

Original Research Article

The susceptibility to Rubella virus infection among pregnant women attending antenatal clinics in Unguja, Zanzibar: the need to employ multiple strategies to control Congenital Rubella syndrome in Tanzania

.Abstract

Aims: This study was conducted to determine the proportion of pregnant women susceptible to Rubella Virus in Zanzibar, the information that might be useful in future control interventions.

Study design: A cross-sectional hospital-based study

Place and Duration of Study: The study was conducted in Unguja Zanzibar between May 2023 and July 2023

Methodology: Sociodemographic and other relevant information were collected from pregnant women attending antenatal clinics using structured questionnaires. Blood samples were collected from each consented woman. Detection of rubella IgG antibodies was done by an indirect Enzyme Linked Immunosorbent Assay (ELISA). Data analysis was done by using STATA version 15.

Results: The median age of enrolled participants was 27 [IQR: 23-31] years while the median gestation age was 28 [IQR: 20-32] weeks. Out of 171 participants, 10/171(5.84%) [95% CI:2-9%] were negative to Rubella IgG antibodies indicating susceptibility to active RV infection that can lead to CRS. On multivariate analysis, history of congenital malformations (OR:27.4, 95% CI:1.29-580.52, p=0.033) was significantly associated with susceptibility to RV infection

Conclusion: Despite high level of natural immunity there is a considerable proportion of pregnant women in Zanzibar susceptible to RV necessitating the need for multiple strategies to reach a goal CRS elimination.

Keywords: Rubella, susceptible pregnant women, CRS, Zanzibar

1. INTRODUCTION

Rubella virus (RV) infection usually causes a mild fever and rash in children and adults. However, if contracted in the first trimester the virus can cause teratogenic effects that can lead to Congenital Rubella Syndrome (CRS) characterized by multiple birth defects. The most common manifestations include heart diseases, bilateral cataracts and deafness among many others [1-3]. CRS occurs in about 90–100% of the infants whose mothers were infected with the virus in the first trimester while fetal manifestations become rare when maternal infection occurs after 16 weeks of gestation[4]. In the year 2010, an estimated 105 000 CRS cases occurred globally[5]. Before the introduction of Rubella vaccine in 1969, RV caused epidemics every 6–9 years. Few data are available on the global burden and epidemiology RV and CRS globally before 1969 while in the USA, 60% of RV cases were among children younger than 10 years and 23% among people older than 15 years[6]. In Africa the RV natural immunity reported to range from 52.9 to 97.9 % while the prevalence of susceptible pregnant women ranged from 2.1 to 47.1 %[7]. In Tanzania mainland IgG seropositivity was reported to be 50.8%, 90.4 and 92.6% among children, adolescent girls and pregnant women respectively while prevalence of active infection was found to be 13%, 10.9 and 8.9% among older children, under five children and pregnant women respectively [3, 8, 9]. A previous report in Mwanza documented 46 out of 55 pregnant women with RV active infection had adverse pregnancy outcomes with 10.9% having babies with CRS[3]. This implies that RV

active infection can cause serious undesirable pregnancy outcomes necessitating the need to ensure all women of reproductive age are immune to RV.

Tanzania government introduced a catchup campaign on Rubella vaccine in October 2014 which was followed by introduction of Rubella vaccine in January 2015. A recent report of surveillance data showed notable decrease in RV active cases in different regions of Tanzania[10]. The world Health Organization (WHO) recommends multiple strategies to be employed including vaccinating susceptible women of reproductive age to reach a goal of CRS elimination[11]. Most of high-income countries (HICs) are nearly close to reach the goal of elimination of CRS. However, in most of low and middle income countries (LMICs) cases of CRS are still reported whereby more than 100,000 children are born with CRS each year [12-14]. Seroepidemiological studies and surveillance data are important in targeting specific groups eligible for vaccination[15]. Despite high level of natural immunity observed in women with of reproductive age in Tanzania; there is considerable proportion of pregnant women susceptible to RV infection that can lead to CRS. Therefore, there is a paramount need to investigate proportion of these women so as to produce information that can be useful in devising appropriate control interventions. In Zanzibar there is limited data on the current status of RV among different population including pregnant women. In a view of this, this study was conducted to determine the proportion of susceptible pregnant women. This information might be useful in future control interventions to reach a goal of elimination of CRS.

