Acute Rubella Virus Infection among Women with Spontaneous Abortion in Mwanza City, Tanzania

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ABSTRACT

Introduction: Acute rubella virus infection in early pregnancy has been associated with poor pregnancy outcome ranging from spontaneous abortion, stillbirth and multiple birth defects known as Congenital Rubella Syndrome (CRS). Despite its importance the prevalence of acute rubella virus infections is not known among women with spontaneous abortion in most centres in developing countries.

Aim: The present study was aimed to determine the seroprevalence of acute rubella infection among women with spontaneous abortion in Mwanza city.

Materials and Methods: A total of 268 women with spontaneous abortion were enrolled from four different hospitals in Mwanza city between November 2015 and April 2016. Blood samples were collected; sera were extracted and stored at -80°C until processing. Acute rubella virus infection was diagnosed by the detection of rubella specific IgM antibodies using indirect Enzyme Linked Immunosorbent Assay (ELISA) as per manufacturer's instructions. Data were analysed by using STATA version 11.

Results: The mean age of enrolled women was 26.3±5.6 years. The prevalence of acute rubella virus infection was found to be 9/268 (3.7%, 95% CI: 1-5). Only women residing in urban areas (AOR: 5.65, 95% CI: 1.15-27.77, p=0.035) were found to predict acute rubella virus infection among cases with spontaneous abortion in Mwanza city.

Conclusion: About four out of hundred women residing in urban areas with spontaneous abortion in Mwanza are acutely infected with rubella virus highlighting the potential of this virus in contributing to poor pregnancy outcome in this setting.

INTRODUCTION

Rubella virus infection in early pregnancy has been frequently associated with adverse pregnancy outcomes due to its teratogenic effects. Apart from causing CRS, it has been implicated as one of the common causes of spontaneous abortion [1]. Rubella virus infection is a major public health concern especially in low and middle income countries where rubella vaccination is not extensively implemented. The infection is most common in children, young adults, child bearing aged women and pregnant women [2-4]. Laboratory serological detection of specific rubella antibodies in suspects remains to be crucial in diagnosis of rubella virus infection since clinical diagnosis is difficult due to non-specific symptoms [5]. Despite being a self-limited disease in children; if contracted by pregnant women during first trimester of pregnancy one of the most common sequels is spontaneous abortion.

About 20% of women experience spontaneous abortions before 20 weeks of pregnancy whereby most of them occur in the first 12 weeks of gestation [6]. In Tanzania the rate of spontaneous abortion was estimated to be around 12%, however the causes of these abortions have never been established [7]. Viral infections such as rubella, cytomegalovirus, parvovirus B19 and many other agents during pregnancy have been implicated as common causes of spontaneous abortions [8,9] and have been found to be common during pregnancy in Tanzania [10].

Despite its importance, the role of rubella virus infection in abortions has never been studied in Tanzania. Regardless of reported high level of rubella natural immunity among child bearing aged women in Tanzania and other African countries, significant proportion of women are still susceptible to acute rubella infections hence risk of poor pregnancy outcome [11,12]. This study was designed to determine the prevalence of acute rubella virus infection among women with spontaneous abortion in Mwanza city, Tanzania, the information that may be useful in improving antenatal care services across the country.

MATERIALS AND METHODS

Study Design and Study Area: A cross-sectional hospital based study involving 268 women with spontaneous abortion was conducted from November 2015 to April 2016 in four conveniently selected hospitals in Mwanza city, Tanzania namely; Sekou Toure Regional Hospital, Bugando Medical Centre, Nyamagana District Hospital and Buzuruga Health Centre. These hospitals provide obstetric care services to a large population of the city.

Sample Size and Sampling Procedures: The sample size was calculated using Kish Lisle formula for cross-sectional study [13]. The prevalence of 10.8% of acute rubella infections among women with spontaneous abortion in Baghdad was used [14]. The minimum sample size obtained was 149 women, however a total of 268 women were enrolled. All women who met inclusion were serially enrolled.

