

Epidemiology of valvular heart diseases in Africa

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INTRODUCTION

One of the earliest cases, if not the first case, of rheumatic fever (RF) with rheumatic heart disease (RHD) reported in Africa was reported by medical officers Procter and Hargreaves in 1932 in the East African Medical Journal.⁽¹⁾ One of the medical officers had been engaged in native practice⁽¹⁾ for eleven years while the other had examined a large number of African school children and neither had found a case of RF or RHD prior. The reported case was that of a 25 year old male from Lumbwa, Kenya admitted to a local hospital with two months duration of painful and swollen joints and a fever. On physical examination, both a systolic and a diastolic murmur were heard consistent with left-sided valvular regurgitation. Infective endocarditis was ruled out since the patient's condition improved with bed rest and salicylates. He was dismissed after about a week of admission and was advised to seek follow up upon discharge.⁽¹⁾ In the 76 years since that case report, RF and RHD have become a major but under-appreciated public health problem in Africa where they account for significant cardiac morbidity and mortality in a substantial number of children and young adults.⁽²⁻⁷⁾

ABSTRACT

Rheumatic heart disease (RHD) resulting from rheumatic fever (RF) is the main form of valve disease in Africa. Other forms of valve diseases such as myxomatous mitral valve disease, age-related valve disease, sub-valvular aneurysms or valve disease related to endomyocardial fibrosis are less common than RHD. In developed countries, RF and RHD are rare and no longer pose a public health problem, but the combination of poverty, lack of awareness, lack of infrastructure and resources, and social instability contribute to the persistence of RF and RHD in Africa. The presence of other major infectious diseases also shifts attention away from RF and RHD. Contemporary population-based epidemiologic data utilising echocardiography to detect valve disease suggests the prevalence of valve diseases in Africa is likely much higher than previously thought, meaning the estimated mortality, morbidity and socio-economic burden they cause could also be much higher than currently appreciated. Increased efforts are needed to define the scope of the problem of valve diseases in Africa to draw attention to these illnesses and step up public health efforts to control and eradicate them as has already been achieved in other parts of the world. This article highlights the public health problem of valve diseases in Africa, the efforts underway to combat them and the attendant challenges.

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ETIOLOGY OF RHEUMATIC FEVER

The current understanding of the pathogenesis RF is that RF is the result of a delayed immune response to Group A B-haemolytic streptococcus (GABHS) pharyngitis after a latent period ranging from 1-5 weeks.⁽⁸⁾ Our understanding of this current working paradigm is based on epidemiologic and experimental data largely from the United States^(9,10) more than half a century ago when RF and RHD were still a major public health problem there. Rheumatic fever rarely affects adults and occurs mainly in children in the age group 5-15 years.^(11,12) About 3% of GABHS pharyngitis cases will develop RF of left untreated, but the risk of RF increases substantially to about 75% with a recurrent episode of GABHS pharyngitis.⁽¹³⁻¹⁵⁾ The precise pathogenic mechanism of RF has not been fully defined.⁽²⁾

Intriguing data from Australian aborigines affected by high incidence of RF suggests GABHS pyoderma or even non-GABHS may be responsible for RF and RHD in that population.⁽¹⁶⁾ However, similar data from other high incidence populations does not exist.⁽¹⁷⁾

SEQUELAE OF RHEUMATIC FEVER AND RHEUMATIC HEART DISEASE

Rheumatic fever affects multiple organs, and the clinical presentation is variable depending on multiple factors including the organs affected, severity of involvement and the time of presentation.⁽¹⁸⁾ The diagnosis of RF is based on the 2002-2003 World Health Organisation (WHO) revised Jones criteria.^(2,19)

Cardiac involvement in RF may be pancarditis, and it is cardiac involvement in the form of valvulitis that is the most important cause of morbidity and mortality.⁽²⁰⁾ There is evidence of cardiac involvement during the acute episode in 40 to 80% of cases of acute RF21,⁽²¹⁻²³⁾ but cardiac involvement almost always occurs in recurrent episodes of RF.⁽²⁴⁾ A large majority of those who have carditis during RF episodes will develop progressive RHD from inflammation and scarring of the heart valves, typically left-sided, which may result in significant valvular regurgitation and or stenosis and heart failure in childhood or early adulthood.⁽²⁵⁾ Determinants of the outcome of RHD are the age of first attack of RF and the frequency and severity of recurrent attacks.⁽²⁶⁾ Cardiac involvement in the attack of RF may range from mild to severe and should be suspected on clinical grounds when a murmur (systolic or diastolic) is heard on physical examination or if there is presence of cardiomegaly or unexplained heart failure.⁽¹⁸⁾

