Prevalence and Risk Factors for Subclinical Rheumatic Heart Disease Among Primary School Children in Dar es Salaam, Tanzania: A Community Based Cross-Sectional Study.

Parvina Kazahura (✉ parvinakoku.pk@gmail.com)  
Jakaya Kikwete Cardiac Institute  
https://orcid.org/0000-0003-1770-4744

Theophylly L. Mushi  
Jakaya Kikwete Cardiac Institute

Pedro Pallangyo  
Jakaya Kikwete Cardiac Institute

Mohamed Janabi  
Jakaya Kikwete Cardiac Institute

Rodrick Kisenge  
Muhimbili University of Health and Allied Sciences

Mazen Albaghdadi  
Harvard Medical School

Naizihijwa Majani  
Jakaya Kikwete Cardiac Institute

Edward Kija  
Muhimbili University of Health and Allied Sciences

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Abstract

**Background:** Rheumatic heart disease (RHD) is the most common acquired heart disease occurring in children and adolescents. RHD is associated with significant morbidity and mortality particularly in low and middle-income countries (LMICs) where the burden is estimated to be higher compared to high income countries. Subclinical RHD is the presence of valvular lesion diagnosed by echocardiography in a person with no clinical manifestation of RHD. This study aimed at determining the prevalence, types and factors associated with subclinical RHD among primary school children in Dar Es Salaam, Tanzania.

**Methods:** We conducted a cross-sectional, descriptive community-based study which recruited primary school children from February to May 2019. A standardized structured questionnaire was used to collect demographic data and information related to prior history of upper respiratory tract infections (URTIs). Anthropometric measurements were taken and chest auscultation and echocardiographic screening were done to all study participants. World Heart Federation echocardiographic classification was used to define the types and prevalence of subclinical RHD.

**Results:** A total of 949 primary school children were enrolled with females being predominant (57.1%). The prevalence of subclinical RHD was 34 per 1000. All the participants had mitral valve disease only whereby 17 had definite disease and 15 had a borderline disease. The associated factors for subclinical RHD were older age of more than 9 years (OR 10.8, 95% CI 1.4-82.2, P=0.02) having three or more episodes of URTI in previous six months (OR 21, 95% CI 9.6-46, P=0.00) and poor hygiene (OR 3, 95% CI 1.3-6.8, P=0.009)

**Conclusion:** Subclinical RHD as detected by echocardiographic screening is prevalent in primary school children, uniformly affects the mitral valve, and is associated with potentially modifiable risk factors. Children with a history of more than three episodes of URTI in six months may represent a particularly high-risk population that should be targeted for RHD.

Background

Rheumatic fever (RF) is a multi-system inflammatory, post infectious disease, which presents as a delayed sequela to Group A streptococcal (GAS) pharyngitis. In developing countries it remains a major health concern due to poor health seeking behaviour, overcrowding, poor nutrition and scarcity of health care resources. RF is mainly a disease of children aged 5 to 14 years old and rare in persons above 30 years. It is hypothesized to have an immune mediated pathogenesis due to the latent period between GAS infection and rheumatic fever.

Rheumatic heart disease (RHD) is the most serious complication of rheumatic fever whereby patients develop heart valve regurgitation or stenosis, atrial dilation, arrhythmias and right ventricular dysfunction. After a patient has had RF, there is often a prolonged period of subclinical disease characterized by changes in valvular morphology and function. It has been shown that 40 to 65% of patients who have had RF get clinically recognizable RHD. Subclinical RHD is a term used to describe the presence of
morphological and functional valvular lesions detected by echocardiography but with no corresponding heart murmur. The latent period of subclinical RHD provides a window of opportunity for screening, initiation of secondary prophylaxis, and referral for valvular intervention when appropriate.

At the Jakaya Kikwete Cardiac Institute (JKCI) in Dar es Salaam, Tanzania, 29.5% and 32.9% of all cardiac surgeries in 2017 and 2018 respectively were performed to treat RHD “(unpublished data)”. The World Heart Federation continues to recommend screening as a component of RHD control in high prevalence areas (8) However, there is a paucity of data in Sub-Saharan Africa with regard to RHD and associated risk factors, particularly in children. (9, 10) In the current study, we utilized WHF echocardiographic screening criteria and a structured questionnaire to evaluate the prevalence and risk factors of subclinical RHD, respectively, in Tanzanian primary school children.

