



Pilot Study on Prevalence of Rheumatic Heart Disease in Urban and Rural Angola by Echocardiography

Michelle Kwok¹, Chi-Ming Chow², Karen Henriksen³, Stephen Foster⁴, Aaron Jones³, Michael Bentley-Taylor^{2,4} and Keith Kwok⁵

¹University of Sydney, Sydney Medical School, Sydney, Australia

²University of Toronto, Department of Cardiology, Toronto, Canada

³Rio da Huila Hospital, Huila, Angola

⁴Clinica Evangélico de Medicina do Lubango, Lubango, Angola

⁵Adjunct Lecturer, Department of Medicine, University of Toronto, Canada

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***Corresponding author:** Michelle Kwok, 2175 Sheppard Ave E, Unit 209, Toronto ON, M2J1W8, Canada, Tel: 416-494-2001; Fax 416-494-2004; Email: miche.kwok@gmail.com

Abstract

Rheumatic heart disease is an important cause of death and disability in young people in sub-Saharan Africa. Prevalence of rheumatic heart disease has been studied in many African countries, but no such report for Angola. The objective of this pilot study is to address rheumatic heart disease prevalence in Angola. Echocardiography has been shown to be much more sensitive than clinical detection of rheumatic heart disease. Portable and handheld echo devices were used to screen for prevalence in urban and rural areas. Five sites with no previous rheumatic heart disease screening were chosen and classified according to levels of healthcare access (Table 1). At each site children between ages 4-20 who consented were screened. Two cardiologists performed onsite echo and diagnosed rheumatic heart disease based on 2012 World Heart Federation criteria. Abnormal studies were externally reviewed to confirm the diagnosis. Positive cases were referred to local clinics for follow-up. 574 cases were screened, with 17 positive. Overall prevalence was 29.6 cases per 1000, with a 95% confidence interval between 17.3-47.0. External review concordance rate was 94%. Level 3 areas (lowest healthcare access) had highest prevalence of rheumatic heart disease. (Level 1 = 0, Level 2 = 23.0, Level 3 = 71.4, per 1000, $p = 0.04$). Mitral valve was predominately affected (MV=17, AV=3). Posterior mitral regurgitation was the dominant lesion in early disease (MR = 17, MS = 3). Average age of positive cases was 10. Rheumatic heart disease is highly prevalent in Angola, and areas with lower access to healthcare had a higher disease rate. Early disease is mainly manifested through posterior mitral regurgitation. This study demonstrates an urgent need for a bigger study involving broader regions to define true disease burden, as well as public health intervention including early detection and secondary prophylaxis in reducing rheumatic heart disease in resource-limited areas.

Keywords

Rheumatic heart disease; Echocardiography; Child; Hand-carried cardiac ultrasound; Screening

Introduction

Rheumatic Heart Disease (RHD) is an important cause of death in young people living in developing countries, particularly in sub-Saharan Africa. Rheumatic Heart Disease results from repeated exposure to Group A streptococcus (GAS) infections, which over time causes valve scarring and dysfunction [1]. Data from previous studies has shown that most patients present as young adults when symptoms are severe enough to cause functional limitations [2,3]. Rheumatic heart disease places a massive healthcare burden on healthcare systems that have

severely limited budgets and human resources.

Worldwide, the prevalence is estimated to be at least 15.6 million cases, with an annual incidence of 282,000 cases and 233,000 deaths per year [4]. Sub-Saharan Africa is the most affected region; with an estimated prevalence of 1-14 per 1000 children aged 5-14, affecting more than 1 million children [4]. However this figure may be a gross underestimation as no prospective population-based study of acute rheumatic fever in Africa is available [5]. Many of the prevalence studies did not use echocardiography as screening tool and may underestimate true

Table 1: Characteristics of study sites according to levels of healthcare access.

Healthcare Level	Site	Location	Accessibility from City	Healthcare Availability
Level 1	Humpata	Suburban school outside Lubango*	5-10 minutes drive	Access to city hospitals
Level 2	Kahima	Village 60km southeast of Lubango	90 minutes drive	Access to rural outreach clinics with vaccination program, outreaches, on-site physician and nurse
	Tchitunda	Village 60km southeast of Lubango	90 minutes drive	
	Tchicombe	Village 100km south of Lubango	120 minutes drive	
Level 3	Cavango	250km northeast of Lubango	Difficult road access	No local health personnel or medical outreach programs. Nearest clinic 4 hours drive; nearest hospital 8 hours drive

*Lubango is the provincial capital of Huila province.

disease burden. In addition, these data were based on studies over 10 years ago and may not reflect current situation.

