Original Research Article

Sero-prevalence of Mumps among Unvaccinated Children Attending Regional Referral Hospitals in Dar es salaam, Tanzania

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ABSTRACT

Aims: Mumps infection and its complication remain under recognized public health problem in Tanzania, as there are no national screening programme and sero-epidemiological surveys. This makes it difficult to devise control interventions including administration of vaccinations. We determined the Sero-prevalence of Mumps among Unvaccinated Children Attending Regional Referral Hospitals in Dar es salaam, Tanzania

Study design: A hospital based cross-sectional study.
Place and Duration of Study: Outpatient departments of three regional hospitals in Dar es Salaam Tanzania: Amana, Mwananyamala, and Temeke hospitals, between March to June 2021.
Methodology: Three hundred and sixty children aged 1- 16 years were included in the study. A structured questionnaire was used to collect participants' information. Serum samples were tested for mumps immunoglobulin G antibodies using an enzyme linked immune-sorbent assay. Proportions were used to describe children's social demographic and clinical characteristics, and binary logistic regression was used to estimate the odds of exposure to mumps virus. A p-value < 0.05 was considered statistically significant.
Results: The mean age was 7.6 ± 4.1, half of them were females. More than three quarters (77%) of the children had Mumps Immunoglobulin-G. Mumps sero-prevalence among under-fives was 58.8%, among 5-8 years was 80%, 9-12 years was 86% and for 13-16 year was 88%. Compared to under-fives, children in the ages of 5-8, 9-12 and 13-16 had four times (OR 4.19 95% CI 1.49-11.7), five times (OR 5.84 95% CI 1.89-18.12) and six times (OR 6.00 95% CI 1.63-21.43) higher odd of mumps exposure respectively. The number of siblings in the house, going to school, and previous history of parotid gland enlargement were not associated with mumps sero-positivity.
Conclusion: The mumps virus is circulating in a high proportion among children in Dar es Salaam and the likelihood of exposure increases with age.

Keywords: *Antibody, mumps, protective antibody titer, sero-prevalence, vaccine*

1. INTRODUCTION

Mumps is a common contagious viral disease caused by mumps virus of the Paramyxoviridae family(1). Although the disease is mild and asymptomatic in 30% to 40% of affected individuals (2). up to 10% develop aseptic meningitis, and 5/100,000 infected children develop sensorinueral deafness(3,4). Moreover, mumps infection in males during or post puberty could lead to orchitis(3), a condition characterized by inflammation of the testes, of which the probability of becoming permanently sterility is up to 30% (5).

There is no specific treatment for mumps but control of Mumps and associated sequel is mainly achieved by vaccination of children using monovalent vaccine or in combination with rubella and measles (MMR) (6). Mumps vaccination is currently being implemented in atleast 122 countries belonging to world health organization (WHO) programe (7), but there is little to no vaccine coverage in majority of African countries (8). To date only four countries in Africa including Seychelles, Mauritius, Cabo Verde and Algeria have included mumps vaccine in their country Expanded Program for Immunization (EPI) (9). Tanzania has neither a vaccination nor surveillance program against mumps. This leaves a lot of Tanzanian children at risk of contracting mumps virus and suffering its complications. Furthermore, the absence of a mumps surveillance program for mumps makes it harder to get accurate information on the magnitude of the disease.

According to the WHO recommendation on routine mumps vaccination, countries with an efficient vaccination program and have achieved more than 80% coverage on the measles and rubella vaccination coverage should consider in cooperating mumps vaccine into their EPI (10). Tanzania had achieved 85% of measles vaccination coverage by 2008 (11), however, mumps vaccination is not offered routinely. Other important considerations for introducing the mumps vaccine include, social and economic impact of the vaccine introduction and the burden of disease in the country (12). Absence of mumps sero-surveillance data in Tanzania makes it difficult to ascertain the burden of disease to justify incorporation of mumps vaccine into EPI in Tanzania.