Data Collection and Laboratory Procedures: After obtaining written informed consent from participants, about 4 ml of blood samples were collected in plain vacutainer tubes (Becton Dickinson, Nairobi, Kenya) and transported to the Bugando multipurpose laboratory whereby sera were extracted and stored at -80°C freezer until processing. Sociodemographic and obstetric information were collected using pre tested data collection tool. Data collected included age, gestation age, residence, education level, parity, occupation, history of blood transfusion and Human Immunodeficiency Virus (HIV) sero-status. Regarding education, "educated" was defined as women with secondary school education and above while "non educated" was defined as those with primary or no formal education. Urban and rural areas were defined based on district municipal distribution.

Laboratory Investigations: Detection of rubella specific IgM antibodies was done by using indirect ELISA (ChemWell® 2910-Awareness Technology Inc., Palm City, USA) according to the manufacturer's instructions with the positive cut off values of ≥ 1 index. The sensitivity and specificity of the test used was >97% [15].

Data Management and Analysis: Data were entered in Microsoft Office Excel 2007 and analysed using the STATA version 11 (College Station, Texas, USA). Continuous variables were summarized as means with standard deviation while categorical variables were presented as proportions. Univariate and multivariate logistic regression models were fitted to determine factors associated with rubella IgM seropositivity. Backward-stepwise selection model to select factors with a p-value <0.2 to be fitted into the multivariate logistic regression analysis was done. Unadjusted (UOR)/Adjusted Odds Ratio (AOR), 95% confidence interval (95% CI) and p-values were noted.

Ethical Clearance: The protocol for carrying out the study was approved by the Joint Catholic University of Health and Allied Sciences/Bugando Medical Centre (CUHAS/BMC) research ethics and review committee with ethical clearance number CREC/106/2015. Written informed consent was obtained from each participant prior to enrolment for the study.

RESULTS

Sociodemographic Characteristic of the Study Participants: A total of 268 women with spontaneous abortion were enrolled from four different hospitals in Mwanza city, Tanzania between November 2015 and April 2016. The mean age of study participants was 26.3±5.6 years. Participants' age was found to range from 16 to 40 years with majority of the participants (33.2%) placed between 21 and 25 years. The mean gestation age of the enrolled women was 12±3.2 weeks. Majority of the enrolled women 175 (65.3%, 95% CI: 59-70) were not employed while 148 (55.2%, 95% CI: 49-61) either attained primary education or had no formal education. A total of 162 (60.5%) and 106 (39.5%) women were residing in rural and urban areas respectively. In addition, majority of the participants 205 (76.5%) were in the first trimester while 63 (23.5%) were in the second trimester. A high percentage of women 187(69.7%) had one or more children as shown in [Table/Fig-1].

Prevalence of Acute Rubella Infection (IgM Seropositivity): The prevalence of acute rubella infection as indicated by the presence of specific rubella IgM antibodies was found to be 9/268 (3.7%, 95%CI: 1-5). The mean age of IgM seropositive women was lower than the mean age of IgM sero negative women (23.6±4.4 vs. 26±5.9 years, p=0.157). Moreover, there was no significant difference between the mean gestation age among IgM seropositive women and IgM sero-negative women (12±2.9 weeks vs. 11.5±3.21, p=0.926).

Factors Associated with Acute Rubella Infection Among Women with Spontaneous Abortion: On univariate logistic regression analysis, it was observed that as the age increases the IgM seroprevalence was found to decrease (UOR: 0.90, 95%CI: 0.79-1.03, p=0.157). In addition as gestation age increases the prevalence of IgM antibodies increased (UOR: 1.09, 95% CI: 0.22-5.55, p=0.926). Women residing in urban areas was found to be significantly associated with increased risk of acquiring acute rubella infection (UOR: 5.65, 95% CI: 1.15-27.77, p=0.033). Other factors found to be associated with acute rubella infections among women with spontaneous abortion with no significant statistical difference were: being uneducated (UOR: 1.01, 95% CI: 0.27-3.86, p=0.984), unemployed (UOR:1.89, 95% CI: 0.38-9.31, p=0.431), being nullipara (UOR: 1.89, 95% CI: 0.49-7.23, p=0.352), having positive HIV sero-status (UOR: 9.29, 95% CI: 0.87-98.93, p=0.065) and having history of blood transfusion (UOR: 3.70, 95% CI: 0.51-26.93, p=0.195). Only women residing in urban areas (AOR: 5.65, 95% CI: 1.13-28.19, p=0.035) were found to predict acute rubella

