Original Research Article

High proportion of school aged children susceptible to mumps virus infections in the city of Mwanza, Tanzania: Should it be included in the national Immunization programme?

ABSTRACT

Aim: This study for the first time in Mwanza, Tanzania aimed at determining seroprevalence of mumps virus in school aged children who are targeted for vaccination.

Study design: Cross-sectional study

Place and duration of the study: This study was conducted in the city of Mwanza from July to September 2018.

Despite being common with reported associated complications in many resource limited countries, there is scarcity of information on its epidemiology in Tanzania.

Methodology: We enrolled 440 school children aged 6-12 years. Data was collected using a pre-tested structured data collection tool. Blood samples were collected, and sera were used for detection of mumps virus antibodies by indirect enzyme linked immune-sorbent assay (ELISA). Data was analyzed using STATA version 13.

Results: The median age of enrolled children was 9(IQR: 8-11) years. The seropositivity of mumps IgG antibodies was found to be 94(21.4%, 95% CI: 17.5-25.1) while that of IgM was 1 (0.23%, 95% CI: 0.02-0.6). By multivariable logistic regression analysis, residing in rural areas (OR: 2.28, 95%CL: 1.42-3.36, P=0.001) and age >10 years (OR: 1.67, 95% CI: 1.03-2.7, P=0.036) independently predicted mumps IgG sero-positivity.

Conclusion: A significant proportion of young children in urban areas of the city of Mwanza are susceptible to mumps virus infection indicating the need to generate more data across the country so as to institute appropriate control measures including measles, mumps and rubella (MMR) vaccination programme.

Keywords: *Mumps virus, seroprevalence, Mwanza, Tanzania*

Introduction

Mumps is an acute highly contagious viral infection caused by a paramyxovirus of the family paramyxoviridiae [1]. The virus is transmitted through respiratory secretions from the infected individual or through direct contact with saliva and contaminated fomites [2]. The disease affects mostly children aged 5 to 9 years with peak incidence occurring during winter and spring in temperate climates, however, infection may occur at any time of the year in hot climates. If not prevented in childhood, mumps can be associated with serious complications such as orchitis which occurs in 20–30%, oophoritis in 5%, aseptic meningitis in 50–60% and mastitis in 31% of women over the age of 14 years [3, 4]. Mumps has also been associated with infertility, encephalopathy, deafness and spontaneous abortions especially if the infections contracted in the first trimester [4-10]. Mumps virus presents as an acute mild or asymptomatic illness in approximately 30% of children. In most cases, the disease is self-limiting and typically presents with few days of fever, headache, myalgia, fatigue, anorexia and these manifestations are usually followed by development of salivary gland swelling within 48 hours. [11]. The incubation period from exposure to mumps virus infection to onset of symptoms ranges 14–21 days [12]. Risk factors of mumps infection include: age, exposure, compromised immunity, season of year, travel, and vaccination status [13, 14]. Before the implementation of large scale childhood vaccination programme, mumps had very negative impacts on children worldwide affecting primarily children 5-9 years old with about 186,000 cases reported each year [15]. The incidence of mumps infection in the absence of immunizations has been found to range from 100–1,000 cases/100,000 populations, with epidemic peaks every 2–5 years [16]. Globally, there were more than 560,000 cases of mumps infection reported between 2005 and 2010

[17]. Seroprevalence of mumps has been found to vary in different age groups and different countries. It has been found to increase with age from 50% at the age of 4-6 to 90% by the age of 15 years [1, 13, 18]. Global efforts in reducing incidences of mumps and associated complications has focused on vaccination. Vaccination programs have dramatically reduced mumps incidences in middle and high income countries. However, in low income countries the incidences are still high and is associated with significant morbidities in these countries[15]. Efforts to introduce vaccine programs must go along with understanding the epidemiology of the virus. In Africa, only few studies have documented the seroprevalence of mumps virus whereby in children aged one month to six years was found to be 9% and 22% in South Africa and Democratic Republic of Congo (DRC), respectively[19, 20]. Despite being common in many countries with reported associated complications, there is scarcity of data regarding its epidemiology in Tanzania. Only one study from Tanzania documented mumps seroprevalence of 16.7% among children with deafness about 20 years ago [21]. Based on mortality and morbidity, the World Health Organization (WHO) consider measles and rubella control programmes to be high priority than mumps in Tanzania due to lack of data regarding its epidemiology. It is well known that, understanding epidemiology of infection is one of the key steps in devising control measures. In a view of that, this study for the first time in Mwanza, Tanzania was done to determine the proportion of school aged children seropositive to mumps antibodies so as to estimate the risk of infection and possible associated complications. Findings from this study might stimulate further epidemiological studies across the country and in other countries in Africa to generate information that may be useful in control interventions

such a policy of inclusion of mumps vaccine in the immunization and vaccination development programme (IVDP).

