

A Review of Acute Rheumatic Fever and Rheumatic Heart Disease Research in Malaysia

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ABSTRACT

A total of 39 titles related to rheumatic fever or rheumatic heart disease in Malaysia were found with online literature search dating back to their inceptions and through 2014. Additional publications from conference journals were included. Nine papers were selected based on clinical relevance and future research implications.

There were no population-based studies on the incidence or prevalence of ARF or RHD. In the 1980s, the incidence of admission due to ARF ranged from 2 to 21.1 per 100 000 paediatric admission per year. The burden of disease was significant in the adult population; 74.5% of patients with RHD were female, of which 77.1% were in the reproductive age group of 15-45 years old. Rheumatic mitral valve disease constituted almost half (46.7%) of all mitral valve repairs, ranging from 44.8 – 55.8 patients per year from 1997 – 2003. From 2010-2012, mitral valve interventions increased to 184 per year, of which 85.7% were mitral valve repair.

In children with ARF, 25.4% - 41.7% had past history of rheumatic fever or RHD. In patients with rheumatic mitral valve disease undergoing surgical or medical interventions, only 6% reported history of ARF, none had history of GABHS pharyngitis or antibiotic prophylaxis. Only 44.7% of patients with RHD on follow-up were on intramuscular benzathine penicillin prophylaxis.

Overall, there is scarcity of publications on ARF and RHD in Malaysia. Priority areas for research include determination of the incidence and prevalence of ARF and RHD, identification of high-risk populations, evaluation on the implementation and adherence of secondary preventive measures, identification of subclinical RHD especially amongst the high-risk population, and a surveillance system to monitor and evaluate preventive measures, disease progression and outcomes.

KEY WORDS:

Acute rheumatic fever, rheumatic heart disease, prevention, penicillin prophylaxis, Malaysia

INTRODUCTION

Acute Rheumatic Fever (ARF) is a postinfectious, immunologic response to untreated or inadequately treated Group A β -Hemolytic *Streptococcus* (GABHS) pharyngitis,

occurring in genetically susceptible individuals. Rheumatic heart disease (RHD) is the only chronic sequel to ARF, with lifelong consequences. As such, ARF and RHD are potentially preventable diseases with timely, adequate and appropriate antibiotic treatment of streptococcal pharyngitis.

Unfortunately, ARF and RHD remain the most important causes of cardiovascular morbidity and mortality in children and young adults living in developing countries,¹⁻³ and the poor and minority groups in developed countries.⁴⁻⁵ RHD is the most commonly acquired heart disease in these socially and economically disadvantaged population.¹⁻⁵ In 2005, it was estimated that 15.6 million people have rheumatic heart disease worldwide; and there were 282,000 new cases of rheumatic fever with 233,000 deaths attributable to rheumatic fever or rheumatic heart disease annually.¹ In Asia, it is estimated that up to 1% of all school children show signs of the disease.³ Studies from South-Central Asia produced prevalence estimates ranging from 0.68-1.3 per 1,000 school-aged children.³ A household survey in rural Pakistan found all-age prevalence of echocardiographically confirmed rheumatic heart disease of 5.7 per 1,000 population.⁶ A school-based survey conducted in Phnom-Penh, Cambodia found a prevalence rate of clinically detected RHD that was echocardiographically confirmed at 2.2 per 1,000 children.⁷ Studies using echocardiography to screen for RHD showed a marked increase in the prevalence,⁷⁻⁹ with a 10-fold increase to 21.5 cases per 1000 children in Cambodia,⁷ and an increase from 0.8/1,000 to 20.4/1,000 school children in India.⁹

The objectives of this review are to summarise the studies on ARF and RHD in Malaysia that have been published, to review the incidence, epidemiology, clinical features, and management of ARF or RHD, and to identify gaps in the management and research on ARF and RHD in Malaysia.

SECTION 1: REVIEW OF LITERATURE

LITERATURE SEARCH Rheumatic Heart Disease; Rheumatic Fever

PubMed search and other searches according to the search methodology of the National Clinical Research Centre¹⁰ with the Medical subheadings (MeSH) Rheumatic Fever OR Rheumatic Heart Disease AND Malaysia from 2000 – 2014 were conducted. Online literature search dating back to their

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inceptions and continuing through 2014 with the same MESH were also conducted. There were a total of 39 titles. Additional studies or publications from conference journals were hand searched and included in the review. The abstracts of the articles were reviewed and 9 papers were considered relevant. Case reports or case series were excluded. The abstracts or the fulltext of these 9 articles were reviewed.