2. MATERIAL AND METHODS

Study Design, duration, study area and study population

From May to July 2023, a cross-sectional study involving pregnant women attending antenatal clinics in Unguja Zanzibar was conducted. Women were enrolled from Mwembeladu and Rahaleo hospitals. Approximately 1500 women attend antenatal clinics per month at Mwembeladu hospital while approximately 30 women attend gynecological clinic per day and Rahaleo hospital.

Sample size estimation, sampling procedures and selection criteria

Sample size was calculated by using Kish Leslie formula using the prevalence of 92.6% from a previous study in Mwanza[16]. A minimum sample size was of 105, however a total of 171 women were enrolled. All pregnant women attending antenatal clinics consented to participate in this study were included.

Data and sample collection and specimen analysis

The structured pre-tested questionnaire was used to obtain sociodemographic, clinical and other relevant information. Under aseptic procedures approximately 3-5mls of whole blood was drawn from medial cubital vein of the forearm and transferred to plain vacutainer tubes (Becton & Dickson Co.LTD, Nairobi) and allowed to clot for serum extraction. The extracted sera were transferred into well labelled cryovials and kept at a -20°C. Sera were analyzed for the presence of RV antibodies by using Indirect enzyme linked immunosorbent assay (ELISA) as per manufacturer's instructions (Viracell, S.L. Parque Tecnológico de la Salud, Avicena 8, Spain).

Data management and analysis

Laboratory results were recorded into laboratory logbook then were sorted and transferred into Microsoft excel sheet for cleaning and coding. Descriptive data analysis was done using STATA version 15 (College Station, TX: Stata Corp LLC). Percentage or fraction was used to summarize categorical variables while mean (STD)/median (IQR) was used for continuous variables. Logistic regression was used to show factors associated with susceptibility to RV infection and a P-value of <0.05 was considered as statistically significant.

3. RESULTS AND DISCUSSION

Sociodemographic and clinical characteristics

A total of 171 participants were enrolled from Mwembeladu and Rahaleo hospitals in Unguja, Zanzibar and analyzed in this study. The median [Interquartile range (IQR)] age of the participants was 27 [IQR: 23-31] years and median gestation age was 28 [IQR: 20-32] weeks. Majority of the participants 152/171 (88.9%) resided in the urban areas and most of them 158/171 (92.4%) were married. Moreover, more than two thirds 125/171 (73%) attained formal education. Furthermore, about more than half 111/171 (64.9%) of the participants were housewives. The median number of household members was 5 [IQR:3-6] members while the median parity was 2[IQR:1-3] children. Regarding the clinical history of the participants during the current pregnancy, 16/171

(9.4%) of the participants reported to have fever and 19/171 (11.1%) reported to have rashes. Majority of them 166 (97.08%) reported no history of stillbirth (Table 1).

Table 1: Sociodemographic and clinical characteristics of enrolled participants

Variables	Category	Frequency	Percentage (%)
Residency	Urban	152	88.9
	Rural	19	11.1
Marital status	Married	158	92.4
	Unmarried	13	7.6
Education level	No formal education	46	26.9
	Primary school	58	33.9
	Secondary school	55	32.2
	Tertiary	12	7
Occupation	Housewife	116	67.84
	Employed	55	32.16
Water source	Tap water	171	100
House type	Brick	168	98.25
	Mud	3	1.75
Fever	Yes	16	9.4
	No	155	90.6
Rash	Yes	19	11.1
	No	152	88.9
Median [IQR] age in years		27[23-31]	
Median gestation age in weeks		28[20-32]	
Median parity [IQR] children		2[1-3]	
Median [IQR] household members		5[3-6]	

Prevalence of women susceptible to RV infection and associated factors among pregnant women attending antenatal clinics in Zanzibar (n=171)

Out of 171 participants, 10/171 (5.84%, 95% CI: 2 - 9.6%) were negative to Rubella IgG antibodies indicating that they are susceptible to active RV infection. On univariate analysis, history of congenital malformations (Fisher's exact 7.16, $p=0.007$) was significantly associated with susceptibility to RV infection. On multivariate analysis history of congenital malformations (OR: 27.4, 95% CI: 1.29-580.52, $p=0.033$) remain to be significantly associated with susceptibility to RV infection (Table 2).

