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Prevalence of Rheumatic Heart Disease in North Madagascar: An echocardiographic screening in young and adult populations

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RESEARCH

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ABSTRACT

Background
Rheumatic Heart Disease (RHD) prevalence in Madagascar is poorly known. Echocardiographic screening detects a higher prevalence of RHD than clinical examination.

Aims
We aimed to describe RHD prevalence in children and adults in North Madagascar using the most updated World Heart Federation (WHF) criteria for RHD echocardiographic diagnosis.

Methods
Children aged 5–19 years (Group One) and adults aged more than 20 years (Group Two) underwent a four-steps visit: clinical questionnaire, physical examination, laboratory test - oropharyngeal swab for Group One and Anti-streptolysin O (ASO) titre for Group Two - and echocardiogram using a portable machine..

Results
Among 859 people (522 in Group One, 337 in Group Two) RHD prevalence was 2.1 per cent. Group Two had a higher risk of having RHD than Group One (OR 4.39, CI 1.39–13.9, p=0.004), while clinical findings were more frequent in Group One (children had a higher risk of heart murmur (O.R. 3.85 C.I. 1.08–13.72; p=0.029)). RHD prevalence was 1.34 per cent in children. Those positive to oropharyngeal swab had a higher risk of RHD (OR 14.5, CI 3.04–69.44, p=0.0024); children with history of fever and sore-throat had a higher risk of positive oropharyngeal swab (OR 15.97, CI 3.14–81.19, p=0.002). RHD prevalence was 3.3 per cent in adults. None of those had history of fever and throat-pain, positive ASO titre and cardiac murmur simultaneously.

Conclusion
This is the first study describing prevalence of RHD in Madagascar. Our results, although preliminary, are important to enhance prevention programs in this country.

Key Words
Rheumatic heart disease, echocardiography, heart valves, Sub-Saharan Africa

What this study adds:

1. What is known about this subject?
Poor is known about Rheumatic Heart Disease (RHD) in Madagascar. The advent of Echocardiography as a screening tool has increased RHD prevalence in developing countries.

2. What new information is offered in this study?
This echocardiographic screening based on the most updated World Heart Federation (WHF) criteria provides preliminary data about RHD prevalence in Madagascar.

3. What are the implications for research, policy, or practice?
Our results are important for future prevention programs in Madagascar in view of cutting the considerable expenses to the health system and reducing the impacts on quality of life and fertility of RHD.

Background

Rheumatic Heart Disease (RHD) is one of the major causes of morbidity and mortality worldwide. More than 15 million people are affected,[1] including a large number of patients who are disabled and an estimated 233,000 deaths each year.[2] This is especially evident in developing countries, where RHD is endemic in regions of Africa, Pacific Islands, Asia and South America that are poor and overcrowded, and where sanitation is underdeveloped.[3] Historically, sub-Saharan Africa has had the highest prevalence of clinically detected RHD, ranging from less than 1–14 per 1,000.[4] In Mozambique, an incidence of 3 per cent has been reported,[5] whereas in Uganda is 1.5 per cent.[4]

Madagascar, off the South-eastern coast of Africa, is the fourth largest island in the world, has 22 million inhabitants, and represents a melting-pot of ethnicities, plus socioeconomic, cultural and hygienic-sanitary substrates that are known to influence risk factors, susceptibility and progression of RHD. However, we know little about RHD in Madagascar, about how significant its impact is on the population, and therefore about the usefulness of screening and prevention programs.

The reported number of RHD cases strongly depends on the screening method.[6] For example, the advent of echocardiography has greatly enhanced the numbers associated with RHD prevalence, because it is able to detect subclinical cases which are missed during clinical screenings.[6] However, the criteria used for echocardiographic screening vary according with different local experiences. In 2012, the World Heart Federation (WHF) has published new evidence-based guidelines of echocardiographic criteria for the diagnosis of RHD, in order to make the identifications and classification of RHD uniform worldwide:[6] according to these guidelines, young individuals and adults must be considered as distinct populations, as the disease itself has different features in these age groups.

To our knowledge, population-based echocardiographic screening for RHD has not been previously performed in Madagascar. For the first time, we aimed to describe the prevalence of RHD in the children and adults of North Madagascar, screened using the updated WHF echocardiographic criteria.