There were 9 studies over a span of 25 years; 6 were retrospective studies,¹¹⁻¹⁶ and 3 prospective observational studies.¹⁷⁻¹⁹ All were hospital- or institution-based studies with 4 papers from the National Heart Institute Kuala Lumpur,¹⁶⁻¹⁹ 2 papers from University Hospital or Universiti Malaya Medical Centre Kuala Lumpur,¹²⁻¹³ and one each from Hospital Universiti Sains Malaysia Kota Baru,¹¹ Hospital Kuala Lumpur,¹⁴ and Queen Elizabeth Hospital II Sabah (Table 1).¹⁵ Six (66.7%) of these papers were recent and were published in 2013 and 2014.¹⁴⁻¹⁹

INCIDENCE AND PREVALENCE

There were no population-based studies on the incidence or prevalence of ARF or RHD in Malaysia.

In the paediatric population, there were 4 retrospective studies.¹¹⁻¹⁴ Two retrospective reviews of paediatric admission in the 1980s showed that the incidence of admission due to ARF ranged from 0.002% or 2 per 100 000 total paediatric admission per year,¹¹ to 21.2 per 100,000 paediatric admission per year.¹² Over a 30 year study period, the overall trend was a gradual decline in the number of new cases of ARF, with a peak of >50 cases in 1970-71 to the lowest of <10 cases per year in 1996-1997 in a single institution.¹³ In a more recent review, there were 20 patients diagnosed to have ARF and RHD over a period of 13 months (Table II).¹⁴

In the adult population, the prevalence of RHD contributed significantly to the workload in a tertiary heart centre, constituting almost half (46.7%) of all mitral valve repairs.¹⁸ From 1997 – 2003, the number of mitral valve repairs due to RHD ranged from 44.8 – 55.8 per year (Table II).^{17,18,19} In a more recent 3-year review from 2010-2012, the total number of patients with RHD who required mitral valve repair or PTMC increased to 184 per year, of which majority (85.7%) were mitral valve repairs.¹⁶ The age ranged from 3-75 years, with a mean age of 32±19 years; 13% were children (Table II).¹⁶

CLINICAL FEATURES AND CARDIAC INVOLVEMENT

In the paediatric population, the peak age for ARF was in school-going children.¹¹⁻¹⁴ Fever and joint pain were the most common presenting features, present in 92.9% and 66.7% of patients respectively, followed by joint swelling in 57.1%.¹¹ Amongst the 37 patients with chorea, carditis remained the most common other feature of ARF (35%), followed by arthralgia (24%), fever (22%), subcutaneous nodules (11%), arthritis (5%), and erythema marginatum in 3% of patients.¹³

In the paediatric studies on ARF and RHD, there was an overall male preponderance with male to female ratio ranging from 1: 1.1 to 1.5:1.^{11,12,14} However, in the studies of both adult and children who required mitral valve repair due to RHD, there was female preponderance in the adult

population,¹⁵⁻¹⁸ with equal number of patients in the paediatric population (Table II).¹⁶ In an adult out-patient audit, 74.5% of the patients with RHD were female, of which 77.1% were in the reproductive age group of 15-45 years old.¹⁵

In both the paediatric and adult populations with ARF or RHD, mitral valve disease remained the most common valve complication.^{11,14-19} In the 1980s, amongst the children with ARF, 66.7% had carditis, of which 89.3% were mitral incompetence, 71.4% congestive heart failure, 28.6% mitral stenosis, and 17.9 % aortic incompetence.¹¹ These findings were similar in a more recent study on paediatric population where mitral regurgitation was present in 92% of patients (41.7% were severe mitral regurgitation) and aortic incompetence in 67% patients, where 16.7% had severe aortic regurgitation on echocardiographic examination.¹⁴ A total of 36.6% of these patients had severe congestive cardiac failure in New York Heart Association (NYHA) functional class III or IV; one patient required intubation and ventilation.¹⁴