Many patients who present to RHD programs already have existing symptoms and advanced disease, overlooking milder or silent cases of RHD that occur. Symptomatic rheumatic heart disease in adult carries high mortality and morbidity, and is often complicated by congestive heart failure, pulmonary hypertension, atrial fibrillation and stroke [6]. A large multinational study determined RHD to be the most frequent cause of heart failure amongst children and young adults, giving a 180-day mortality as high as 17.8% [7]. Treatment of these patients are very challenging, especially in resource limited areas [6]. Early detection including asymptomatic cases with secondary prophylaxis may prevent progression of valve damage and is a much more cost-effective public health measure.

Echocardiography has become the method of choice for screening rheumatic heart disease. It has been shown to be ten times more sensitive than clinical auscultation of murmurs [8]. The prevalence detected by echocardiography in children with clinically silent RHD in sub-Saharan Africa is estimated to 7.5-51.6 per 1000 children [9]. In the past there were no standardized echo criteria for diagnosing RHD, so different studies used different criteria, making the comparison of prevalence data challenging. In 2012 the World Heart Federation (WHF) defined specific criteria for the echocardiographic diagnosis of RHD for both symptomatic and silent RHD ([Appendix](#)). This allows for comparison of prevalence data between studies.

To date, most prevalence studies have been based on schools, clinics or hospitals. With portable technology becoming increasingly available worldwide, echocardiography can easily be used in rural and remote settings to diagnose RHD [10]. There is a need to study both school and non-school children to obtain real world data.

Although there have been estimates done for sub-Saharan Africa as a whole and in specific countries in sub-Saharan Africa such as Senegal, Uganda, Mozambique, Cameroon, and Democratic Republic of Congo [8,11-14] no known such study has been performed in Angola. Rheumatic heart disease prevalence shows a high regional variation between countries. There is also regional variation within a country. Therefore each country needs to establish its own data. Such data need to be established before effective prevention measures can be planned. We performed an initial screening study in Angola to determine the prevalence of RHD using portable echocardiography.

Materials and Methods

Site Selection

We conducted our screening in five sites in Angola over two weeks in August 2013. Four of these sites were located in the province of Huila (Humpata, Kahima, Tchitunda, Tchicombe) and one was in the neighbouring province of Huambo (Cavango.) Sites were chosen based on the availability of local contacts through two Angolan hospitals (Centro Evangélico de Medicina, Lubango and Centro Médico do Rio da Huila, Chibia), and the ability of local healthcare services to follow up on positive findings. None of the sites had undergone previous screening for RHD.

Categorization of sites

We categorized our five sites into three levels of healthcare access. Level 1 was a urban/suburban area with easy access to city hospital; Level 2 was rural with onsite basic primary care level healthcare facility/clinic, and Level 3 was rural with no onsite healthcare facility and difficult access to health facilities.

Diagnostic Criteria

Prior to the study the investigating cardiologists agreed upon using the 2012 WHF diagnostic criteria for RHD ([Appendix](#)).

Echocardiographic protocol and study population

This study involved patients aged 4-20. Two cardiologists with experience in rural echocardiography (KK and MBT) performed all on-site echocardiographic examinations. At each site, local clinical contacts promoted free heart screening for children who had previously never been examined for heart disease. Children whose parents consented verbally were included for screening. 80-120 children from each site were screened. Equipment used for screening involved handheld V-Scan (GE Medical Systems, Milwaukee, WI) with a 4V2-A

phased array transducer or SonoSiteMicromaxx (Providian Medical Equipment, Willowick, OH) with a 5-1 MHz 17mm broadband phased array transducer. A paediatric probe (Sonosite) was also used. Cases found positive by screening were given a more detailed focused echocardiographic study using the SonoSiteMicromaxx. Another expert in echocardiography (CMC) blindly reviewed the echo images independently to confirm or refute the diagnosis. Patients found positive were referred back to local clinics for follow-up and secondary prophylaxis. Research Ethics Board approval for the project was obtained from North York General Hospital (Figure 1).