**Methods**

A community based descriptive cross-sectional study was conducted at Muhimbili and Mjimpya primary schools in Dar es salaam, Tanzania. Both are public, mixed-sex schools, and the former represents a middle-class population while the latter represents a lower socioeconomic class population. Muhimbili primary school has a total number of 1120 students while Mjimpya primary school has a total number of 1067 students which were selected consecutively for participation.

School children aged 7 to 18 years were recruited from February to May 2019. They were provided with questionnaires and consent forms for parents to fill at home and children were asked for assent. Those who brought back the filled questionnaires with a signed consent within two weeks after being given were recruited for the study.

All the children with established rheumatic heart disease determined by transthoracic echocardiography and those who denied consent and assent were excluded from the study.

The risk factors, socioeconomic and demographic characteristics, hygiene status, overcrowding, and history of sore throat for past six months were recorded. Those who had at least 3 episodes of upper respiratory tract infectious symptoms were regarded to have recurrent upper respiratory tract infection (URTI). Anthropometric measurements for height, weight and BMI were interpreted from WHO BMI charts for children aged 5 to 19 years.

Cardiac auscultation and echocardiographic screening were conducted at school in a room with a door and curtains. Cardiac auscultation using a stethoscope and transthoracic Doppler echocardiography (2D echo) (Siemens ACUSON P500) with a paediatric cardiac probe were performed by PK and T.L.M. 2D echo images were taken using the apical four chamber view, parasternal long and short axes views, with and without colour Doppler. Screened participants found to have any morphological valvular pathology as per World Heart Federation (WHF) criteria were referred to JKCI for detailed echocardiography that was performed by the paediatric cardiologist using a Siemens ACUSON X300 PE Premium Edition. The interpretations of echocardiographic findings were defined according to the WHF echocardiographic
criteria for RHD. (11) Statistical analysis was done using SPSS version 20.0 (IBM®), statistical software for data analysis. A univariate regression analysis using Chi-square was performed to examine predictors of subclinical RHD. All factors with a p-value < 0.2 were included in the logistic regression model. All statistical analyses were two sided and a p-value < 0.05 was used to denote statistical significance.

Results

A total of 1023 were screened for eligibility and 949 children were enrolled into this study (Fig. 1). Table 1 displays the socio-demographic characteristics of the study population. The mean age of participants was 10.8 ± 1.7 and their ages ranged from 7 to 17 years. There was a female predominance (57.1%) and over three quarters of all participants had a normal BMI. Most parents were small scale business owners and had attained primary school as the highest level of education.
Table 1
Socio-Demographic characteristics of the study participants (n = 949)

| Demographics                        | Mean ± SD / Frequency (%) |
|-------------------------------------|---------------------------|
| **Age of Children**, Mean ± SD; Range | 10.8 ± 1.7, 7–17 years    |
| **Sex** N (%); Female, Male         | 542 (57.1) ; 407 (42.9)   |
| **BMI** N (%)                       |                           |
| Normal                              | 742 (78.2)                |
| Severe underweight                  | 20 (2.1)                  |
| Underweight                         | 156 (16.4)                |
| Overweight                          | 23 (2.4)                  |
| Obese                               | 8 (0.8)                   |
| **Age of the parents**              |                           |
| Mean ± SD                           | Mother                    |
| Range                               | Father                    |
| 22–54 years                         | 42 ± 9.3                  |
| **Parents’ education level** N (%)  |                           |
| No formal education                 | Mother                    |
|                                    | Father                    |
| 12 (1.3)                            | 327 (34.5)                |
| Primary education                   | 28 (3)                    |
|                                    | 336 (35.4)                |
| Secondary education                 | 461 (48.6)                |
| Above secondary education           | 298(31.4) 140 (14.8)      |
|                                    | 198 (20.9)                |
| **Parents’ occupation** N (%)       |                           |
| None                                | Mother                    |
|                                    | Father                    |
| 224 (23.6)                          | 37 (3.9)                  |
| Rural Farmer                        | 23 (2.4)                  |
|                                    | 50 (5.3)                  |
| Small scale business                | 517 (54.5)                |
|                                    | 417 (43.9)                |
| Large scale business                | 43 (4.5)                  |
|                                    | 114 (12)                  |
| Employed                            | 127 (13.4)                |
|                                    | 264 (27.8)                |
| **People living in one house** N (%)|                           |
| > 6 people                          | Mother                    |
|                                    | Father                    |
| 315 (33.2)                          | < 6 people                |
| **People sharing bedroom with the child** N (%) |       |
| > 2                                 | Mother                    |
|                                    | Father                    |
| 206 (21.7)                          | < 2                       |
| 692 (72.9)                          |                           |