Understanding epidemiology of infection and level of natural protective immunity are the key steps in devising control measures. Hence in the current study, we provide evidence of mumps virus circulation among children 1-16 years residing in Tanzania's largest city and financial hub, Dar es Salaam. Findings from this study might be useful in the prevention and control interventions as they can be used as evidence for making decision to curb mumps infection in Tanzania. Furthermore, this study will ascertain the gap for future studies across the country in understanding mumps sero-epidemiology

2. MATERIAL AND METHODS

2.1. Study design, duration and study site

We conducted a hospital based cross-sectional design from March to June 2021 at the outpatient departments (OPD) of three regional referral hospitals in Dar es Salaam: Amana, Mwananyamala, and Temeke hospitals. The three hospitals were selected due to high volume of patients from different communities in Dar es Salaam serving up to 3000 children per month.

2.2. Study Population, Sampling and Sample size estimation

Children aged 1-16 years attending the outpatient department (OPD) at the hospitals were enrolled. A probability proportional to size was used to determine the total number of participants to be enrolled from each hospital and a systematic sampling method for enrolment of study participants was employed. The first child was randomly selected and the subsequent ones enrolled using a sampling interval.
The sample size was calculated using the Kish Leslie formula (1965), considering the prevalence of 63.6% obtained from a hospital-based study conducted in Sudan (11). Mumps immunized children, those who received blood transfusions three months before data collection, and those younger than one year were excluded.

2.3. Data Collection

A structured questionnaire was used to collect study participants' demographic and clinical information. The collected data included age, sex, school level, family history, vaccination status, and the reason for hospital attendance. The clinical information included symptoms of mumps such as fever, painful swelling of the parotid gland, fatigue, and loss of appetite

2.4. Sample processing and mumps IgG detection

About 4mL of whole blood was collected from each participant in ethylene-diamine-tetra-acetic acid (EDTA) tubes. The blood was centrifuged at 1500 r.p.m for 10 minutes to obtain plasma, which was aliquoted into a cryovial tube and transported in a cool box to MUHAS immunology laboratory for storage (at -20°C) and testing. The Mumps specific IgG antibodies were detected using ELISA (Vircell, S.L.parque Tecnologico de la Salud, Avicena, Granada Spain) as described in the manufacturer's instructions (13). Briefly wash solution was prepared by filling 50ml of wash buffer with distilled water to get one liter. By using the plates provided, 100µl of serum diluent was added to all the wells to be used. In the four wells used for control, 5µl of IgG cut-off control (in duplicate) was added, 5µl of IgG negative control and 5µl of positive IgG control were also added. In the rest of the wells, 5µl of plasma was added. The plate was placed on a plate shaker for 2 minutes to achieve a homogenous mixture. The wells were covered with a sealing sheet and incubated at 37°C for 45 minutes. After incubation, the liquid was aspirated, and the plate was washed five times. The rest of the liquid was drained. After washing, 100µl of IgG conjugate was added, the plate was covered with a sealing sheet and incubated at 37°C for 30 minutes. After incubation, the wells were washed five times and incubated again at room temperature in a dark environment. Immediately 50µl of stop solution was added to all the wells. The wells were then be placed in a spectrophotometer at 450nm/620nm to obtain the optical densities. Samples were considered reactive if the antibody index of mumps specific IgG antibodies was more than 11.

2.5. Data Analysis

Data were analyzed using Statistical Package for the Social Sciences (SPSS) version 23. We used proportions to report the sero-prevalence of mumps in different age groups, and the difference in exposure to mumps virus between age groups was analyzed using

Pearson's Chi-square test. Binary logistic regression was used to determine factors associated with exposure to the mumps virus. The variables with *P* value less than 0.05 were considered statistically significant.

3. RESULTS AND DISCUSSION

3.1. Baseline characteristics of study participants

The study enrolled 360 children with a mean age of 7.7 ± 4.1 years; half were males. Most of the children 292/360 (81.1%) attended school, and nearly a third 118/360 (32.8%), lived with more than six people in the house. Fever was the most common reason for seeking medical treatment 271/360 (75.3%), followed by generalized body fatigue 171/360 (47.5%) and headache 162/360 (45.5%). Most of the children did not have swollen parotid glands 350(97.2%) or history of previous parotid gland enlargement 289(80.3%) in (**Table 1**).