Methods

This observational study was performed in 6 non-consecutive weeks spread in the months of October 2013, May 2014 and October 2015. The 3 recruitment sites in region of Antsiranana, North Madagascar were: “Clinique Médico-Surgicale St. Damien” and the Catholic schools “SE.VE.MA” in Ambanja, the "St. Anthony High-School" in the village of Bemaneviky, and the "Don Bosco University" of Antsohihy.

Study design as follows: based on the most recent updated WHF guidelines, and to be consistent with their RHD classification, our population was divided into two groups: “children” aged from 5–19 years and “adults” older than 20 years. In primary and following higher school, children aged 5–19 years (Group One) were randomly recruited from one class for each school level. Individuals older than 20 years (Group Two) were consecutively enrolled from people who accessed the “Clinique St. Damien” (staff members, volunteers, outpatients without major cardiac diseases) or attended other schools or religious institutions. Epidemiological data were recorded for each individual into our database, in order to allow tracing and follow-up. Each patient underwent four steps during the visit: (i) questionnaire about their history of tonsillitis, other clinical signs of Group A Streptococcus (GAS) infection or Acute Rheumatic Fever (ARF) and their housing conditions; (ii) their measurements (weight and height, with body mass index (BMI) calculation, blood pressure, heart rate) and cardiac auscultation were registered; (iii) an echocardiogram, focused on the study of the four valves and to exclude major cardiac congenital abnormalities (e.g.,

atrial and ventricular septal defects); (iv) past exposure to GAS infection was also recorded: since taking a blood sample from children would have required bigger efforts, longer time and specialized operators, Group One underwent an oropharyngeal swab, processed via a rapid GAS antigen detection kit (ImmunoCard Stat! Strep A, Meridian Bioscience, Inc., Cincinnati. OH, sensitivity 96 per cent, specificity 97.8 per cent) which gave qualitative results in about 15 minutes, whereas Group Two underwent a blood test to determine the Anti-streptolysin O (ASO) titre; serum samples were collected, stored at 4°C and analysed by ELISA at our laboratory at "Policlinico Campus-Bio Medico" in Rome. ASO titre was defined as positive or negative when above or below the upper limit of 200 IU/mL respectively, according to the producer instructions.

Echocardiograms were performed using a portable ultrasound machine Esoaote MyLab 25 (Esaote, Genova, Italy) and an 8-3MHz phased array transducer, as appropriate. Each echocardiogram was focused on the study of the four valves in the parasternal long and short axis, apical four and two chambers and apical long-axis views. The 2-D mode was used for morphologic evaluation, colour-flow and Doppler signal, to detect functional valve defects (either regurgitation or stenosis). Individuals with major cardiac congenital abnormalities - including interatrial or interventricular septal defects, valves, and myocardium anomalies - were excluded from the study. All echoes were performed and reviewed online by one of four visiting cardiologists. Exams were stored on appropriate portable supports for review.

Auscultation was performed by a cardiologist, using a standard approach. Murmurs, if present, were categorized as "systolic" or "diastolic" and their intensity graded from 1 to 6 based on the Levine scale. The clinical questionnaire was administered by a cardiologist, with the aid of a local interpreter; teachers helped the younger children understand and answer questions.

Consent was obtained verbally at the time of enrolment from adults and by the school authority or from family/guardians prior the day of the visit for children.

Given the natural history of the RHD across decades of life, WHF guidelines recommend that "definite" RHD cases be distinguished from "borderline" in people less than 20 years old, while for adults who are >20 years old only the "definite" category exists (Table 1). RHD "definite" cases were defined as the presence of either pathological MR and at least two morphological features of RHD of the Mitral Valve (MV), or Mitral Stenosis (MS) with mean gradient ≥4 mmHg, or pathological Aortic Regurgitation (AR) and at least two morphological features of RHD of the Aortic Valve (AV), only in individuals aged less than 35 years or borderline disease of both the AV and MV for individuals younger than 20 years, or pathological AR and at least two morphological features of RHD of the MV – see Table 1. We considered as "definite" cases those patients who had undergone previous valve replacement for documented RHD. "Borderline" cases were defined as either at least two morphological features of RHD of the MV without pathological MR or MS, or pathological MR or pathological AR – see Table 1. They were recorder and listed for future echocardiographic follow-up. All RHD cases were prescribed penicillin prophylaxis once every 4 weeks, according with the availability of local health systems and medications, to rural or urban provenience and individual or family compliance.