Hospital-based studies and cause of death studies across Africa are all consistent and show that RHD is the main cause of cardiac morbidity and mortality in children and young adults,⁽⁴⁾ with heart failure being the predominant cause of morbidity and mortality, followed by other complications such as native valve infective endocarditis, systemic embolisation, pulmonary hypertension, atrial arrhythmias, or complications related to valve surgery.⁽²⁶⁻³²⁾

The leading cause of heart failure in the forms of RHD typically seen in Africa affecting young individuals in their first or second

decades is valve regurgitation mainly of the mitral and aortic valves.^(26,28) It is common clinical course for RF and RHD to result in death in these young individuals⁽²⁸⁾ and the reasons for this malignant course are not entirely clear, but may partly be related to recurrent episodes of RF with inadequate secondary prophylaxis and multivalvular involvement.⁽²⁸⁾ Delayed clinical presentation also contributes to high morbidity and mortality.⁽³²⁾

The mechanism of mitral valve regurgitation is related to inflammation of the mitral valve apparatus leading to dilatation of the mitral anulus and elongation of the chordae and leaflets which results in prolapse of the anterior mitral leaflet.^(26,33) Aortic valve regurgitation, and less commonly tricuspid valve and pulmonary valve regurgitation are also related to inflammation of the valve leaflets and anuli.⁽³⁴⁾ The presence of mixed valve regurgitation and stenosis or pure valve stenosis is more common in older individuals with chronic and less active rheumatic carditis.^(26,34)

Infective endocarditis is a devastating sequelae of RHD where RHD accounts for up to 76.6% of the underlying predisposing condition in some studies.⁽³⁵⁾ Again, those affected by infective endocarditis are typically young where morbidity and mortality are high due largely to new or worsening heart failure or neurologic complications.^(27,35,36) In the 3-year prospective epidemiology study of infective endocarditis, Koegelenberg and colleagues found a six month mortality of 35.6%.⁽³⁵⁾

Rheumatic valve diseases, namely mitral valve stenosis with or without regurgitation, is the most common underlying cardiac condition complicating pregnancies in young women in Africa^(37,38) with a maternal mortality rate of up to 9.5%.⁽³⁹⁾ It is not unusual for the diagnosis of RHD to be made for the first time late during pregnancy⁽⁴⁰⁾ and the attendant consequences of late diagnosis are serious for both mother and child^(40,41) Nqayana and colleagues recently published a retrospective review of all patients admitted with cardiac disease in pregnancy over a 1-year period at their tertiary hospital.⁽⁴²⁾ RHD (mitral valve disease) was the commonest aetiology of cardiac disease in the 95 patients included with the majority aged 21-25 years. There was high maternal morbidity with 13 patients admitted in cardiac failure, 9 with atrial fibrillation, 3 required intensive-care management, 8 required balloon mitral valvuloplasty and 1 underwent valve replacement at 32 weeks' gestation.⁽⁴²⁾ There were adverse fetal outcomes with

86 live births of the 97 deliveries due largely to problems with anti-coagulation.⁽⁴²⁾

INCIDENCE AND PREVALENCE OF RF AND RHD IN AFRICA

The number of new cases of RF per 100 000 per year in Tunisia was 30 in 1990 and in Algeria 11, 1 in 1997 and 6.2 in 2000.^(43,44) There are no reliable data on the number of new cases of RF per year in sub-Saharan Africa⁽⁴⁵⁾ and the estimated 13 per 100 000 per year is based on incidence rates from the Middle East and North Africa.⁽⁴³⁾ Identifying new cases of RF demands active surveillance systems which requires enough skilled manpower and other resources such as laboratories which do not exist in many parts of Africa.⁽²⁾ The World Health Organisation (WHO) has however demonstrated previously that setting up such surveillance systems is feasible in Africa, but that such systems falter operationally over time.⁽⁴⁶⁾