Table 1: Baseline characteristics of study participants

Variable	Frequency
Sex	
Female	178(49.4)
Male	182(50.6)
Age (yrs)	
1-4	80(22.2)
5-8	143(39.7)
9-12	87(24.2)
13-16	50(13.9)
Number of siblings	
1	77(21.4)
2	81(22.5)
3	80(22.2)
4	63(17.5)
≥5	59(16.4)
Total number of people in a household	
2	2(0.56)
3	47(13.1)
4	60(16.7)
5	70(19.4)
6	63(17.5)
>6	118(32.8)
Attending school	
Yes	292(81.1)
No	68(18.9)

Residence	
Ilala	115(31.9)
Temeke	107(29.7)
Kinondoni	106(29.4)
Ubungo	23(6.4)
Kigamboni	9(2.5)
Swelling of the parotid gland	
Yes	10(2.8)
No	350(97.2)
History of parotid gland enlargement	
Yes	71(19.7)
No	289(80.3)

3.2. Sero-prevalence of mumps in children

A high sero-prevalence was observed, with more than three quarters 277(77%) of the children having Immunoglobulin G antibodies against mumps virus in **figure 1**.

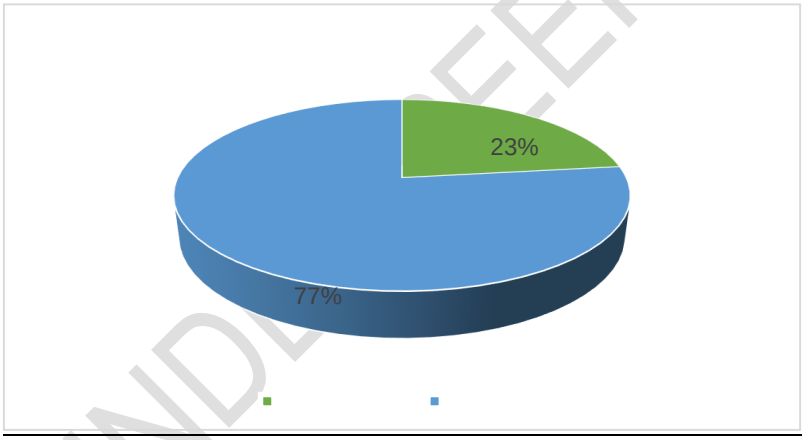

Figure 1: Sero-prevalence of mumps in children

3.3. Sero-prevalence of mumps in different age categories

Mumps sero-prevalence among under- fives was 58.8%, 5-8 years was 80%, age 9-12 had sero-prevalence of 86% and those at 13-16 had sero-prevalence of 88% in (**Figure 2**)