Clinical findings suggestive of past GAS infection and/or sequela were considered: fever associated with sore-throat, heart murmur, positive swab for Group One or ASO titre for Group Two.

We considered overcrowding, defined as more than one person per room living in the house,[7] as an indicator of the socio-economic state of the population.

Odds ratios (OR) and their 95 per cent confidence intervals (95 per cent CI) were calculated to evaluate the association between echocardiographic diagnosis subtypes of RHD and signs of past GAS infections or clinical history of RHD at the univariate level. Chi-square and Fisher's exact test were used to confirm the statistical significance. All p-values <0.05 were considered statistically significant. The statistical analysis was conducted using Epi Info version 7.2. (Division of Health Informatics & Surveillance (DHIS), Center for Surveillance, Epidemiology & Laboratory Services (CSELS).

Results

Overall analysis

We screened 859 people (522 children, Group One, and 337 adults, Group Two). The demographic and clinical features of the population divided by the two study groups are showed in Table 2. No major congenital heart diseases were found: only two asymptomatic patients had bicuspid aortic valve and one was operated for pulmonary stenosis few years earlier.

According with the WHF echocardiographic RHD criteria, overall prevalence in our population was 2.1 per cent (18/859). Fifteen (83 per cent) cases had definite RHD, 3

were borderline (17 per cent). RHD valvular involvement in both adults and children groups is shown in Table 3.

Group two had a 4-fold higher risk of being diagnosed of RHD by echocardiography than Group One (OR 4.39, CI 1.39–13.9, p=0.004). Clinical findings were more frequent in Group One than Group Two (5.9 per cent *vs.* 4.5 per cent), although without statistical significance (p=NS).

Prophylaxis with benzathine penicillin was prescribed to all RHD cases based on adequate cardiological assessment by means of echocardiogram interpretation.

Analysis by groups

Group one: among the young population, RHD prevalence was 1.34 per cent (7/522) and three cases (43 per cent) were borderline. Table 3 shows the detail of valvular involvement. Among the seven cases, five (71 per cent) showed the contemporary presence of clinical murmur and history of fever and sore throat. Children with positive oropharyngeal swab had 14-fold higher risk of having RHD than those without (OR 14.5, CI 3.04–69.44, p=0.0024, data available for 386 children). Children with history of fever and sore-throat had 16-fold risk of being positive to oropharyngeal swab than those without (OR 15.97, CI 3.14–81.19, p=0.002, data available for 386 children). No correlation was found between RHD diagnosis and overcrowding (6/384 (1.6 per cent) RHD cases in overcrowded group *vs.* 1/116 (0.9 per cent) RHD cases in the non-overcrowded group, p=NS, data available for 500 children), although children living in an overcrowded environment had the highest probability of joint pain and fever associated with sore-throat (OR 14.6, CI 2.8–76.8, p=0.0006 and OR 9.5, CI 1.1–79.9, p=0.008, respectively).

Group two: among adults, eleven RHD cases were found, resulting in a prevalence of 3.3 per cent (11/337) - see Table 3 for details. None was positive at the same time for history of fever associated with throat-pain, cardiac murmur and ASO titre (available for 120 people). Among RHD cases 4 (4/11, 36 per cent) had heart murmur, 1 (1/11, 9 per cent) had fever and sore-throat, and none was positive to ASO titre. They had a higher risk of having a heart murmur than non-RHD cases (O.R. 3.85 C.I. 1.08–13.72; p=0.029). There was non-significant correlation between RHD and overcrowding (7/217 (3.2 per cent) RHD cases in overcrowded group *vs.* 2/66 (3.0 per cent) RHD cases in non-overcrowded group, p=NS, data available for 283 people).