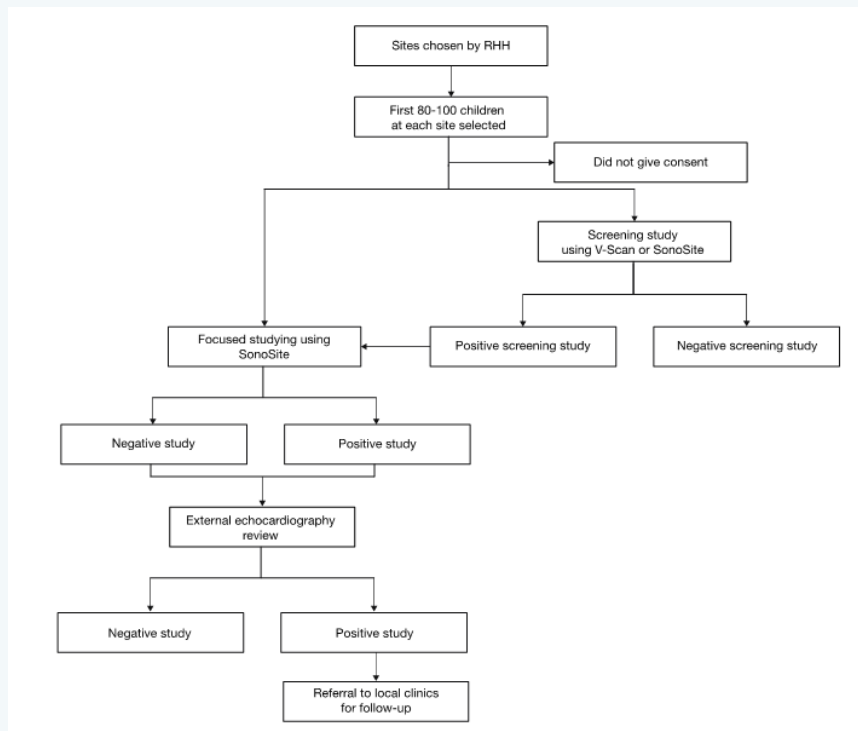


Figure 1: Methodology of Echocardiographic Screening for Rheumatic Heart Disease in Angola.

Statistical Analysis

The study had 73% power to detect a difference in prevalence among levels of access to healthcare at the 0.05 significance level. The data were analysed using contingency tables to compare the prevalence of rheumatic heart disease between areas of varying access to healthcare, and also by age and sex. A two-sided Fisher’s exact test was used due to small cell counts, and Holm’s method was used to control the family-wise error rate for pair wise comparisons.

Results

The study examined 574 children over 5 sites, which were grouped into the three previously discussed levels of access to healthcare. The mean age of the children was 10.14 years, and 56% of them were female. Echocardiographic screening detected evidence of rheumatic heart disease in 17 of the children, with

10 definite and 7 borderline according to the 2012 WHF criteria, resulting in an overall prevalence of 29.6 per thousand (95% confidence Interval, 17.3 – 47.0). Table 2 One 4-year old patient met the revised Jones Criteria for acute rheumatic fever and was referred to a local physician for treatment and follow-up (Figure 2 & Table 2).

The prevalence of rheumatic heart disease varied dramatically by access to healthcare ranging from 0.0 (95% CI, 0 – 36.2) per thousand in the area where healthcare was most readily available, to 70.9 (95% CI, 33.2 – 131.3) per thousand in the Level 3 areas (p=0.004) (Table 2). While controlling for the family-wise error rate, significant differences in the prevalence of rheumatic heart disease were detected between the highest level of healthcare access and the lowest level (p=0.015), and between highest level of healthcare access and the middle level (p=0.043) (Table 3).

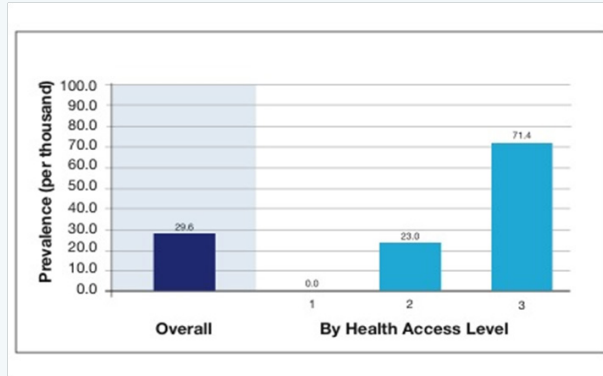


Figure 2: Prevalence of Rheumatic Heart Disease by Level of Healthcare Access.