About one third of all participants came from families of six or more and the screened child shared a bedroom with at least two other family members in over 21% of families.
Prevalence of subclinical RHD among primary school children

As shown in Fig. 2, a total of 949 asymptomatic primary school children were recruited and screened for subclinical RHD and 32 of them, 23 girls and 9 boys, were found to have subclinical RHD making a prevalence of 34 per 1000, out of which 17 had a definite disease and 15 had a borderline disease. The prevalence of subclinical RHD did not differ between Muhimbili and Mjimpya primary schools (3.2% and 3.6% respectively). One child had clinically detected RHD by a grade 3 pan systolic murmur on the apex, which was later confirmed by echocardiography with the presence of pathological mitral regurgitation (MR) and anterior mitral valve leaflet (AMVL) thickening. Also one child was diagnosed with a 2mm patent ductus arteriosus with a pressure gradient of 65mmHg.

Types of valvular lesions

All 32 primary school children who were found to have subclinical RHD had lesions of the mitral valve. There was no child with mitral stenosis or disease of the aortic valve as shown in Fig. 3. The following valvular lesions were most commonly observed: anterior mitral valve leaflet (AMVL) thickening >3mm, chordal thickening in 12 of 32 (36.5%), and pathological MR in 11 of 32 (33%)

Socioeconomic and Clinical Risk Factors for Subclinical RHD

Risk factors that were associated with subclinical RHD are shown in Table 2. Recurrent URTI, poor hygiene and age greater than nine years of age were associated with the greatest univariate risk of subclinical RHD. We then performed a multivariate logistic regression model comprised of 4 predictors of subclinical RHD from our univariate analysis. As shown in Table 3, school children aged more than 9 years, recurrent URTI and poor hygiene showed statistical significance as associated factors for subclinical RHD.
| Factor          | N (%) | Chi-square | p-value |
|----------------|-------|------------|---------|
| **Age**        |       |            |         |
| >9 years       | 31(4.3) | 8.3         | 0.004   |
| ≤9 years       | 1(0.4)      | 0.4         | 0.79    |
| **Hygiene**    |       |            |         |
| Poor           | 10 (2)  | 5.9         | 0.015   |
| *Good          | 22(4.9) | 0.4         | 0.79    |
| **Overcrowding** |      |            |         |
| Yes            | 19(4.6) | 3           | 0.08    |
| *No            | 13(2.5) | 0.4         | 0.79    |
| **Mothers education** |  |            |         |
| Low            | 18(3.9) | 0.16        | 0.69    |
| *High          | 14(3.2) | 0.4         | 0.79    |
| **Family income** |   |            |         |
| Low            | 20 (4)  | 1.7         | 0.19    |
| *Middle        | 12 (2.9)| 0.4         | 0.79    |
| **URTI**       |       |            |         |
| Recurrent      | 20(22)  | 29.3        | 0.00    |
| *Non-recurrent | 12 (4.1)| 0.4         | 0.79    |
| **Nutrition**  |       |            |         |
| Underweight    | 8 (4.5) | 0.9         | 0.34    |
| *Not underweight | 24(3.1) | 0.4         | 0.79    |
| *Reference     |       |            |         |
Table 3
Multivariate Predictors of Subclinical RHD

| Factor      | COR (95% CI) | p-value | AOR (95% CI) | p -value |
|-------------|--------------|---------|--------------|----------|
| Age         |              |         |              |          |
| > 9 years   | 10.6 (1.4–78.2) | 0.02     | 10.8 (1.4–82.2) | 0.02     |
| ≤ 9 years   | 2.5 (1.2–5.3)  | 0.02     | 3 (1.3–6.8)   | 0.009    |

Hygiene

|          |              |         |              |          |
|----------|--------------|---------|--------------|----------|
| Poor     |              |         |              |          |
| *Good    | 10.8 (1.4–82.2) | 0.02     | 3 (1.3–6.8)   | 0.02     |

Overcrowding

|          |              |         |              |          |
|----------|--------------|---------|--------------|----------|
| Yes      | 1.9 (0.9–3.8) | 0.09    | -            | -        |
| *No      |              |         |              |          |