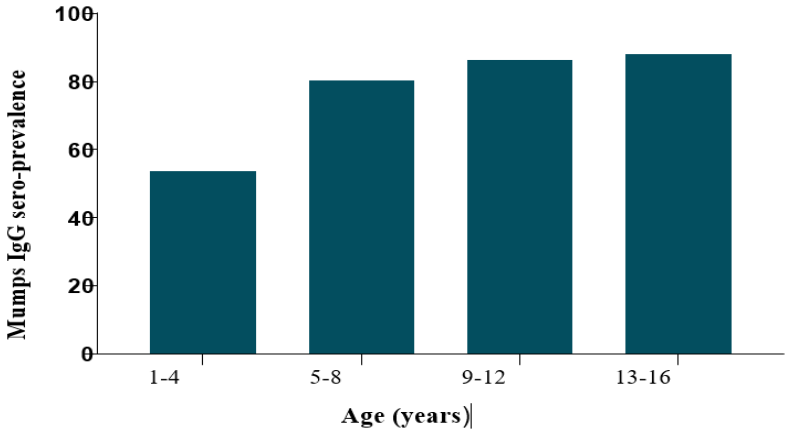

Figure 2: Sero-prevalence of mumps in different age categories

3.4. Factors associated with mumps infection in children

Binary logistic regression was used to assess factors associated with exposure to the mumps virus. In univariable logistic regression analysis, sex, age, and school attendance were associated with mumps IgG sero-positivity. The odds of contracting the mumps virus among female children was 78% higher than males (OR 1.78, 95%CI 1.08-2.93). Children in the age categories of 5-8, 9-12 and 13-16 years had three times (OR 2.88, 95% CI 1.57-5.29), five times (OR 4.85, 95% CI 2.23- 10.5) and eight times (OR 8.07, 95% CI 2.65-24) higher odds of exposure to mumps virus than children younger than five years. In addition, the likelihood of mumps virus exposure among children who were going to school was three times higher than those who were not going to school (OR 3.0, 95% CI 1.68-5.33). In adjusted analysis, only age was independently associated with exposure to mumps virus. Compared to under-fives, the odds of exposure to mumps virus were 4.2, 5.8, and 6 times higher in 5-8 years (OR 4.19 95% CI 1.49-11.7), 9-12, (OR 5.84 95% CI 1.89-18.12) and 13–16-year olds, (OR 6.00 95% CI 1.63-21.43) respectively. (**Table 2**).

Table 2: Factors associated with mumps infection in children

Variables	Mumps sero-positivity	IgG Univariable		Multivariable	
	n (%)	cOR (95% CI)	*P value*	aOR (95% CI)	*P* value
Sex					
Female	146(82.02)	1.78(1.08-2.93)	0.025	1.50(0.88-2.55)	0.139
Male	131(71.98)	Ref			0.317
Age (yrs)					
1-4	43 (53.75)	Ref			
5-8	115 (80.42)	2.88(1.57-5.29)	0.01	4.19(1.49-11.7)	0.007
9-12	75 (86.21)	4.85(2.23-10.5)	0.01	5.84(1.89-18.12)	0.002
13-16	44 (88)	8.07(2.65-24)	0.01	6.00(1.63-21.43)	0.007
Attending school					
Yes	242(82.88)	3.00(1.68-5.33)	0.001	1.10(0.39-3.12)	0.853
No	42(61.76)	Ref			

No of people in the household					
2	1(50)	Ref			
3	25(65)	1.76(0.10-30.1)	0.695	2.25(0.06-81.05)	0.129
4	29(63.04)	2.16(0.13-36.40)	0.594	3.48(0.10-122.49)	0.221
5	51(78.46)	2.89(0.17-48.6)	0.461	4.21(0.12-147.87)	0.196
6	51(85.00)	5.30(0.31-91.9)	0.252	8.89(0.24-327.25)	0.100
>6	90(85.71)	5.56(0.33-92.9)	0.233	9.24(0.25-345.42)	0.914
Number of siblings					
1	36(69.23)	Ref			
2	50(68.49)	1.73(0.82-3.66)	0.150	0.454(0.16-1.26)	0.129
3	60(81.08)	1.7(0.76-3.78)	0.194	0.453(0.12-1.61)	0.221
4	50(86.21)	1.75(0.70-4.36)	0.230	0.40(0.10-1.60)	0.196
≥5	43(85.72)	6.0(0.75-48.2)	0.092	0.27(0.06-1.28)	0.100
History of parotid gland enlargement					
Yes	60(84.51)	2.08(1.98-4.40)	0.056	1.64(0.625-4.13)	0.292
No	217(75.09)	Ref			

4. DISCUSSION

The current study reports a relatively high sero-prevalence of mumps IgG among unvaccinated children. In addition, the likelihood of exposure to mumps virus increased with age, with the odds being higher among older children compared to those under five years.