Table 2: Characteristics of study population according to levels of healthcare access.

Measure	Access to Health Care			
	Low	Mid	High	Overall
N	100	348	126	574
Mean (\pm SD) Age	8.4 \pm 1.6	10.8 \pm 4.5	9.7 \pm 4.1	10.1 \pm 4.1
Median Age	9	10	8	10
% Male	36.00%	43.40%	52.80%	44.20%
# of cases	0	8	9	17

Table 3: Prevalence of RHD according to age.

Measure	Age Group		p-value
	<10 yrs	\geq 10 yrs	
N*	283	290	0.002
# of cases	2	15	
Prevalence	7.1 (8.6 - 25.3)	51.7 (29.2 - 83.4)	

Rheumatic heart disease was also more prevalent in older children, with the prevalence ranging from 7.1 per thousand among children less 10 years old, to 51.7 per thousand in children over 10 years and older ($p=0.002$) (Table 3). No significant difference was observed based on sex. A multivariate analysis undertaken with firth logistic regression suggests that the minor differences in age distributions between the accesses to healthcare groups did not significantly confound the healthcare access effect (Tables 4 & 5).

Table 4: Characteristics of study population according to gender.

Measure	Gender		p-value
	Male	Female	
N	253	320	0.32
# of cases	5	12	
Prevalence	19.8 (6.4 - 45.5)	37.5 (18.5 - 65.0)	

Table 5: P-value of data according to levels of healthcare access.

Access to Health Care Comparisons	p-value
Global	0.004
Low - Mid	0.208
Low - High	0.015
Mid - High	0.043

Morphology of valve lesions

The mitral valve was the most commonly affected valve (17/17 cases, 100%). Aortic valve involvement was found in only 3 cases (17.6%) and was always concomitant with mitral valve involvement. All cases with aortic valve involvement were patients older than 10 years of age.

Mitral stenosis was uncommon in early disease (3/7 cases), with mitral regurgitation being the most common functional abnormality (16/17 cases). The mitral regurgitation was mostly posteriorly directed, suggesting an anterior leaflet problem.

Table 6: Criteria for diagnosis of RHD.

Definite	A: Pathological MR and at least 2 morphological features of RHD of MV
(either of)	B: MS mean gradient \geq 4mm Hg
	C: Pathological MR and at least 2 morphological features of RHD of AV
	D: Borderline disease of both AV and MV
Borderline	A: At least 2 morphological features of RHD of MV without pathological MR or MS
(either of)	B: Pathological MR
	C: Pathological AR
Normal	Physiological MR (MR not meeting all 4 Doppler echocardiographic criteria)
	Physiological AR (AR not meeting all 4 Doppler echocardiographic criteria)
	Isolated morphological feature of RHD of MV without associated pathological stenosis or regurgitation
	Morphological feature of RHD of AV without associated pathological stenosis or regurgitation

Table 7: Morphological features of RHD.

MV Features	AMVL thickening \geq 3mm (age specific)
	Chordal thickening
	Restricted leaflet motion
	Excessive leaflet tip motion during systole
AV Features	Irregular or focal thickening
	Coaptation defect
	Restricted leaflet motion
	Prolapse

Table 8: Criteria for pathological regurgitation.

Pathological MR	Seen in two views
	In at least one view, jet length \geq 2 cm
	Velocity \geq 3m/s for one complete envelope
	Pan-systolic jet in at least one envelope
Pathological AR	Seen in two views
	In at least one view, jet length \geq 1 cm
	Velocity \geq 3m/s for one complete envelope
	Pan-diastolic jet in at least one envelope

Based on the 2012 WHF Criteria [22].

All definite cases had both WHF defined morphologic features of rheumatic mitral valve and pathologic MR. Three definite cases also met the WHF 2012 mitral stenosis criteria. The borderline cases were mainly qualified by presence of pathologic MR based on WHF criteria.

Discussion

We found the overall prevalence of RHD to be 29.6 per 1000 children aged 4-20 in our selected sites in Huila and Humpata provinces. This high prevalence is consistent with similar echocardiographic studies conducted in sub-Saharan Africa and other developing countries such as Cambodia, Fiji, India, Laos, Mozambique, New Caledonia, Nicaragua, Pakistan, Samoa, South Africa, Tonga, and Yemen [10].