Table 2: Factors associated with RV susceptibility among pregnant women in Zanzibar (n=171)

Variable	Total	Rubella susceptibility N (%) / median (IQR)	Univariate analysis		Multivariate analysis	
			Fisher exact	P value	OR [95%]	P Value
Age (years)	10	27(24-37)		0.503	1.09(0.966-1.23)	0.155
Gestation Age (weeks)	10	30(28-32)		0.379		
Household number	10	5.5(3-8)		0.544		
Rash						
No	152	9(5.92)				
Yes	19	1(5.26)	0.014	0.908		
Stillbirth						
No	166	9(5.42)				
Yes	5	1(20.0)	1.975	0.171	4.2(0.35-50.55)	0.254
Occupation						
Formal employed	55	1(1.82)				
Housewife	116	9(7.76)	0.171	0.111	4.7(0.555-39.57)	0.156
Marital status						
Not married	13	0(0.0)				
Married	158	10(6.3)	1.00	0.443		
Congenital malformation						
NO	169	9(5.33)				
Yes	2	1(50)	7.16	0.007	27.4(1.29-580.52)	0.033

Seroepidemiological studies are important in understanding the burden of disease and its associated consequences in different populations. This study documents the proportion of pregnant women susceptible to RV attending antenatal clinics in Unguja-Zanzibar, Tanzania. Despite the high level of natural immunity observed among pregnant women in Zanzibar, there is a considerable proportion of these women susceptible to acute RV infection that can lead to CRS. The data from the current study are in agreement with a previous report in Tanzania mainland which reported the prevalence of susceptible pregnant women to be 7.4% [16]. Moreover, in comparison to previous reports from other African countries the prevalence is comparable to reports from Eldoret-Kenya, Zaria-Nigeria, Osogbo-Nigeria, Maputo-Mozambique, Khartoum state-Sudan which reported prevalence of 7%, 2.4%, 12.5%, 4.7%, and 4.9% respectively [17-21]. Considering the consequences of acute RV in pregnant women, there is a great risk of these women to contract RV infection that can result into adverse pregnancy outcomes as previously documented in Mwanza [3].

The Tanzania government introduced RV vaccine in January 2015 targeting children under five years of age which is given in combination with Measles vaccine (MR) in two doses. The WHO recommends multiple strategies to be employed to reach a goal of elimination of CRS and most of the countries employing these strategies are in CRS elimination phase. Despite the efforts made by Tanzania government to introduce RV vaccine and the impact of its implementation [10], there is a paramount need to consider other strategies including screening and vaccinating women of child bearing age and susceptible pregnant women during postpartum period as recommended previously [22]. This has been reported to be more cost-effective in HICs than vaccinating all children and adolescents blindly. Furthermore, introducing screening in the antenatal package can be a useful strategy to identify susceptible women so that they can be vaccinated after delivery. Combination of these strategies has been found to be effective in other countries that are in the CRS elimination phase.

Among the factors studied, history of congenital malformations was significantly associated with susceptibility to RV infection requiring further studies for this particular population to investigate their vulnerability to other pathogens that can lead to congenital malformations [23-25]. In conclusion Tanzania government should ensure sustained high vaccination coverage across the country to break transmission cycle and employ multiple strategies to reach a goal of CRS elimination.

4. CONCLUSION

In conclusion Tanzania government should ensure sustained high vaccination coverage across the country to break transmission cycle and employ multiple strategies to reach a goal of CRS elimination.

CONSENT

The importance of the study was explained well to the participants and those agreed to participate were asked for the consent by signing in the consent form. Confidentiality was maintained throughout the study.

ETHICAL APPROVAL

Ethical clearance to conduct the study sought from CUHAS/BMC research ethics and review committee (CREC) with clearance number 2603/2023 and Zanzibar health research institute (ZAHRI) with reference number 2023/100. Permission to conduct the study was sought from relevant authorities.

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DEFINITIONS, ACRONYMS, ABBREVIATIONS

BMC	Bugando Medical Centre
CRS	Congenital rubella Syndrome
ELISA	Enzyme linked immune sorbent Assay
CUHAS	Catholic University of Health and Allied Sciences

IgG
OR
CI
IQR
IVDP

Immunoglobulin G
Odds ratio
Confidence interval
Interquartile range
Immunization and Vaccination Development Programme

UNDER PEER REVIEW