Discussion

To the best of our knowledge, this is the first study describing the prevalence of RHD in Madagascar through an echocardiographic screening based on the most recent WHF criteria. Although our numbers are lower than those of previous reports, RHD prevalence found in our study is comparable to that in other Sub-Saharan countries[2] and appears to be higher than that in Pacific Ocean populations.[8] Interpretation of the global burden, however, is complicated by the enormous heterogeneity of studies in terms of screening methodology, age groups, provenience, risk category.[9] It is worth noticing that there can be difference of prevalence among states, districts, ethnicities or regions of the same country. This could be also the case of Madagascar, a mixture of ethnical groups carrying their own habits and predisposition to infectious diseases such as ARF and RHD. Our results should be considered as strictly related to the Northern population of the West side of the Island. Further studies in other regions should be conducted in order to describe RHD prevalence across the entire country.

Our study shows that RHD prevalence in children is relatively low (1.34 per cent) compared to previous studies.[10,11] This is likely since our young population has a wider age range, as it includes children from 5–19 years old. Although we did not conduct a further stratification of data due to the small sample, it is assumable that RHD prevalence progressively increases along years of age also in this group, as it has been suggested by Kane et al.[11]

Accordingly with previous evidences[5,12] we found a higher prevalence of mitral than aortic disease in both adults and children. We also found a higher number of mitral than aortic lesions which did not meet the criteria for RHD diagnosis. Although RHD valvular lesions generally need one or two decades to develop, a spectrum of findings can be identified even in the young population. WHF standardized criteria[6] have shown to have more power in detecting incipient RHD cases compared to the previously used WHO criteria.[8] Therefore we chose these criteria to discriminate RHD lesions from others. Moreover, WHF criteria have been the used in the second edition of the Australian guidelines for prevention, diagnosis and management of ARF and RHD.[13] Australia is a country where indigenous and non-indigenous populations are present together and RHD prevalence is significantly different among them. Similarly, we considered WHF criteria the most appropriate in a heterogeneous context as that in Madagascar and we promote their use in further studies.

Several studies stated that auscultation is poorly sensitive and specific, and that echocardiography is the best method for RHD screening.[1,8,10] In fact, in asymptomatic school pupils from South Africa and Ethiopia, the prevalence of RHD defined by echocardiography was of 20–30 per 1000,[14] while previous estimates in South Africa based on clinical auscultation reported a number of 6.9 per 1000.[15] Establishing how many people did or did not have ARF in the past would have been difficult because of several limitations, such as language barriers or lack of facilities (e.g., electrocardiographer). Thus, we searched only for clinical findings suggestive of past GAS infection. Overall, we found that more children than adults had clinical suggestive findings, while echocardiographic RHD diagnosis was more frequent in adults than in children. Our results are comparable to other evidences showing that adults have more frequently echocardiographic lesions than children.[11,16,17] Among children with RHD we found 71 per cent of them having pathological heart murmurs and history of fever associated with sore-throat. Similarly, children with RHD and those with history of fever associated with sore-throat had a significantly higher risk of positivity to GAS oropharyngeal swab than those without. On the contrary, only 36 per cent of RHD adults had pathological heart murmur, 9 per cent had history of fever and none was positive to ASO titre. Consistently, adults with RHD had a higher risk of having heart murmur (i.e., sign of the established RHD lesion) than non-RHD adults but positivity to ASO titre was already masked (non-significant correlation between RHD and ASO titre). To explain this, we postulated that acute infection and its sequela (i.e., ARF) are more recent in children than in adults, although it has not developed echocardiographic lesions yet. Clinical findings identify people at high risk of GAS infection and subsequent cardiac involvement. We suggest that, in the view of optimizing efforts of humanitarian expeditions in the setting of poor resources and in countries where portable ultrasound machines are not always available locally, two different screening strategies should be planned for the young and adult population. Since adults have low signs of past GAS infection and auscultation is poorly sensitive, especially when performed by non-cardiologist, they should undergo echocardiographic screening as first line. Oppositely, children could take a "two-step model" screening: a first clinical screening, via history taking and oropharyngeal swab, then those found to be positive at this first step should be selected for a specialist medical contact with echocardiography. This strategy could rationalize efforts and resources and speed up the work of medical groups travelling from the Western World, often confined in limited time frames. However, it is worth underlying that clinical history taking, as we experienced, is extremely challenging with children, especially if they only speak the local idiom, and translation by local interpreters could often be misleading if they are not previously educated about the disease. Ideally, we suggest that the first step of clinical screening for children should be performed by local professionals or operators, such as teachers, tutors, assistants or religious figures in schools after an intense "in loco" educational program and training about RHD. This would increase awareness of the local community, essential for school health services development, and especially helpful for chronic conditions (e.g., RHD) prevention, as it has been advocated by numerous voices.[18] However, further studies are needed to test our strategy.