Material and Methods

Study design, duration and study area

This was a cross-sectional study which was carried out for a period of three months from July to September 2018 in different primary schools in urban and rural areas of Ilemela and Nyamagana districts in the city of Mwanza. As of 2018 survey, the population of primary school children was 81,907 and 101,173 for Ilemela and Nyamagana districts, respectively (Demographic Education Survey data). The study involved only public primary schools to get participants with different socioeconomic levels.

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A cross-sectional study was carried-----add

Study population and selection criteria

All children aged between 6-12 years old from selected schools whose parents agreed to participate in the study were enrolled. The study excluded all children who were coming from countries with MMR vaccination coverage with confirmed history of vaccination.

Sample size estimation and sampling technique

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Sample size was estimated by using the Yamane Taro formula[22]. As of 2018 survey, the population of primary school children was 81,907 and 101,173 for Ilemela and Nyamagana districts respectively (Demographic Education Survey data). Using school children population, the sample size of 400 was obtained after adding 10% of non-response. A stratified multistage cluster sampling technique was used to obtain the sampling unit of the study. The first stage was sampling of the wards and the second was sampling of the primary schools in both Ilemela and Nyamagana districts. Ilemela has 20 wards while Nyamagana has 18 wards. From 38 wards,

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three wards were selected by a simple random sampling (two from Ilemela and 1 from Nyamagana). This ensured representation of the study population from all geographical location in the two districts. From Ilemela district Nyamanoro and Bugogwa wards were selected randomly while in Nyamagana district, Pamba ward was selected. From Nyamanoro ward Karume primary school was selected and from Bugogwa ward Bugogwa and Igombe primary schools were selected. From Pamba ward Bugarika and Bugando primary schools were involved. The selection ensured representation of urban and rural schools.

Data and sample collection

Children whose parents/guardians gave consent and children who gave assent were enrolled in the study. Information regarding personal history, place of resident, sex, age etc. were collected using a pre-tested data collection tool. Detailed anthropometric data such as weight, height and body temperature were also collected. Under aseptic procedures, 3-5 ml of venous blood sample was drawn from each participant in plain vacutainer tubes. Samples were transported to CUHAS microbiology laboratory whereby blood was centrifuged to obtain sera which was stored in cryovials at -80^{0}C until analysis. Detection of specific mumps IgM and IgG antibodies were done by using indirect Enzyme linked immune-sorbent Assay (ELISA) as per manufacturer's instructions (vircell, S.L.parque Tecnologico de la salud, Avicena, Granada, Spain). The test has sensitivity and specificity of 98% and 95% for IgG and 91 and 99% for IgM, respectively.

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Ethical considerations

Ethical approval was sought from the joint Catholic University of Health and Allied Sciences (CUHAS)/Bugando Medical Centre (BMC) research ethics and review committee (CREC) with

ethical clearance number CREC/296/2018. Permission to conduct the study in the selected schools was sought from the respective district administrative secretaries and from the headmasters/mistresses of the schools. The consent form containing all information pertaining the study (the aim, duration, risk and benefits of the study etc.) was attached to the information sheet and provided to children a day before enrollment and sample collection. Phone numbers were provided in the information sheet in case further clarifications were required. Written informed consent was obtained from each parents/guardian before enrollment to the study. After receiving the parent/guardian's consent the child was asked if she/he agrees/disagree to participate in the study; only children who agreed to participate were enrolled. Confidentiality was assured, and no unauthorized person had access to the collected data. Each participant was assigned a study identification number which was kept confidential throughout the study period.

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Data management and analysis

Data was entered into a computer using Excel 2007, cleaned and analyzed using a STATA version 13. Categorical variables were summarized as proportions while continuous variables were summarized as mean (standard deviation) and median (interquartile range). Wilcoxon Ranksum (Man Whitney) test was used to compare median age of different groups. Socioeconomic status (SES) was determined by considering combination of proxy indicators such as parent's/guardian's education level, occupation, type of house, source of water and type of toilet. Univariable and multivariable logistic regression analyses were used to determine factors associated with mumps virus seropositivity whereby factors with p value of <0.2 on univariable analysis were subjected into the multivariate analysis. However, SES was not

included in multivariable analysis because of its collinearity with residency. Odds ratio and 95% confidence intervals were determined; variables with p value of less than 0.05 were considered to have statistically significant differences.