Over three-quarters of children in the current study had mounted IgG immune response against mumps virus infection. Studies reported elsewhere showed more or less similar results: studies in Sudan, Iran, and Turkey reported mumps sero-prevalence among unvaccinated children, to range from 63% to 80% (11,14,15). Reports on mumps in Tanzania are scarce. However, one recent study in Mwanza reported a much lower mumps IgG sero-prevalence of 21% among 6-12-year-old children (16). The difference could be attributed to the age range since mumps sero-prevalence increase with age (17). Nonetheless, mumps herd immunity to block mumps virus transmission requires a threshold ≥ 85 % (18). The percentage rate in the current study shows that mumps infection transmission will likely continue amongst other children, hence there is a need to consider incorporating mumps vaccine in the Expanded Program for immunization (EPI) in Tanzania.

Sero-prevalence of mumps IgG increased with age, whereby children in the 9-12 and 13-16 years' categories had six times the odds of having mumps immune-globulins compared to those below five years. Previous sero-surveys have reported similar results where 50% of children had been exposed to mumps virus by the age of 6 years, and the exposure increased to 90% by 14-15 years (3). By 30 years, the sero-positivity ranged from 90-100% (18,19). These findings show that almost all unvaccinated individuals will eventually get infected (20).

Of note, nearly a quarter of children in the present study were still susceptible to infection. These include 14% and 12% for those ages 9-12 and 13-16, respectively. Acquiring mumps infection during and post-puberty is characterized by an increased risk of orchitis, that could result to infertility in males (5). High inflammation in the testis impair the blood-testis barrier,

exposing immune-privileged antigens and producing autoantibodies (21). Hence-why, children before puberty rarely experience this because the spermatids have not yet been produced in the testes. These findings highlight the need to consider incorporation of mumps vaccine in the EPI in-order to prevent mumps associated complications such as secondary infertility that could occur at this age.

The current study did not find an association between the previous history of parotid gland enlargement and an increase in IgG sero-positivity. Likewise, Rakiru et al. had similar observations among school-aged children in Tanzania (16). Our finding is contrary to a report from Sudan, where IgG sero-positivity was significantly higher among children who had reported experiencing the swelling of the parotid gland before (11). The high rate of asymptomatic mumps infection (2) and atypical symptoms (16) could explain the lack of association in the current study.

Although there was a trend in the increase of mumps IgG sero-positivity with the increase in the number of people and number of siblings in the house, the two factors were not independently associated with exposure to the mumps virus in the current study. These findings Coincide with Rakiru et al., who reported the lack of association of exposure to mumps virus with number siblings among school-going children in Mwanza (16). However, Gürgöze et al. reported that the lack of a sibling in a house significantly lowered mumps sero-prevalence among unvaccinated 3-5-year-old children in Spain(15). Additionally, Arroyo et al. found that mumps sero-prevalence among unvaccinated children in Turkey increased as the number of siblings increased (22). Geographical and climatic conditions could be the reason for the variations of the findings in the current study.

Although our findings argue for the need to incorporate the mumps vaccine in the expanded program for immunization in Tanzania, they should be interpreted with caution because this was a health facility-based study. The subjects may not represent the entire infected population. Nonetheless, it does not take away from the fact that our findings are among the few available data in the country, highlighting important findings on the sero-prevalence of mumps among unvaccinated children in Tanzania. Furthermore compare to the initial published study in Tanzania, our study has a wider age range and hence more informative on which age presents a high risk of infection for consideration of vaccine strategies in the country.

5. CONCLUSION AND RECCOMENDATION

The mumps virus is circulating in high proportion among children, and the likelihood of exposure increases with age. The presence of a substantial proportion of children between the age of 9-16 where puberty generally begins who did not have mumps IgG underscores the need for the mumps vaccine in childhood immunization to prevent mumps-related complications.

CONSENT

As per international standard or university standard, Participants' written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

The MUHAS Senate Research and Publications Committee provided ethical approval to conduct this study with reference number MUHAS-REC-2-2020-098. Participation was

voluntary, and parents and children were free to decline to participate without compromising their healthcare services. The collected information was entered into computers using study identification numbers. To ensure confidentiality, only authorized persons accessed the data. All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

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