Family income

|          |              |         |              |          |
|----------|--------------|---------|--------------|----------|
| Low      | 1.7 (0.8–3.6) | 0.19    | -            | -        |
| *Middle  |              |         |              |          |

URTI

|          |              |         |              |          |
|----------|--------------|---------|--------------|----------|
| Recurrent| 19.6 (9.1–41.2) | 0.00    | 21 (9.6–46)  | 0.00     |
| *Non-recurrent |          |         |              |          |

Discussion

Echocardiographic screening for the identification of subclinical RHD is the gold-standard method for understanding disease burden and severity in endemic regions. Insights from echocardiography-based RHD screening programs are vital to informing advocacy and public health responses to reduce the burden of RHD, however data from sub-Saharan Africa are limited. In this study, we sought to provide insights into the epidemiology and echocardiographic characteristics of subclinical RHD in Tanzanian school-children. We found that subclinical RHD as detected by echocardiographic screening is not uncommon in primary school children in Dar es salaam, uniformly affects the mitral valve, and is associated with potentially modifiable risk factors.

We observed that thirty-two out of 949 screened children were found to have subclinical RHD, including seventeen with definite subclinical RHD. The prevalence of subclinical RHD in this study is comparable to that found in other studies in Africa including: Senegal, Brazzaville, Uganda, Ethiopia, Mozambique and Malawi which ranges between 4.95 per 1000 to 32.6 per 1000.(12–16) Furthermore our findings are very
similar to the reported prevalence of subclinical RHD in Malawi with the difference being in the number of
definite and borderline cases whereby their study had more borderline cases than definite cases
compared to this study. The similarity could be explained by both studies having been conducted in sub-
Saharan Africa where sociodemographic characteristics are similar. (12) The number of definite cases in
this study was slightly higher than the number of borderline cases which was also demonstrated in the
studies done in Eastern Nepal and Mozambique. This is because in all three studies the RHD was more
prevalent in children of 9 years of age and above when significant valvular changes have taken place for
a definite disease to occur. (13, 17). The prevalence of RHD detected by clinical examination was
approximately 1 per 1000 compared to the prevalence detected by echocardiography which was
approximately 34 per 1000. Several studies have shown that, regardless of the experience of the
examiner, the sensitivity and specificity of echocardiography is greater than cardiac auscultation. (18–
20) The early progressive valvular changes in RHD are silent and hence it is difficult to pick them by
cardiac auscultation unless they are visualized by echocardiography.

In this study, all the participants who were found to have RHD had mitral valve disease without
involvement of any other valve. Typical features of mitral valve disease observed in our study include
regurgitation, AMVL thickening, chordal thickening and excessive mitral valve leaflet motion. Several
studies from Sub-Saharan African have highlighted the predominance of mitral valve disease among
individuals with subclinical RHD. Other studies have shown that aortic valve disease may be associated
with mitral valve disease though only in a small percentage of individuals. (5, 21) Pure mitral stenosis is
commonly seen in the third decade of life and given that our study population was all less than the age
of 17, we did not observe a high prevalence of rheumatic mitral stenosis as would be expected in this
younger population (22). This pattern is similar to that seen by Chimalizeni et al in Malawi school
children screened whereby mitral regurgitation was the most common valvular lesion, there was only one
child with aortic valve disease and there was no mitral stenosis. (12) Moreover, this finding is in
agreement with other RHD echocardiographic screening studies in Cambodia, Mozambique and Senegal
which also were conducted in school children to determine the prevalence of subclinical RHD that
showed that the mitral valve was the most affected valve although it was associated with aortic valve
disease and without the presence of mitral stenosis. (13, 14) In subclinical RHD, mitral stenosis is not a
common lesion of mitral valve disease as it has not been reported in several studies except the screening
done in school children from Ethiopia where mitral stenosis was found in only 7% of children. (16) The
mitral valve is more commonly involved in RHD probably because the mitral valve cusps are exposed to
the pressure of the left ventricle during contraction in systole but the aortic cusps are exposed to the
aortic diastolic pressure during closure and so the shear stress on the large mitral leaflets is more than on
the small aortic cusps thus making the mitral valve more prone to injury during the RF attacks. The
findings of the current study have important implications for the design of future echocardiographic
screening studies that could be directed at only the mitral valve in resource-limited settings.

