Rheumatic Heart Disease: The Tip of the Iceberg

Running title: Sliwa et al.; RHD-tip of iceberg

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Journal Subject Codes: [19] Valvular heart disease; [100] Health policy and outcome research

Key words: Editorials; race/ethnicity; rheumatic heart disease; valve replacement; valvular regurgitation; Africa
Rheumatic heart disease (RHD) remains one of the largest preventable burdens of disease in the world. It is perceived as a disease of childhood as it is acquired by streptococcal throat infection of the tonsillo-pharynx, leading to an inflammatory reaction that involves many organs, including the heart. However, cases in children of 5-14 years are likely to represent only 15-20% of all cases within all age groups of vulnerable populations.1

As a disease of poverty and low socio-economic circumstances, RHD is prevalent in the developing world. This association with the poorest and weakest of society represents a double tragedy: while the lack of access to education, infrastructure and medical facilities turns a preventable and surgically treatable condition into a major cause of suffering, incapacity and death, global awareness remains depressingly low.

Although RHD has received increasing attention in the past few years, leading to declarations,2 definition of areas of research3 and new diagnostic criteria on echocardiography, as well as suggestions for prevention programs insight into incidences, disease progression and mortality remains largely speculative due to a lack of data.

With the adoption of echocardiography to project-funded screening programs, it emerged that previous estimates may have distinctly under-estimated the prevalence of the disease.4 As screening programs generally focus on school children, they concentrate on the most accessible and reliable cohort for the assessment of disease-incidence. Yet, echo-based incidences of RHD in school children are age-dependent,5 as a 71% increase in children younger than 9 years, to those older than 12 years,4 was shown. Although the ten times higher sensitivity of echo-screening over clinical assessment4 detects in 90% of cases clinically silent RHD, almost half of these valve lesions are already functionally moderate to severe.6 Therefore, together with the effectiveness of secondary penicillin prophylaxis, the case for echo screening programs is strong.
However, as important as school-screening programs are for secondary prophylaxis, they address only the tip of the iceberg, in view of the disease progression in the undiagnosed post-school-age population groups. In contrast to the assessment of early disease incidence in school children, data on disease progression rely on the screening of adult population cohorts, years after manifestation of the disease. Historical knowledge largely comes from the developed world, prior to disease eradication, when the natural history of RHD was already mitigated by high socio-economic standards. In developing countries, pregnancy screenings provide some insight\textsuperscript{6} but require a more advanced level of socio-economic development of a society than the screening of school children. One of the few follow-up studies to date reports a 16\% progression rate from acute rheumatic fever (RF) to severe, clinically relevant chronic valve lesions within less than 15 years in Brazil.\textsuperscript{7} Given an estimated 60\% progression rate from RF to RHD,\textsuperscript{8} the actual progression rate of echocardiographically diagnosed cases would therefore be closer to 25\%. The proportion of these patients that eventually die remains the biggest unknown in the natural history of RHD. Sporadic reports from countries like Ethiopia suggest that 70\% of patients die before they are 26 years old.\textsuperscript{9} Previous global estimates of 500,000 deaths/year\textsuperscript{5} have been recently increased to 1.4 million/year.\textsuperscript{10} Apart from prophylactic prevention, the vast majority of these deaths might be preventable through surgical valve repairs or replacements.

Thus, as the political will for funding and implementation of both prophylaxis programs and the roll-out of cardiac surgery will depend on better insight into the impact of RHD on population health, productivity and premature mortality, the next big challenge in the combat of RHD will be better insight into the natural history of the disease.\textsuperscript{11} Yet, early detection by using the newest screening guidelines (2006 NIH/WHO) does represent a crucial first step.

The study by Beaton et al,\textsuperscript{12} performed in Kampala, Uganda, addresses the limited data
from Sub-Saharan Africa on echocardiography in children. Auscultation and portable echocardiography was used to screen 4869 randomly selected schoolchildren, aged 5-16 years. The strengths of the study are the large sample size, the carefully planned prospective design and the systematic application of criteria for diagnosis. The study design is interesting and novel in that it provided simple pre-screening and, if any abnormality was detected, very detailed assessment by a cardiologist at Mulago Hospital, Kampala. Through this novel approach the researchers were able to screen 200-250 children with one sonographer, in one day, while two other staff members served as organizers and data tabulators. Each school-based screening took approximately two minutes to complete. Echocardiography detected 3 times as many cases of RHD than auscultation. Lower socioeconomic groups had significantly more RHD, with also more advanced disease presentation. The burden of disease in that cohort was 15 cases per 1000. The authors interestingly expanded their calculation to the Ugandan population of an estimated 18 million children in the age group 5-16 years. By this calculation, 266,400 cases would be detected, while only 88,200 would be detected by clinical examination. Their data suggest that screening efforts targeting 10-year-old children in lower socioeconomic cohorts may maximize sub-clinical detection.