Characteristics (N)	IgM sero-positivity n (%)	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
Age* (Years)	23±4.44	0.90(0.79-1.03)	0.157	0.919 (0.80-1.05)	0.229
Gestation age* (Weeks)	12±2.95	1.09(0.22-5.55)	0.926		
Education					
Educated(120)	4(3.3%)	1			
Uneducated (148)	5(3.9%)	1.01(0.27-3.86)	0.984		
Occupation					
Employed (93)	2(2.2%)	1			
Unemployed (175)	7(4%)	1.89(0.38-9.31)	0.431		
Parity					
≥1 children (187)	5(2.7%)	1			
Nullipara (81)	4(4.9%)	1.89(0.49-7.23)	0.352		
Residence					
Rural (162)	2(2.3%)	1			
Urban (106)	7(6.6%)	5.65(1.15-27.77)	0.033	5.65 (1.13-28.19)	0.035
HIV status					
Negative (190)	4(2.1%)	1			
Unknown (72)	4(5.7%)	2.73(0.66-11.24)	0.163		
Positive (6)	1(16.7%)	9.29(0.87-98.93)	0.065	2.77 (0.89-8.61)	0.077
Blood transfusion					
No (206)	2(0.9%)	1			
Yes(57)	2(3.5%)	3.70(0.51-26.93)	0.195		

[Table/Fig-1]: Univariate and multivariate logistic regression analysis of factors associated with acute rubella infection among 268 women with spontaneous abortion in Mwanza city.
*Mean age and mean gestation age for IgM seropositive women.

infection among women with spontaneous abortion in Mwanza city on multivariate logistic regression analysis when adjusted for age and HIV status [Table/Fig-1].

DISCUSSION

Viral infections during pregnancy have been associated with poor pregnancy outcome [8,16]. Rubella virus infection in early pregnancy has been implicated as one of the causes of spontaneous abortion. This is the first study to report seroprevalence of acute rubella virus infection among women with spontaneous abortion in Tanzania. In this study, compared to previous study in the same setting among women with term pregnancy [11], significant proportion of women were acutely infected with rubella virus (3.7% vs. 0.3%, p=0.003). In Africa, the prevalence of women susceptible to rubella virus infection ranges from 2.1-47.1% [12]. Specifically in Tanzania the prevalence of susceptible pregnant women is about 10% hence in the population studied, about 30 women were at risk of acute rubella infection giving the possibility that rubella virus might have contributed to spontaneous abortion in 30% of susceptible women. This observation signifies the possible role of rubella virus as one of the causes of spontaneous abortion in this setting. Apart from rubella, being associated with spontaneous abortion in the current study, the previous study in the same setting documented congenital rubella syndrome cases [4].

The prevalence of 3.7% reported in this study is significantly lower than what was reported elsewhere among women with spontaneous abortion [14,17]. The difference could be due to geographical variation as rubella virus is endemic in most of African countries, with majority of women being naturally immune [10,12,18,19]. Further studies on rubella transmission and seasonal variation particularly in women with spontaneous abortion are highly recommended in this setting.

In the present study, urban residence has been found to predict rubella virus infection among women with spontaneous abortion.

Our findings are consistent with previous studies which had similar findings [14,20]. In the contrary to the previous study among under-fives in the same settings [4]; most of the urban residents in Mwanza city live in highly populated squatters which has been found to favour rubella virus transmission [21,22]. Furthermore, the differences could be explained by study population and seasonal variation whereby the current study was done among adult population from November 2015 to April 2016 while the previous study was done among children from September to October 2014.

LIMITATION

The major limitations in this study is inability to perform sensitive techniques like PCR in placental tissues as well as to rule out other causes of spontaneous abortion which would give more concrete evidence on the role of rubella virus in causing spontaneous abortion. In addition captured IgM ELISA would be of beneficial for confirmation of positive cases. However, the study has highlighted the possible role of rubella virus infection in causing spontaneous abortion in developing countries.

CONCLUSION

A significant proportion of women with spontaneous abortion residing in urban setting are acutely infected with rubella; and these infections might have a role to play in poor pregnancy outcome, in Mwanza city, Tanzania. Rubella virus screening coupled by appropriate counseling during antenatal visits should be considered routinely. In addition screening and vaccinating sero-susceptible women before conception is recommended.

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