By applying our findings to the urban/rural demographics

of Huila province, we can estimate that there are 28,600 cases of RHD in the province in children aged 4-20 (**Appendix**). Our confidence in this estimate however is limited by our method of site selection. The non-randomized nature of the selection raises concerns about the generalizability of the results. However it does give a snapshot of disease prevalence and its regional variation in the areas screened. There is a need for urgent action including bigger scale study and health policy change.

The association between RHD with environmental factors is well known, however there are few good-quality prevalence surveys of rheumatic heart disease in developing countries. Previous studies are also inconsistent in the timing and quality of their surveys making comparisons difficult. Known factors associated with RHD include overcrowding, urbanization, and poor early childhood nutrition. The best-studied factor is low

socio-economic status [14-19]. While it has been suggested that access to medical services and prophylaxis programs can also explain the difference in RHD between developed and developing countries, this factor has not been well studied [15,20].

Our study is unique in that it is the one of the first studies to examine the link between access to healthcare services and rheumatic heart disease. We were surprised by the high burden of disease in the site with the lowest access to healthcare. Cavango had by far the highest prevalence of RHD, and also had the highest level of definite disease. Not only the remote access site has the highest prevalence, it also has the most severe cases. Three cases of severe rheumatic disease, characterized by moderate to severe mitral regurgitation and severe pulmonary hypertension (RVSP 66-90mmHg) were identified in the study, and all of them were in Cavango. This kind of regional variation has important resource planning implication. The difficult to reach areas tend to be underserved. Our study suggests that areas with poor access to health facility can benefit the most from rheumatic disease screening and improved access to health services.

Most prevalence studies of RHD to date have either been based in clinics or schools. However, the usage of mobile echocardiography also allowed us to be the one of first studies we are aware of that did not screen schoolchildren in clinics, but rather gathered a broader sample of children by visiting communities directly. This avoids a potential bias in that school attendance is likely to be negatively associated with major risk factors of rheumatic heart disease [1]. The children with symptomatic disease are also less likely to be able to attend school.

Echocardiography has been proven to be more sensitive and specific than auscultation, identifying roughly ten times more cases with RHD [8,10]. Although echocardiography machines are costly, especially for low-income countries, the increased availability of handheld ultrasound machines has allowed RHD to be screened systematically at lower cost. Handheld echocardiography has shown to be highly sensitive (90.2%) and specific (92.9%) at distinguishing between normal and definite RHD patients. It is best used as a screening tool in early detection of RHD, with positive results to be confirmed by fully functioning echocardiography machines [16].

In our study we employed the 2012 World Heart Foundation guidelines for the diagnosis of RHD. Previous criteria include the 2005 joint WHO and National Institute of Health expert definitions, which were limited due to insufficient experience with echocardiographic findings in children and not considering the full morphological spectrum of RHD. Studies done prior to the WHF criteria employed different criteria to define disease morphology and function, often based on local experience with RHD. Hence, prevalence reporting has varied widely, making comparison difficult [10]. Our application of the WHF

guidelines allows us to report disease prevalence based on an internationally endorsed evidence-based echocardiographic diagnostic guideline for asymptomatic patients.

In contrast to mature disease which is usually characterized by mitral stenosis and/or multiple valve involvement, early rheumatic disease predominately showed single valve involvement, and mainly mitral regurgitation. Interestingly the MR jet is mainly posterior directed suggesting anterior leaflet lesion. Another interesting observation was that mitral valve is affected much more commonly and earlier than aortic valve. This is consistent with a recent study [6]. The reason for mitral more than aortic valve involvement is partly secondary to different hemodynamic stress on the valves. Current research also links genetic predisposition and immunologic factors in pathogenesis of valvular damage [22].

Conclusion

While our study suffered from limitations of non-randomized site selection and small sample sizes, this is the first study that has attempted to assess the prevalence of RHD in Angola. The disease started at early age, and has high regional variation. Our results have important implications for forming national and regional control strategies to reduce the burden of disease. Bigger scale study involving randomized sites and broader regions to attain better estimates of the prevalence of RHD in Angola, with particular emphasis on prospective cohort studies to chart the progression of disease for children with subclinical disease. Such children will receive the highest benefit from early detection and subsequent secondary prophylaxis. On a public health scale, the impact of RHD on disability and mortality and health economics can also be studied. Above all, urgent action including public health interventions are needed to reduce the burden of disease [16,21].

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