Their data are different to another study using echocardiography based screening in sub-Saharan Africa. The study performed by Marijon et al\(^4\) in 2170 otherwise healthy school children in Mozambique, between 2001-2002, found a substantially higher burden of disease (30.4 cases per 1000), corresponding with 33/1000 in Tonga,\(^13\) 24/1000 in New Zealand’s Maoris\(^14\) and 51/1000 in India.\(^12\) Apart from including children as young as 5 years and, as such, encountering an expectably lower incidence, the difference might also be explained by difference in region, socioeconomic circumstances or echocardiographic criteria used.
The authors critically discuss various levels of screening by echocardiography via careful clinical assessment and comment on the use of various guidelines, including the new criteria from the World Heart Federation, published February 2012.15 The study supports the inclusion of portable echocardiography in screening protocols, even in resource- and medical staff-constrained settings.

A recent study from the Heart of Soweto cohort, reporting on the incidence and clinical characteristics of newly diagnosed rheumatic heart disease in adulthood from an urban African community, found an estimated incidence of new cases of RHD for those aged > 14 years to be in the region of 23.5 cases/100 000 per annum.6 Many of those patients presented late, with an echocardiographic ejection fraction of less than 45% in 17% of the cases and an elevated right-sided pressure in 18% of the cases. Therefore 22% of this cohort of 344 cases had valve replacement or repair within one year, with a further 26% being admitted for initial diagnosis of suspected bacterial endocarditis within 30 months.

A further burden of late diagnosis of RHD is the fact that women often only present with symptomatic RHD when pregnant. A 4-year audit of cardiac disease in pregnancy in a South African hospital found an etiology of 63.5% of RHD and 20.1% of prosthetic VHD, probably of RHD origin, which contributes to the unacceptably high maternal mortality in South Africa.16 While a predominant lesion in RHD patients presenting in pregnancy is mitral stenosis which is amenable to balloon- or surgically-closed mitral valvotomy, 60%17 to 84%9 of cases presenting outside of pregnancy involve mitral regurgitation and 1517 to 4018 aortic regurgitation, eventually making open heart surgery inevitable.

Even extrapolating the authors’ relatively low incidence of 15/1000 to an African population of one billion would result in 15 million RHD patients with almost 400,000 new cases
per year of which 100,000/year may need heart valve surgery at some stage in their lives. Taking the higher incidences reported from Mozambique, this number would be as high as 200,000/year. At present, only South Africa, Egypt, Sudan, Kenya and, most recently, Namibia have established independent cardiac surgical programs that do not rely on sporadic ‘fly-in’ missions. Yet, even there, a majority of hospitals cater for the few private patients, while the largely indigent RHD patients rely on a small number of public hospitals. Therefore, the already dismal access to 18 open heart surgeries/million population as opposed to 1222/million in the USA19 is in reality distinctly lower. In South Africa – which boast two-thirds of all hospitals that provide cardiac surgery on the African continent - only 15% of these cater to the indigent patients with RHD. Thus, over 50 million patients compete for limited access to 7 public centres in the one African country that has the best established cardiac surgical facilities. The situation is even more dramatic in countries like Uganda, where the incidence highlighted by the authors contrasts with the almost complete inability of routine referral to cardiac surgery.

This study, as with all studies, also has weaknesses. Only left-sided valves were examined for features of RHD. This is by far the most common area for RHD, but a number of cases involving the right side may have been missed. Spending only approximately 2 minutes per child and doing screening on more than 200 cases a day, by one sonographer, might have led to missing a number of cases. The number of views recorded for secondary evaluation must have been limited by this approach.

The authors did not include a cost calculation. This would have been of particular interest, as this study was carried out in a developing world set-up with limited funding. In the cost calculation the salaries of the three staff members, as well as the equipment needed for cardiac ultrasound, would need to be included.
Furthermore, the use of the much cheaper hand-held portable echocardiography to detect rheumatic heart disease in children and adults with symptoms should be explored, as the image quality might be sufficient for screening purposes (Figure 1). Interestingly the World Health Organization supported the development of a simple, affordable, solar-powered blood-pressure device. Support for other cheaper devices, as for cardiac ultrasound, would be laudable.

In conclusion, the authors have provided a significant contribution to the knowledge of childhood incidence of RHD in a hitherto unreported part of Sub-Saharan Africa. Well conducted studies like this will continue to be important for creating awareness for the fact that we only begin to see the tip of an iceberg which developed countries have long erased from their radar screen. Without deeper understanding of the disease progression and the actual impact of RHD on the respective countries, however, the necessary political pressure for the roll-out of secondary prophylaxis and surgical therapy will be insufficient.

Conflicts of Interest Disclosures: None

References:


**Figure Legend:**

**Figure 1.** A. Patient with rheumatic mitral valve disease imaged with a top-of-the range cardiac ultrasound machine. B. Patient with rheumatic mitral valve disease imaged with a hand held cardiac ultrasound machine.