Mitral regurgitation was the predominant valvular dysfunction in the paediatric patients with ARF or RHD,^{11,14} as well as in the adult patients with RHD.¹⁵ In the studies involving rheumatic mitral valve repair, most patients had mitral regurgitation; concomitant mitral regurgitation and stenosis occurred in 10.0 - 22.6% of all patients,^{17,18,19} whereas isolated mitral stenosis was present only in 1.9% of patients.¹⁸ (Table II). More than three quarters of all patients who required rheumatic mitral valve repair were in congestive cardiac failure in NYHA functional class II or more, and about a quarter had atrial fibrillation.^{17,18} No patients were reported to have stroke or endocarditis in these series of patients undergoing valve repair.

DIAGNOSIS AND MEDICAL MANAGEMENT

There were no studies on the clinical or echocardiographic criteria used for the diagnosis of ARF or RHD in Malaysia. In a study from year 2010-2012, most patients with rheumatic mitral valve disease who required surgical or medical intervention did not have a past history of ARF, only 6% reported history of ARF.¹⁶ In an earlier study from 1968-1975, a past history of rheumatic fever was elicited in less than half (43.8%) of pregnancies with rheumatic valvular lesions.²⁰

There were also no studies on the acute medical management of ARF, effectiveness of aspirin, steroids or other anti-inflammatory drugs and the outcome of the disease.

PROGRESSION OF DISEASE AND QUALITY OF LIFE

There were no studies on the progression of disease or the quality of life in patients with RHD.

PREGNACY AND RHD

Pregnancy increases the morbidity and mortality of both mother and baby in women with RHD and requires additional close monitoring by the obstetricians and the cardiologists. Amongst the female patients with RHD in the reproductive age group of 15-45 years old, 55.6% were given

Table 1: List of relevant articles on Acute Rheumatic Fever (ARF) and Rheumatic Heart Disease (RHD) from Malaysia

Author	Year Published	Title	Type of Study	Population	Time Frame	Sample Size
Studies on epidemiology of Acute Rheumatic Fever / Rheumatic Heart Disease						
Gururaj AK <i>et al</i> ¹¹	1990	A Clinical, Laboratory and Echocardiographic Profile of Children with Acute Rheumatic Fever	Retrospective clinical study	Paediatric patients admitted to Hospital Universiti Sains Malaysia, who were diagnosed with ARF	Apr 1985-Mar 1989	42
Omar A ¹²	1995	Pattern of Acute Rheumatic Fever in a Local Teaching Hospital	Retrospective clinical study	Patients admitted to Department of Paediatrics, University Hospital who were diagnosed with ARF	Jan 1981 – Dec 1990	134
Chew NK <i>et al</i> ¹³	2002	A clinical study of Sydenham's chorea at University Malaya Medical Centre (UMMMC)	Retrospective clinical study	Patients admitted to UMIMC presenting with acute rheumatic fever	1967-1997	313
Hung LC <i>et al</i> ¹⁴	2013	Rheumatic heart disease in a tertiary hospital in Malaysia	Retrospective clinical study	Patients diagnosed with ARF or RHD in Paediatric Cardiology Unit, Hospital Kuala Lumpur	Jul 2011 – Jul 2012	20
Studies on Rheumatic Heart Disease, Consequences and Treatment						
Liew HB ¹⁵	2014	Audit of rheumatic heart disease outpatient service	Retrospective clinical study	RHD outpatients at Queen Elizabeth Hospital, Sabah	May – Jun 2013	47
Levin BR <i>et al</i> ¹⁶	2014	Epidemiology, clinical profile and cardiac remodeling of severe rheumatic heart disease in Malaysia	Retrospective clinical study	Patients with clinically severe RHD who underwent either PTMC or surgery, IJN	2010 - 2012	552
Dillon J <i>et al</i> ¹⁷	2013	Leaflet extension in rheumatic mitral valve reconstruction	Prospective clinical Study	Patients with RHD who underwent leaflet extension, National Heart Institute (IJN)	Jan 2003 – Dec 2010	62
Mohd Azhari Yakub <i>et al</i> ¹⁸	2013	Contemporary long-term results of mitral valve repair in rheumatic heart disease	Prospective clinical study	Patients who underwent MV repair for rheumatic mitral disease at IJN	Jan 1997 – Dec 2010	627
Dillon J, <i>et al</i> ¹⁹	2014	Comparative long-term results of mitral valve repair in adults with chronic rheumatic disease and degenerative disease	Prospective clinical Study	Patients admitted to IJN for rheumatic and degenerative mitral valve repair	1997 - 2010	401