Using overcrowding as indicator of socio-economic conditions in both adult and children, although there was a significantly higher risk of joint pain and fever associated with sore-throat, we found RHD to be more frequent in overcrowded zones but without statistically significant difference. Although the small sample size should be considered, this may find its explanation in the lack of a net difference in population strati in Madagascar. In fact in developing countries differences between socio-economic groups cannot be detected because the threshold level where higher socio-economic status is associated with reduced prevalence of RHD is not always reached.[19] Moreover, children selected among school attendants come from families with more homogeneous level of education and economic status.

Study Limitations

The first limit of this study is the small sample size, as it is not representative of the entire population of the Island. The small size bias has been compensated by extending the number of sites of screening. The variety of ethnicity in Madagascar is not fully represented in this study as we mainly screened people of the Sakalava ethnicity, the majority in North territories. Thus, our numbers could change by extending the geographical area of investigation. The age variety can represent a limit to the homogeneity of the survey while it also gives a wider view on the population. Our selection of school children, is another limit. There is a well-known gap between school enrolment and the rest of population, as demonstrated by a drop in school participation among boys after the age of 10 years at the South Africa site.[20] Another important limit is the language barrier. The vast majority of individuals only spoke local idioms. Although interpreters have been helpful, they were not medical operators and had poor knowledge of the disease. Thus we found difficulties in translating medical

terms or specific questions into the local idiom. This may result in lack of accuracy for some answers (i.e., symptoms of arthritis, cutaneous manifestations, etc.).

Conclusion

This is the first study describing prevalence of RHD in Madagascar based on the most recent WHF criteria for echocardiographic diagnosis. Since RHD results in a considerable expense to the health system and impacts on career choices, quality of life, and fertility, a prevention program in this country is strongly desirable. Our results create the necessary, although preliminary, knowledge about the dimension of RHD in Madagascar.