The WHO estimated that there were 12 million people worldwide in 1994 with RF and RHD, the majority of them in developing countries.⁽²⁾ An update of the worldwide burden of RF and RHD estimated that 15.6-19.6 million people were affected by RHD with 2.4 million of those being children in the age group 5-14 years.^(4,43) Forty-two percent of the estimated 2.4 million children affected by RHD are located in sub-Saharan Africa. The number of people with previous RF who need secondary prophylaxis was estimated to be 1.88 million and the estimated number of deaths per year from RHD based on an annual mortality of 1.5% per year was 233 364-294 398.⁽⁴⁾

The prevalence of RHD in the update was estimated to be highest in sub-Saharan Africa with a prevalence of 5.7 per 1 000, compared to 1.8 per 1 000 in North Africa, 2.2 per 1 000 in South central Asia and 0.3% in developed countries.⁽⁴⁾ These estimates were based on large population-based data from the 1980s and 1990s where school age children were screened for RHD by clinical examination confirmed by echocardiographic and Doppler studies in some studies.^(4,47,48)

Previous studies in school children on prevalence of RHD utilising clinical screening plus or minus echocardiography show variation in the prevalence of RHD from region to region within Africa⁽⁴⁾

ranging from 1.0 per 1 000 in Inanda, South Africa to as high as 14.0 per 1 000 in Kinshasa, Democratic Republic of Congo and 14.6 per 1 000 Lusaka, Zambia.^(6,43) These studies have also shown that the prevalence of RHD is higher in poorer communities as demonstrated by the study in Addis Ababa, Ethiopia where the prevalence of RHD was 1.0 per 1 000 in children of high socio-economic status compared to 7.1 per 1 000 in those of low socio-economic status.⁽⁴⁹⁾

A seminal epidemiologic study on the prevalence of RHD in Africa in school children was recently conducted and was published by Marijon and colleagues in the *New England Journal of Medicine* in 2007.⁽⁷⁾ The study was conducted from May through October 2005 where 2 170 children age 6 to 17 years were randomly selected from six public primary schools among the 1 140 000 children living in the capital city Maputo in Mozambique.⁽⁷⁾ All children underwent a detailed clinical examination performed by physicians experienced in the diagnosis of murmurs and RHD and all children underwent a detailed echocardiographic examination.⁽⁷⁾ Only left-sided valves were assessed for features of RHD. Echocardiographic criteria for RHD were the presence of any definite evidence of mitral or aortic regurgitation in two planes accompanied by at least two of the following morphologic abnormalities: restricted leaflet mobility, focal or generalised valve thickening, and abnormal subvalvular thickening.⁽⁷⁾ Children who were found to have an organic murmur by clinical examination and RHD was confirmed by echocardiography were classified as having clinically detected RHD.⁽⁷⁾

The findings of the study were striking with respect to both the overall prevalence of RHD found in the children as well as the gross underestimation of RHD prevalence by clinical examination alone. Out of 2 170 children enrolled, 3 had a prior history of acute RF, 1 had known RHD, and only 2 were found to have acute RF.⁽⁷⁾ The number of cases of RHD detected by clinical examination alone was 5 (2.3 per 1 000 children), and by echocardiographic examination 66 (30.4 per 1 000), and by echocardiographic examination but not clinical examination 61 (28.1 per 1 000).⁽⁷⁾ Therefore, 92.4% of the cases of rheumatic valve diseases were clinically silent and occurred in children who were asymptomatic without an audible murmur.⁽⁷⁾ By extension, of the 1 140 000 children age 6-17 years in Maputo, an estimated 2 622 cases of RHD would be detected by clinical screening compared to 34 656 cases by echocardiographic screening.⁽⁷⁾

ECHOCARDIOGRAPHIC SCREENING OF VALVE DISEASE

Echocardiographic directed screening of valve diseases will undoubtedly uncover substantially higher prevalence of RHD across the continent. The geographic distribution will likely be similar to what has been documented, namely that the burden of disease will be highest in poorer countries and communities.