Results

Socio-demographic characteristics of the enrolled children in Mwanza city

A total of 440 children aged 6-12 years were enrolled with the median age of 9 (IQR: 8-11) years. The majority of the children 279 (63.4%) were female while most of them 269 (61.1%) were enrolled from urban areas. Most of the female parents /guardians 300 (68.2%) and male parents/guardians 296 (67.3%) of the enrolled children had primary level of education. More than a half of children 262 (59.5%) were coming from families with low socioeconomic status (SES). Almost a half 218 (49.6%) of children reported to have habit of sharing utensils while the median size of household was 6 (IQR: 5-8) members (table 1)

Table 1: Sociodemographic characteristics of the enrolled children in Mwanza city (n=440)

Characteristics	**Frequency**	**%**
***Age**	9	8-11
Sex		
Female	279	63.4
Male	161	36.6
Residency		
Rural	171	38.9
Urban	269	61.1
Female parent/guardian's education		
None	22	5
Primary	300	68.2
Secondary	103	23.4
Tertiary	15	3.4
Male parent/guardian's education		
None	25	5.7
Primary	296	67.3
Secondary	97	22
Tertiary	22	5
***Number siblings**	4	3-5
***Number of household**	6	5-8
House type		
Low quality house	303	68.9
High quality house	137	31.1
Sharing utensils		
Yes	218	49.6
No	222	50.4
Socioeconomic status (SES)		
Low	262	59.5
High	178	40.5

** The second and third columns indicate median and interquartile range respectively*

Clinical characteristics of the enrolled children

The mean temperature of the enrolled children was 36.6±0.4 ^{0}C while the mean body mass index (BMI) was 17.5±2.0. Of 440 enrolled children, 151(34.3) reported to have previous history of mumps while 6(1.4%) reported to have previous clinical signs suggestive of parotitis. Regarding face appearance, most of the enrolled children 437(99.3) had no swollen face (table 2).

Table 2: Clinical characteristics of enrolled children in Mwanza city (n=440)

Characteristics	Frequency	%
***BMI**	17.5	2.0
***Body Temperature**	36.6	0.4
Swelling of face		
Yes	3	0.7
No	437	99.3
Parotitis		
Yes	6	1.4
No	434	98.6
Previous history of mumps		
Yes	151	34.3
No	289	65.7
Painful swallowing		
Yes	47	10.7
No	393	89.3
Tonsillitis		
Yes	7	1.6
No	433	98.4

**The second and third columns indicate mean and standard deviation respectively*

Seropositivity of mumps antibodies and proportion of susceptible children in Mwanza city

The seropositivity of mumps IgG antibodies was found to be 94(21.4%, 95% CI:17.5-25.1) while only 1 (0.23%, 95% CI:0.02-0.6) was seropositive for IgM antibodies indicating an acute mumps infection (figure 1). By Wilcoxon ranksum (man Whitney) test, there was no significant

difference in age between IgG seropositive children and IgG seronegative children [10 (IQR: 8-11) years vs. 9 (IQR: 8-11) years, p=0.221)]. Overall, 345 (78.4%, 95% CI: 74.5-82.2) of enrolled children were found to be susceptible to mumps virus infection i.e. had no detectable levels of antibodies to mumps virus (Figure 1).

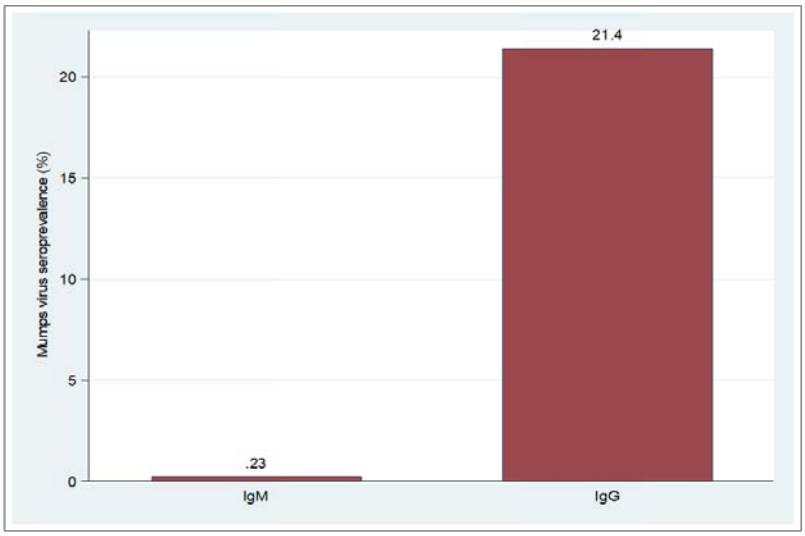

Figure 1: Seroprevalence of mumps IgM and IgG antibodies

Factors associated with mumps IgG antibodies seropositivity among children in Mwanza city.