References

1. Carapetis JR, McDonald M, Wilson NJ. Acute rheumatic fever. Lancet. 2005;366(9480):155-168.
2. Carapetis JR, Steer AC, Mulholland EK, et al. The global burden of group A streptococcal diseases. Lancet Infect Dis. 2005;5(11):685-694.
3. Marijon E, Mirabel M, Celermajer DS, et al. Rheumatic heart disease. Lancet. 2012;379(9819):953-964.
4. Beaton A, Okello E, Lwabi P, et al. Echocardiography screening for rheumatic heart disease in ugandan schoolchildren. Circulation. 2012;125(25):3127-3132.
5. Marijon E, Ou P, Celermajer DS, et al. Prevalence of rheumatic heart disease detected by echocardiographic screening. N Engl J Med. 2007;357(5):470-476.
6. Remenyi B, Wilson N, Steer A, et al. World Heart Federation criteria for echocardiographic diagnosis of rheumatic heart disease--an evidence-based guideline. Nat Rev Cardiol. 2012;9(5):297-309.
7. U.S. Department of Housing and Urban Development, “Measuring overcrowding in housing,” Off. Policy Dev. Res., p. 38, 2007.
8. Colquhoun SM, Kado JH, Remenyi B, et al. Echocardiographic screening in a resource poor setting: Borderline rheumatic heart disease could be a normal variant. Int J Cardiol. 2014;173(2)284-289.
9. Zühlke LJ, Steer AC. Estimates of the Global Burden of Rheumatic Heart Disease. Glob Heart. 2013;8(3):189-195.
10. Webb RH, Wilson NJ, Lennon DR, et al. Optimising echocardiographic screening for rheumatic heart disease in New Zealand: not all valve disease is rheumatic. Cardiol Young. 2011;21(4):436-443.
11. Kane A, Mirabel M, Touré K, et al. Echocardiographic screening for rheumatic heart disease: Age matters. Int J Cardiol. 2013;168(2):888-891.
12. Kingué S, Ba SA, Balde D, et al. The VALVAFRIC study: A registry of rheumatic heart disease in Western and Central Africa. Arch Cardiovasc Dis. 2012;109(5):321-329.
13. Carapetis J, Brown A, Maguire G, et al. The Australian guideline for prevention, diagnosis and management of acute rheumatic fever and rheumatic heart disease. RHD Australia, National Heart Foundation of Australia and the Cardiac Society of Australia and New Zealand. 2012.
14. Engel ME, Haileamlak A, Zuhlke L, et al. Prevalence of rheumatic heart disease in 4720 asymptomatic scholars from South Africa and Ethiopia. Heart. 2015;1-6.
15. McLaren MJ, Hawkins DM, Koornhof HJ, et al. Epidemiology of rheumatic heart disease in black school children of Soweto, Johannesburg. Br Med J. 1975;3(5981):474-478.
16. Sliwa K, Carrington M, Mayosi BM, et al. Incidence and characteristics of newly diagnosed rheumatic heart disease in Urban African adults: Insights from the Heart of Soweto Study. Eur Heart J. 2010;31(6)719-727.
17. Parnaby MG, Carapetis JR. Rheumatic fever in Indigenous Australian children. J Paediatr Child Health. 2010;46(9)527-533.
18. Robertson KA, Volmink JA, Mayosi BM. Towards a uniform plan for the control of rheumatic fever and rheumatic heart disease in Africa – the Awareness. S Afr Med J. 2006;96(3):241-245.
19. Steer AC, Carapetis JR, Nolan TM, et al. Systematic review of rheumatic heart disease prevalence in children in developing countries: the role of environmental factors. J Paediatr Child Health. 2002;38(3):229-34.
20. Gustafsson M. The gap between school enrolments and population in South Africa. Stellenbosch: Stellenbosch University Bureau for Economic Research. 2012 Dec.

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PEER REVIEW

Not commissioned. Externally peer reviewed.

CONFLICTS OF INTEREST

The authors declare that they have no competing interests.

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ETHICS COMMITTEE APPROVAL

Ethics approval was not required.

Table 1: Echocardiographic criteria for the diagnosis of RHD, pathological regurgitation and morphological features of RHD (adapted from WHF; Reményi et al. Nat Rev Cardiol. 2012;9:297–309)

Individuals aged ≤20 years	Individuals aged >20 years
Definite RHD (either A, B, C, or D):	**Definite RHD (either A, B, C, or D):**
A) Pathological MR and at least two morphological features of RHD of the MV B) MS mean gradient ≥4mmHg* C) Pathological AR and at least two morphological features of RHD of the AV‡ D) Borderline disease of both the AV and MV§	A) Pathological MR and at least two morphological features of RHD of the MV B) MS mean gradient ≥4mmHg* C) Pathological AR and at least two morphological features of RHD of the AV, only in individuals aged <35 years‡ D) Pathological AR and at least two morphological features of RHD of the MV
Borderline RHD (either A, B, or C):	
A) At least two morphological features of RHD of the MV without pathological MR or MS B) Pathological MR C) Pathological AR	
Pathological Regurgitation	**Morphological features**
Mitral Valve	**Mitral Valve**
(All four Doppler echocardiographic criteria must be met) Seen in two views; In at least one view, jet length ≥2cm**; Velocity ≥3m/s for one complete envelope; Pan-systolic jet in at least one envelope.	AMVL thickening## ≥3mm (age-specific)‡‡; Chordal thickening; Restricted leaflet motion§§; Excessive leaflet tip motion during systole||||.
Aortic Valve	**Aortic Valve**
(All four Doppler echocardiographic criteria must be met) Seen in two views; In at least one view, jet length ≥1cm**; Velocity ≥3m/s in early diastole; Pan-diastolic jet in at least one envelope.	Irregular or focal thickening¶¶; Coaptation defect; Restricted leaflet motion; Prolapse.