Subclinical valve diseases in all stages of RF is not uncommon⁽⁵⁰⁻⁵²⁾ and is not necessarily transient as demonstrated by Figueoa and colleagues in Chile, South America, in a long-term prospective follow up study of patients with subclinical rheumatic valvulitis.⁽⁵³⁾ Although there is a lack of data in Africa documenting the incidence of echocardiographically detected subclinical disease in cases of acute RF, the study by Marijon and colleagues in Mozambique sheds light on what appears to be an enormous problem of subclinical valve disease.⁽⁷⁾ The argument against the standard use of echocardiography to detect valve diseases in Africa centers around cost, lack of equipment and echocardiographic expertise, and potential over diagnosis of valve disease when physiologic regurgitation is found.⁽²⁾ However, the counter argument for the use of echocardiographic screening and diagnosing of RHD in high prevalent settings is being correctly advanced by some.^(2,17,53,54) Echocardiography is superior to physical examination in diagnosing valve disease and it makes sense to try to find models and establish guidelines for proper application of echocardiography for the sake of determining true incidence and prevalence of disease and to identify cases needing secondary prophylaxis.^(7,17)

PREVENTION AND MANAGEMENT OF VALVE DISEASES

The prevention and control of RF and RHD in Africa is now a priority. The Pan African Society of Cardiology (PASCAR) convened a workshop in 2005 to frame a road map and action plan for the prevention and elimination of RF and RHD in Africa during this lifetime.^(5,55) The action plan adopted at the workshop was called the Awareness Surveillance Advocacy Prevention (ASAP) Programme⁽⁵⁶⁾ which aims to (1) raise general awareness about RF and RHD (2) establish surveillance systems for the detection and treatment of cases of RF and RHD (3) champion

advocacy for RF and RHD and (4) implement proven primary and secondary prevention strategies.

The road to achieving the goal of eradicating RF and RHD has obvious barriers.⁽⁵⁶⁾ There is widespread lack of awareness about the causes, symptoms, risks and other problems associated with RF and RHD.⁽⁵⁶⁾ Part of this may be related to coexistent high rates of other public health problems such as HIV/AIDS, malaria, and tuberculosis which shift attention away from RF and RHD.^(17,56) However, even those affected by RF and RHD often do not receive adequate education or do not understand much of what they are told about the illness.⁽⁵⁷⁾ Setting up surveillance systems to capture new cases and regularly follow identified cases requires concerted coordinated effort by an aware, dedicated and well supported health care system with laboratory capabilities.⁽²⁾ Advocacy for RF and RHD faded largely due to the virtual disappearance of these diseases in developed nations and the lack of reliable epidemiologic data in Africa and other developing countries that highlight RF and RHD as major public health problems.^(17,56)

Primary prevention requires timely treatment of suspected or confirmed GABHS to prevent RF, but laboratory confirmation of GABHS remains the gold standard and these laboratory capabilities are not readily available.⁽²⁾ Rapid diagnostic kits are helpful, but cannot substitute for a laboratory and a negative kit result requires laboratory confirmation.⁽⁵⁸⁾ It is recommended that in communities where RF is endemic, all cases of sore throat in children 3-15 years old be treated as GABHS pharyngitis unless there is ulceration, or hoarseness, or watery nasal congestion, and/or conjunctivitis which argue against GABHS pharyngitis.⁽⁵⁹⁾ The WHO Acute Respiratory Infection Guideline lacks sensitivity for the diagnosis of GABHS pharyngitis since it requires both pharyngeal exudate and tender, enlarged lymph nodes to make the diagnosis.⁽⁶⁰⁾ Complicating primary prevention strategies is the absence of symptoms of pharyngitis in a significant proportion of those who develop RF.⁽⁶¹⁾

Secondary prevention is the long-term administration of penicillin after the first episode of RF to prevent recurrence and duration of treatment is tailored to the presence and severity of valve disease according to the WHO recommendations.^(2,59) Secondary prevention is the strategy so far proven most cost effective in

the control of RF and RHD and is the main strategy supported by the WHO.⁽²⁾ This strategy requires identification of cases and establishment of registries of patients to ensure continued coordinated administration of antibiotics every 3-4 weeks.⁽²⁾ However, whether administration of secondary prevention for all children with echocardiographically detected subclinical valve disease is warranted has not been shown.⁽⁵⁴⁾