On univariable logistics regression analysis, residing in rural areas (OR: 2.23, 95%CI: 1.40-3.54, p=0.001) significantly protected children from being mumps IgG seropositive. Moreover, sharing of utensils (OR:1.67, 95%CI:1.05-2.66, p=0.029), coming from families with low socioeconomic status (SES) (OR:1.93, 95%CI:1.22-3.07, p=0.005) and age>10 years (OR:1.64, 95%CI:1.03-2.61, P=0.038) were significantly associated with mumps IgG seropositivity. Having parents with secondary education (OR:1.61, 95%CI:0.46-5.6, p=0.456) and primary education

(OR:2.32, 95%CI:0.63-8.49, p=0.204) were found to have non-statistical increased risk of being IgG seropositive. By multivariable logistic regression analysis, residing in rural areas (OR: 2.28, 95%CL: 1.42-3.36, P=0.001) and age >10 years (OR:1.67, 95% CI:1.03-2.7, P=0.036) independently predicted IgG seropositivity (table 3)

Table 3: univariate and multivariate logistic regression analysis on the factors associated with mumps igg seropositivity

**SES was not included in multivariate analysis because it has collinearity with residence*

Characteristics	IgG seropositivity (N, %)	Univariate		Multivariate	
		OR (95% CI)	P value	OR (95% CI)	P value
Age					
6-10 years (238)	53(18.4)	1			
>10 years (152)	41(27.0)	1.64(1.03-2.61)	0.038	1.67(1.03-2.71)	**0.036**
Sex					
Female (279)	55(19.7)	1.0			
Male (161)	39(24.2)	1.3(0.82-2.07)	0.267		
Residency					
Urban (269)	43(15.99)	1.0			
Rural (171)	51(29.82)	2.23(1.40-3.54)	**0.001**	2.28(1.42-3.66)	**0.001**
Parent/guardian's education					
Tertiary (22)	3(13.64)	1.0			
Secondary (97)	26(26.8)	1.61(0.46-5.6)	0.456		
Primary (321)	65(20.25)	2.32(0.63-8.49)	0.204		
Previous history of mumps					
No (289)	65(22.49)	1.0			
Yes (151)	29(19.21)	0.82(0.50-1.34)	0.425		
Number of siblings	4(IQR 3-5)	0.94(0.84-1.06)	0.328		
Social economic status (SES)					
High (262)	44(16.79)	1.0			
Low (178)	50(28,09)	1.93(1.22-3.07)	**0.005**		
BMI	17.2(IQR16.4-18.8)	0.99(0.88-1.11)	0.882		
Parotitis					
No (434)	93(21.43)	1.0			
Yes (6)	1(16.67)	0.73(0.85-6.35)	0.778		
Previous h/ parotitis					
No (332)	76(22.89)	1.0			
Yes (108)	18(16.67)	0.67(0.38-1.19)	0.172	0.64(0.35-1.17)	0.148
Painful swallowing					
No (393)	89(22.65)	1.0			
Yes (47)	5(10.64)	0.407(0.16-1.06)	0.065	1.77(0.66-4.78)	0.257
Sharing of utensils					
No (222)	38(17.12)	1			
Yes (218)	56(25.69)	1.67(1.05-2.66)	**0.029**	1.44(0.88-2.35)	0.141

Discussion

This is the first study to assess seropositivity of mumps antibodies among school aged children in Mwanza, Tanzania. The median age of enrolled children was high and most of the enrolled

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children were female. In relation to age and sex, this population is similar to previous studies in the U.S.A and Ankara [23, 24] and different from another study where most of the enrolled children were male [1]. Moreover, in this study almost half of children reported to share utensils and the majority of the children were enrolled from rural areas of the city. This observation is similar to a previous study in Colombia and different from another study in DRC whereby the majority of participants were from urban settings [19, 25].