Table II: Reported prevalence, demographics and cardiac involvement of ARF and RHD from 1985 through 2013 in Malaysia

Population	Time Frame	Sample Size	Incidence/prevalence	Demographics	Cardiac Involvement
Gururaj AK <i>et al</i> ¹¹	Apr 1985-Mar 1989	42	2 /100 000 paediatric admission per year	Range: 5.75 years to 11.9 years. All children were Malays. Male to female ratio: 1: 1.1	MI: 89.3%, MS: 28.6% AI: 17.9 % CCF: 71.4% Past history ARF/RHD: 26.2% There were 34 episodes of recurrent attacks in 20 patients.
Omar A ¹²	Jan 1981 – Dec 1990	134	21.2 /100 000 paediatric admission per year (15.8 first attack of ARF, 5.4 recurrent ARF)	Peak: 6 – 11 years, >63% Youngest: 4 years old Male to female ratio: 1.4: 1	35% had carditis during the first presentation of chorea.
Chew NK <i>et al</i> ¹³	1967-1997	Total: 313 Chorea: 37 (12%)	1970-1971: >50 cases/year 1996-1997: <10 cases/year	Onset of chorea: Mean age: 11.5 years Range: 2-12 years	MI: 92% AI: 67% 5/12 (41.7%) of ARF were recurrent ARF.
Hung LC <i>et al</i> ¹⁴	Jul 2011 – Jul 2012	20	20 patients over 13 months	Peak: 5-9 years old, 58.3% Male to female ratio: 1.5:1	
Liew HB ¹⁵	May – Jun 2013	47	47 patients over 2 months	Mean age 37 years old Female: 74.5%	MI: 74.5%
Levin BR <i>et al</i> ¹⁶	2010 - 2012	Total: 552 Surgery: 85.7%	Overall: 184 patients per year Surgery: 157.7 per year.	Adult:480. Surgery:403 Child:72. Surgery:70 Adult: female 66% Child: female 50%	Adult: none had reported history of GABHS pharyngitis or antibiotic prophylaxis. 6% reported history of ARF.
Dillon J <i>et al</i> ¹⁷	Jan 2003 – Dec 2010	Total 446 LE: 62	Total: 55.8 patients per year LE: 7.8 patients per year	Mean age 20.2+11.7 years, range 3-60 years. Female: 75.8%, male: 24.2%	MI: 77.4% MI + MS: 22.6% AF: 22.6%
Mohd Azhari Yakub <i>et al</i> ¹⁸	Jan 1997 – Dec 2010	627	44.8 patients per year	Mean age: 32±19 years Range 3-75 years, median 28 years. Female: 54%, male 46%	CCF: 77.4% MI: 85.6% MI + MS: 12.4% Isolated MS: 1.9% AF: 22.6%
Dillon J, <i>et al</i> ¹⁹	1997 - 2010	Total: 401 R: 268 D: 157	R: 19.1 patients per year D: 11.2 patients per year	R: mean 53.9±8.4, median 53 yrs D: mean 55.8±7.4, median 55 yrs	CCF: 76.8% R: 90% MI, 10% MI + MS R: 90% MI, 10% MI + MS

AF: Atrial Fibrillation. AI: Aortic Incompetence. CCF: Congestive Cardiac Failure, NYHA II or more. D: Degenerative. LE: Leaflet Extension. MI: Mitral Incompetence. MS: Mitral Stenosis. R: Rheumatic.

