preventing rubella and CRS is ensuring sufficient population immunity through natural disease or through vaccination programs that achieve high coverage. However, a vaccination policy should be implemented for unvaccinated males and females rather than pregnant women should get rubella vaccination to protect unborn life, also, a vaccination policy should be implemented for women neither pregnant women at risk, which may be carried out either through the vaccination of whole cohorts of women of child bearing age (e.g., 15-44 years) or cohort of particular groups of women such as health care workers, schoolgirls, college students, or premarital couple. Some countries set up the rubella vaccination program only for young women; however, this strategy had proved to be ineffective for preventing the spread of rubella. A supplementary vaccination for male adults was recommended to achieve rubella elimination after an outbreak in Japan (Minakami *et al.*, 2014).

Meanwhile, in this present study a few limitations were encountered throughout the duration of the study; the main limitation of the study is that the results were limited to only preparatory year students, thus the findings of this study may not reflect the seroprevalence of whole community; rather they reflect only the seroprevalence of those who actually included in the study. Therefore, the findings need to be interpreted within the context of study limitations.

In our study, the susceptibility was found to be 11%, nevertheless, further studies among different age groups in rural and urban settings, preferably large-scale screening, are needed in order to determine the need for a national rubella vaccination program among population in different settings and determine whether CRS is a substantial problem will also help in the future planning of appropriate interventions. The most important result of this study is that 11 (15.3%) of adolescent girls are still susceptible to rubella infection in our region. These girls could be candidates for CRS if they are not immunized.

CONCLUSION

The results of the present study demonstrate that a substantial risk of rubella infection is still exist among Yemeni adults and supported the presence of virus circulation all over Yemen. The current health care policy has left a substantial number of adults reaching reproductive age with susceptibility to acquire rubella infection. Therefore is a great need for health education about risk and protection of rubella in communities. Considering the importance of protection against rubella, a booster dose of MMR vaccine should be considered for young adults in Yemen rather than pregnant women.

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