*Congenital MV anomalies must be excluded. Furthermore, inflow obstruction due to non-rheumatic mitral annular calcification must be excluded in adults.

‡Bicuspid AV, dilated aortic root, and hypertension must be excluded.

§Combined AR and MR in high prevalence regions and in the absence of congenital heart disease is regarded as rheumatic.

Abbreviations: AR = aortic regurgitation; AV = aortic valve; MR = mitral regurgitation; MS = mitral stenosis; MV = mitral valve; RHD = rheumatic heart disease; WHF = World Heart Federation.

**A regurgitant jet length should be measured from the vena contracta to the last pixel of regurgitant color (blue or red).

##AMVL thickness should be measured during diastole at full excursion. Measurement should be taken at the thickest portion of the leaflet, including focal thickening, beading, and nodularity. Measurement should be performed on a frame with maximal separation of chordae from the leaflet tissue. Valve thickness can only be assessed if the images were acquired at optimal gain settings without harmonics and with a frequency ≥2.0MHz.

‡‡Abnormal thickening of the AMVL is age-specific and defined as follows: ≥3mm for individuals aged ≤20 years; ≥4mm for individuals aged 21–40 years; ≥5mm for individuals aged >40 years. Valve thickness measurements obtained using harmonic imaging should be cautiously interpreted and a thickness up to 4mm should be considered normal in those aged ≤20 years.
§§Restricted leaflet motion of either the anterior or the posterior MV leaflet is usually the result of chordal shortening or fusion, commissural fusion, or leaflet thickening.
||||Excessive leaflet tip motion is the result of elongation of the primary chords, and is defined as displacement of the tip or edge of an involved leaflet towards the left atrium resulting in abnormal coaptation and regurgitation. Excessive leaflet tip motion does not need to meet the standard echocardiographic definition of MV prolapse disease, as that refers to a different disease process. This feature applies to only those aged <35 years. In the presence of a flail MV leaflet in the young (≤20 years), this single morphological feature is sufficient to meet the morphological criteria for RHD (that is, where the criteria state "at least two morphological features of RHD of the MV" a flail leaflet in a person aged ≤20 years is sufficient).
¶¶In the parasternal short axis view, the right and non-coronary aortic cusp closure line often appears echogenic (thickened) in healthy individuals and this should be considered as normal.
Abbreviations: AMVL = anterior mitral valve leaflet; AV = aortic valve; MV = mitral valve; RHD = rheumatic heart disease; WHF = World Heart Federation.

Table 2: Baseline characteristics of study population

	Children	**Adults**	**Total**
n	**522**	**337**	**859**
Female sex, n (%)	300 (57.4)	201 (59.6)	501 (58.3)
Age, years (min-max)	10±4.2 (4-19)	35.6±12.4 (20-75)	20.1±15.1
Height, cm	130.5±20.1	167±22.2	151.2±21.2
Weight, kg	29.7±12.2	65±15.6	48.2±13.8
BMI, kg/m^2	16.7±3.8	23±4.5	19.1±5
BSA, m^2	1±0.3	1.6±0.2	1.2±0.4
SBP, mmHg	109.8±12.1	123.2±17.2	114.4±16.2
DBP, mmHg	67.8±9.6	76.2±12	71±11.3
HR, bpm	98.1±17.5	78.9±13.1	90.4±18.4

Values are expressed as number with percentages. Continuous variables are expressed as mean ± standard deviation.
Abbreviations: BMI = body mass index; BSA = body surface area; DBP = diastolic blood pressure; HR= heart rate; SBP = systolic blood pressure.

Table 3: RHD valvular involvement in our population divided by groups

	Aortic	**Mitral**	**Aortic + Mitral**	**Total**
Children, Group One, n (%): 522	0 (0%)	6 (85.7%) (3 borderline cases)	1 (14.3%)	7 (1.3%)
Adults, Group Two, n (%): 337	3 (27.3%)	6 (54.5%)	2 (18.2%) (both valves replacement)	11 (3.3%)
Total n (%): 859	3 (16.7%)	12 (66.6%)	3 (16.7%)	18 (2.1%)