Table III: Freedom from reoperation and valve failure, comparing mitral valve repair performed for RHD versus degenerative disease

Author / Study Year	Condition	In-hospital or early mortality (%)	Freedom from reoperation at 5 years (%)	Freedom from reoperation at 10 years (%)	Freedom from valve failure at 5 years (%)	Freedom from valve failure at 10 years (%)
Mitral Valve Repair						
Mohd Azhari <i>et al</i> ¹⁸ 1997 – 2010	RHD	Overall 2.4	91.8 ± 4.8	87.3 ± 3.9	85.6 ± 2.3	72.8 ± 4.6
	Degenerative valve disease		92.0 ± 1.7	91.8 ± 4.8	88.7 ± 5.1	82.4 ± 7.7
Dillon J <i>et al</i> ¹⁹ 1997 - 2010	RHD	4.8	97.9	96.5	95.3	89.9
	Degenerative valve disease	1.9	94.3	94.3	92.0	89.4
Leaflet extension						
Dillon J, <i>et al</i> ¹⁷ 2003-2010	RHD	-	96.8	-	91.6	-

education on family planning, but only 25.9% had formal referral to family planning services.¹⁵

In a hospital-based study from the year 1968 – 1975 in University Hospital Kuala Lumpur, out of a total of 20,903 deliveries, 151 patients had cardiac diseases, of which 137 (0.66%) were associated with RHD. Mitral valve disease constituted 74.8% of the cardiac lesions, followed by 18.5% of both mitral and aortic valve involvement, and 5.9% isolated aortic valve disease. Less than 50% of these pregnancies ended up as normal vaginal deliveries compared to 78.1% in the hospital population over the same period. There was one maternal death amongst the 151 deliveries in mothers with cardiac lesions, giving a maternal mortality rate of 6.6 per 1000 deliveries.²⁰

RECURRENT ATTACKS OF RHEUMATIC FEVER AND PREVENTION

In the paediatric series, 25.4% - 41.7% of patients with ARF had past history of rheumatic fever or RHD.^{11, 12, 14} There were no data on secondary antibiotic prophylaxis in these studies.^{11,12,14}

Secondary prophylaxis is an important aspect of RHD management. In a recent outpatient audit of adults with RHD in Queen Elizabeth Hospital II, Sabah, it was found that only 44.7% were on intramuscular benzathine penicillin prophylaxis; 38.3% were not on any prophylaxis and 17.0% were on oral penicillin. Amongst those who were not on prophylaxis, 29.8% were patients aged more than 40 years old, whom were considered less vulnerable to recurrent carditis.¹⁵

In the study of 552 patients who required mitral valve repair or percutaneous transvenous mitral commissurotomy (PTMC) from 2010-2012, none had reported history of GABHS pharyngitis or antibiotic prophylaxis.¹⁶

There were no studies on primary or primordial prevention of ARF.

CARDIAC SURGERY AND OUTCOME

There were 3 studies from a single institution focusing on the surgical techniques and procedures and the outcomes of surgical repair of the rheumatic mitral valve.^{17,18,19} One study

from the same institution focused on the cardiac re-modelling after mitral valve repair or PTMC.¹⁶

Repair of rheumatic mitral valvular disease contributed 46.7% of the total number of mitral valve repairs in a major cardiac institution in the country.¹⁸ The number of mitral valve repairs increased over the last 2 decades from 44.8 per year from 1997-2010, to 157.7 per year from 2010 to 2012 (Table II).¹⁶

Early mortality from rheumatic mitral valve repair ranged from none in the leaflet extension group¹⁷ to 4.8%,¹⁸ whereas the in-hospital mortality rate for mitral valve repair in adults with degenerative valve disease was 1.9%.¹⁹

In all studies, the freedom from reoperation 5 years after the initial mitral valve repair was more than 90%, while the freedom from valve failure at 5 years was lower, ranging between 86 – 95%.^{17,18,19} At 10 years post-surgery, freedom from valve failure for the RHD group dropped further to 73% in one study,¹⁸ worse than the degenerative mitral valve disease at 82 - 89%.^{18, 19} (Table III)

LIMITATIONS OF REVIEW

Of the 9 papers, 4 were abstracts presented at conferences.^{14,15,16,19} Of the 5 full articles, 3 were retrospective review of medical records^{11,12,13} and 2 were based on prospective observational registry data^{17,18} that could have inherent potential biases.

SECTION 2: RELEVANCE OF FINDINGS FOR CLINICAL PRACTICE

Overall, there is lack of research and good data on ARF and RHD in Malaysia.