Multiple studies from Sub-Saharan African, including Mozambique, Uganda, Senegal, and Malawi, have
observed that children above the age of 9 have a higher observed prevalence of subclinical RHD
compared to younger. (12–15, 17) At an older age of 9 years and above, there are notable valvular
changes after the child has had a number of RF attacks. Although the development of RHD is associated with poor hygiene(23), few studies have examined the association between hygiene, respiratory tract infections, and RHD. Not adhering to handwashing practices has been associated with predisposing a child to streptococcal infections like impetigo which is regarded as a risk factor for URTI (23). In a systematic review by Wilson et al exploring the impact of simple hygiene interventions introduced in primary schools and day care centres on respiratory and gastrointestinal infections, it was found that hand hygiene can reduce the incidence of URTI(24) In Pakistan, poor hygienic conditions was reported as a major risk factor for RF and RHD, however, their sample size was smaller compared to this study and included only children diagnosed with acute rheumatic fever or RHD in the outpatient clinic by echocardiography. (23) Our findings are also consistent with those reported by Ngaide et al from Senegal and Vlajinac H et al in Yugoslavia, where repeated sore throat was observed to be a predisposing factor for the development of RHD especially for those who had definite RHD by echocardiography. (14, 25) Similarly, in the present study, we observed that children aged more than 9 years, recurrent URTI, and poor hygiene were associated with prevalent RHD. Our results highlight the importance and relevance of current guidelines and expert opinion regarding the prevention of rheumatic fever and rheumatic heart disease through the prompt recognition and treatment of GAS pharyngitis, supporting access to clean water for adequate hygiene, and access to healthcare. (29, 30)

**Conclusion**

Subclinical RHD detected by echocardiography is common in primary school children in Tanzania. Mitral valve pathology was the only type of valvular lesion found. Factors associated with subclinical RHD were age greater than 9 years, recurrent URTI, and poor hygiene. These characteristics may be considered as possible criteria for identifying children at highest risk for RHD and thus likely to benefit from screening and secondary prevention programs. Prospective studies are needed to understand the natural history of RHD detected by echocardiography in Sub-Saharan Africa and to understand how screening programs can be utilized by government health programs to reduce the burden of RHD.

**Strength and Limitations of the study**

Our study recruited children from semi-urban and rural areas representing a middle-class and a lower socioeconomic class populations, thus representing the population of the majority of people in Dar Es Salaam. Recall bias might have affected the recollection of URTIs in the previous six months thus potentially affecting its impact on the subclinical RHD. Furthermore, we were not able to ascertain any history of treatment with antibiotics (or other potential confounders) which may have confounded the association between individual characteristics and the detection of subclinical RHD.

**Abbreviations**

AMVL: Anterior mitral valve leaflet, BMI: Body mass index, DRC: Democratic Republic of Congo, GAS: Group A streptococcus, MR: Mitral regurgitation, RF: Rheumatic fever, URTI: Upper respiratory tract
infection

Declarations

Ethical approval and consent to participate

Ethical clearance was provided by the Muhimbili University of Health and Allied Sciences Directorate of Research and Publications with Ref.No.DA.287/298/01A. Permission to conduct the study was obtained from the respective municipal authorities as well as schools where the study was conducted. Consent forms were given to children to take to their parents/guardians at home. The parents/guardians who provided a signed written consent, an assent was requested from the children.

Consent for publication

Not applicable

Availability of data and materials

Data and materials are available upon request to the authors.

Competing interests

The authors declare that they have no competing interests.

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Authors` contributions

PK, RK and EK Conceptualized and planned the study. PK, TLM and NM participated in data collection. PK, EK and PP worked on the results analysis. Manuscript drafting was done by PK,EK. Corrections and critical revision were done by MJ, RK, MA, EK and NM. All authors read and approved the final manuscript.

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Author details

1Department of Paediatrics and Child Health, Muhimbili University of Health and Allied Sciences, P.O Box 65001, Dar es Salaam, Tanzania
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Figures

**Figure 1**

CONSORT Flow Diagram
Figure 2

Prevalence of subclinical RHD among screened primary school children in Dar es Salaam. (n=949)
MORPHOLOGICAL AND FUNCTIONAL FEATURES OF RHD OF MITRAL VALVE

Figure 3

Morphological and functional features of RHD of the MV. The prevalence of various (n=33)