Valve surgery is the way to managed valve disease causing heart failure, unless the risk is deemed to high. The difficulties associated with valve surgery in Africa are immediately apparent. The majority of the patients needing valve surgery are young and poor and availability of surgical resources and expertise is not widespread.⁽⁶²⁾ Tissue prosthesis are not durable in young patients⁽⁶³⁾ and mechanical prosthesis are complicated by inadequate anticoagulation due to difficulties with follow up, thromboembolic events, hemorrhage, or infective endocarditis.⁽⁶⁴⁾ Mitral valve repair is preferable to mitral valve replacement and is feasible in a number of patients, but there is risk of needing reoperation, particularly if valve repair is performed in the presence of active rheumatic carditis.⁽⁶⁵⁾ Cardiopulmonary bypass during pregnancy is associated with high fetal loss.⁽⁶⁶⁾ Mitral valve replacement during pregnancy, if deemed the only option, should be delayed until after delivery whenever possible.^(66,67)

Options for management of symptomatic mitral stenosis refractory to medical therapy and particularly complicating pregnancy include percutaneous balloon valvotomy or closed mitral commissurotomy.⁽⁶⁷⁻⁶⁹⁾ Mitral balloon valvotomy is preferred for severe mitral stenosis with pliable leaflets and without heavy commissural calcification,⁽⁶⁸⁾ but closed mitral commissurotomy, which can be performed without need for cardiopulmonary bypass, remains a viable options when balloon valvotomy cannot be performed.⁽⁶⁹⁾

NON-RHEUMATIC VALVE DISEASE

Other forms of valve disease previously reported in Africa include myxomatous mitral valve disease, age-related valve disease, sub-valvular aneurysms, and valve disease related to endomyocardial fibrosis. Myxomatous mitral valve disease was first described in South Africa by Barlow and Bosman in 1966⁽⁷⁰⁾ and is characterised by variable myxomatous degeneration of the mitral valve

leaflets and chordae associated with mitral leaflet prolapse or flail leaflets and mitral regurgitation. Myxomatous mitral valve disease is the leading indication for mitral valve surgery in developed countries,⁽⁷¹⁾ but is an uncommon indication for mitral valve surgery in surgical series reported from Africa.⁽⁶⁾ Valve diseases related to aging are the most common form of valve diseases in developed countries,⁽⁷²⁾ and are also encountered in the elderly in Africa.⁽⁷³⁾ However, age-related valve diseases of clinical significance were not part of the spectrum of heart disease and risk factors in a recent cohort study of a large black urban population in Soweto, South Africa.⁽⁷⁴⁾ Congenital subvalvular aneurysms are rare and were also first described in Africa.^(75,76) These aneurysm may be located below the mitral or aortic valve and be associated with regurgitation, systemic embolisation, or rupture and are thought to be related to congenital weakness between the muscular ventricular wall and fibrous skeleton of the valve annulus.⁽⁷⁷⁾ The cause of endomyocardial fibrosis is not well understood, but it is the most common cause of restrictive cardiomyopathy worldwide caused by deposition of fibrous tissue on endocardial surfaces causing heart failure associated with atrioventricular valve regurgitation.^(78,79) There is no medical therapy for this illness and surgical results of advanced disease are poor.⁽⁷⁹⁾ Mocumbi and colleagues recently performed a large transthoracic echocardiographic survey in a rural area of Mozambique and found a high prevalence of endomyocardial fibrosis of 19.8%.⁽⁷⁹⁾ Most of those affected had mild-to-moderate abnormalities and it is hoped that early detection of disease with echocardiography will help in the study of the pathogenesis and in the development of new management strategies of this common disease.⁽⁷⁹⁾

CONCLUSION

Valve diseases are common and are a serious public health problem in Africa. Recent epidemiologic data suggests the prevalence of valve disease is underestimated. More epidemiologic data utilising echocardiographic detection of valve disease is needed to define the full extent of the problem. The bulk of valve diseases are preventable and controllable through primary and secondary prevention measures, but these have not been implemented fully in Africa. PASCAR has appropriately created a sense of urgency in the efforts to eradicate RF and RHD and their efforts should be supported fully.

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