INCIDENCE, PREVALENCE AND BURDEN OF DISEASE

Malaysia has made significant progress and development over the last few decades. As such, it is generally perceived that the incidence or prevalence of RHD is on the decline. Though there were no population-based studies on the incidence or prevalence of ARF or RHD in Malaysia, there was an overall decrease in incidence of ARF between 1967 to 1997 in a retrospective institutional-based review of clinical records.¹³

However, recent publications show that the prevalence of ARF and RHD is still significant.¹⁴⁻¹⁹ Rheumatic mitral valve repair constituted almost half (46.7%) of the workload of mitral valve repair in institutional prospective studies.¹⁸ Over the last two decades, the number of rheumatic mitral valve repairs has increased from 44.8 per year from 1997-2010, to 157.7 per year from 2010 to 2012 (Table II).¹⁶ These figures might not reflect the trend of disease as other factors such as increased awareness amongst healthcare professionals regarding the disease, lower threshold or criteria for surgical repair, and geographical or institutional bias in the pattern of referral for cardiac intervention may play a role.

From 1997 - 2010, the ages of the 627 patients who underwent rheumatic mitral valve repair ranged from children as young as 3 years old to the elderly of 75 years old,¹⁸ suggesting that ARF and RHD affected almost all age groups, except infants. Cardiac surgery indicates severe disease or eventual sequel of RHD, and the number of patients undergoing cardiac surgery merely represented the tip of the iceberg.²¹ In this study,¹⁸ the criteria for diagnosis of RHD were not discussed.

In addition to lack of data on the incidence and prevalence of RHD in the general population, Malaysia also lacks data on the incidence or prevalence of RHD amongst the indigenous population in the country. Studies in Australasia and Canada reported higher incidence of ARF and RHD in members of the minority or indigenous groups.^{4,5}

DIAGNOSIS OF ARF AND SUBCLINICAL RHD

There is no specific clinical feature or definite laboratory test to diagnose ARF. Since 1944, a constellation of clinical features and laboratory tests included in the Jones criteria have been used for guidance in the diagnosis of ARF. The American Heart Association (AHA) made several modifications and revisions to the Jones criteria over the last few decades.^{22,23} These revised or modified Jones criteria were used in the studies on ARF.^{11,12,13} With the development of echocardiography, some national and regional guidelines have included the use of echocardiography and Doppler studies in the guidelines for the diagnosis of ARF.^{24,25} In 2015, the AHA has included Doppler echocardiography in the revised Jones criteria for the diagnosis of ARF.²⁶

In a study from 1968-1975, a past history of rheumatic fever was elicited in less than half (43.8%) of pregnancies with rheumatic valvular lesions.²⁰ A more recent study from 2010-2012 on adult patients who required rheumatic valvular repair or PTMV revealed that none had reported history of GABHS pharyngitis or on antibiotic prophylaxis and only 6% reported a history of ARF.¹⁶ These might be due to lack of awareness regarding the importance of GABHS pharyngitis, ARF and its recurrence among healthcare providers and the community, poor patient education, or a high incidence of subclinical ARF or RHD.

Screening and early detection of subclinical RHD could reduce the prevalence and severity of RHD by effective implementation of secondary antibiotic prophylaxis and surveillance. Numerous studies have shown that transthoracic echocardiography examination could detect

mild or subclinical rheumatic valvular disease which could not be diagnosed by clinical examination, and revealed a much higher RHD burden than previously thought.^{7,8,9,27,28,29} In 2012, the World Heart Federation developed and published an evidence-based guideline on the echocardiographic criteria for the diagnosis of RHD.³⁰ To minimise the utilisation of resources in these resource-poor developing countries, different approaches were also studied to determine the accuracy of echocardiographic screening.^{31,32} Handheld echocardiographic screening for RHD by non-experts had shown reasonable sensitivity (74.4%) and specificity (78.8%) for both borderline and definite RHD, and improved to 90.9% for definite RHD.³²

PROGRESSION OF DISEASE, QUALITY OF LIFE AND OUTCOME

Good health and well-being are the goal of medicine. However, medical and surgical treatment of severe rheumatic valvular disease are at best palliative, and these are neither accessible nor affordable to the majority of the affected patients who are poor and young. The mean age for mitral valve repair was 20-30 years old.^{17,18} This is the young and productive age-group when an individual is at their prime. Unfortunately, RHD has compromised their quality of life from a young age.