In this study, the seropositivity of mumps IgG antibodies was 21.4% among children aged 6-12years group which implies that more than two thirds of the children in Mwanza are susceptible to mumps virus infections. This means that the population is susceptible for more outbreak and subsequent complications. It is known that complication of mumps like orchitis occur in post pubertal age. Studies have shown that orchitis and testicular atrophy with reduced infertility is commonly observed among unvaccinated individuals who had mumps infection[27, 28].This necessitates the need to have more data across the country so as to have evidence-based implementation of vaccination and other control programmes in future. Moreover, studies on outcomes of mumps virus infection in different populations in Tanzania are warranted. The seroprevalence is comparable to a previous study in the DRC that reported the seropositivity of 22% among children[19].

History of mumps in this study did not correlate with IgG seroprevalence in the current study; this could be due to misinterpretation of clinical symptoms suggestive of mumps and tonsillitis or recall bias. Mumps typically begins with a few days of fever, headache, myalgia, fatigue, and anorexia and followed by development of salivary gland swelling within 48 hours. Also

asymptomatic infection occur in 20 to 30% and some may have nonspecific symptom therefore may not present for clinical evaluation[29].

In comparison to a previous study in South Africa which reported 9% of children with meningitis to have mumps virus, the reported seropositivity in this current study is indeed high [20]. When compared to previous studies in other countries outside Africa; the reported seropositivity in the current study is low compared to 80.2%, 71.9%, 89.1, 71.1 and 69.4% reported in Iran, Yemen, Ankara turkey, Eastern Turkey and Brazil, respectively [1, 18, 24, 26, 30]. The possible explanation for these variations could be due to differences in seasonality, study populations, geographical and climatic conditions. The current study was conducted from July to September which is a dry season compared to the previous studies. As previously reported, seropositivity of mumps tend to be high during winter in temperate regions while in the hot climates transmission can be high at any time of the year [13, 31]. Further studies in different seasons of the year are recommended in this setting. In addition, differences in the utility of the test used could explain differences in seropositivity of mumps IgG antibodies observed. The current study used indirect Enzyme linked immune-sorbent Assay (ELISA) with specificity and sensitivity of 95% and 98%, respectively which might be different from previous studies. Furthermore, the seropositivity in the current study is significantly low compared to studies from USA and Colombia which reported the seropositivity of 87.6% and 91.6%, respectively [23, 25]. This could be explained by the fact that these countries have included mumps vaccine in their national immunization programme and that could explain high levels of IgG antibodies. It has been shown that, in countries where there is no mumps vaccination, the incidence of acquiring the infection is very high compared to those countries that have included

MMR in the national immunization programme therefore antibodies would be high in countries with vaccination due to vaccine induced immunity [14, 25]. Regarding mumps IgM seropositivity in the current study, it was found to be low which is inconsistent with previous studies that did not report mumps IgM seropositivity [19, 20].

Regarding factors associated with mumps IgG seropositivity, residing in rural areas was found to predict mumps IgG seropositivity. This observation is similar to a previous study in Eastern Turkey and different from other studies in DRC and Ankara Turkey [18, 19, 24]. This could be explained by the fact that most of viral infections including mumps virus are associated with low living standards which is most common in rural areas in Tanzania and other low income countries. This has been confirmed in the current study whereby the majority of the children were from low quality houses and most of them were coming from families with low socioeconomic status as previously reported [32]. As in previous reports [1, 19, 32], the odds of being IgG seropositive was significantly higher in older children than young children. This could be explained by the fact that as age increases, the risk of exposure to the virus also increases. Mumps is highly infectious and is transmitted by respiratory droplets, direct contact, or fomites[33]. Therefore spreads rapidly among susceptible individuals living in close contacts school children with family members by sharing utensils which was also observed in this study.

Study limitations

One of the major limitations in this study could be a recall bias some of the clinical factors, this might contributes to poor association of clinical factors and IgG seropositivity.

Conclusion and recommendations

A significant proportion of young children in urban areas of Mwanza city are susceptible to mumps virus infection. Having high proportion of children without immunity to mumps virus

underscores the need to have vaccination and more epidemiological studies across the country so as to have evidence-based control interventions.

Consent for publication

Not applicable

Ethical approval

Ethical approval was sought from the joint Catholic University of Health and Allied Sciences (CUHAS)/Bugando Medical Centre (BMC) research ethics and review committee (CREC) with ethical clearance number CREC/296/2018. Permission to conduct the study in the selected schools was sought from the respective district administrative secretaries and from the headmasters/mistresses of the schools. Written informed consent was obtained from each parents/guardian before enrollment to the study.

Comment [S7]: Omit, already stated in methodology

References

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