In addition, amongst the adult patients who required rheumatic mitral valve repair or intervention, there was female preponderance.¹⁵⁻¹⁸ In an adult out-patient audit, 74.5% of the patients with RHD were female, of which 77.1% were in the reproductive age group of 15-45 years old.¹⁵ These patients require more medical care during their antenatal, intrapartum and postnatal period; and have higher rates of morbidity and mortality for both the mother and the baby. There were no recent publications on the outcome of pregnancy in these patients.

ARF recurrences cause progressive valvular damage and can lead to complications such as congestive cardiac failure, atrial fibrillation, stroke or infective endocarditis. About three quarter of patients undergoing rheumatic mitral valve surgery had congestive cardiac failure and a quarter had atrial fibrillation.^{17,18}

RECURRENT ATTACK OF RHEUMATIC FEVER AND PREVENTION

Secondary prevention of recurrent ARF with regular intramuscular benzathine penicillin injection to prevent recurrent streptococcal pharyngitis and progressive valvular damage, is an important and proven cost-effective measure to reduce the burden of ARF and RHD on both the population and the healthcare system.^{33,34}

In Malaysia, the recurrence rate of ARF was high, ranging from 26.2% to 41.7% amongst children with ARF or RHD.^{11,12,14} In an outpatient audit, less than half the adult patients received intramuscular benzathine penicillin.¹⁵ In the patients who required mitral valve repair or PTMC, none had reported history of GABHS pharyngitis or antibiotic prophylaxis.¹⁶

As such, ensuring appropriate implementation of secondary antibiotic prophylaxis, and a surveillance system to monitor adherence to treatment are important measures to prevent recurrent streptococcal pharyngitis and progressive valvular damage, in order to reduce the burden of ARF and RHD in the country.

Primary prevention, which includes accurate diagnosis, and adequate and timely treatment of the initial acute streptococcal infection with an appropriate antibiotic, is the other important preventive measure. Ultimately, primordial prevention with eradication of poverty and provision of proper housing should be the goals of the authority or the government.

CARDIAC SURGERY

As the disease progresses, valve repair or replacement often becomes necessary. Patients who do not have access to such expensive surgery may have poor quality of life and die prematurely from RHD or its complications. ARF and RHD are neglected diseases of the poor and the marginalised in their youth or young adulthood, who usually do not have access to such expensive surgery. Even with valve surgery, the longterm outcome maybe worse than degenerative valves.¹⁸ As such, prevention of ARF and RHD is imperative.

SECTION 3: FUTURE RESEARCH DIRECTIONS

Overall, there is scarcity of publications on ARF and RHD in Malaysia. Priority areas for research include determination of the incidence and prevalence of ARF and RHD in Malaysia, identification of high-risk populations, evaluation of the implementation of secondary preventive measures and adherence to intramuscular benzathine penicillin injection, identification of subclinical RHD especially amongst the high-risk population, and a surveillance system to monitor and evaluate preventive measures, as well as disease progression and outcome.

In Malaysia, most patients who required cardiac surgical intervention had subclinical RHD. Research in the detection of subclinical RHD in high-risk populations with transthoracic echocardiographic examination, and proper implementation of secondary antibiotic prophylaxis with intramuscular penicillin injection in these high-risk population should be another area to explore. Progression of disease, quality of life, morbidity and premature deaths can then be determined.

Evaluation of the human, social and economic costs, cost-effectiveness of early detection of subclinical RHD, and implementation of preventive measures and their effectiveness, can help in the future development of policies, planning of RHD programmes, resource allocation for primary and primordial prevention, as well as tertiary cardiac care programmes and surveillance programmes.

ARF and RHD contributed significantly to the surgical burden of mitral valve repair or replacement in the country. Since the reduction in disease progression or severity has a long lag time, reduction in the burden of surgical repair of rheumatic

mitral valve may be seen only at a much later date. In addition to the provision of data on the surgical repair of rheumatic heart valves, the National Cardiothoracic Registry that was launched in 2015 can be a source of data for research on the epidemiology, demographic and quality of life in Malaysia.

Public health priorities may include research on the evaluation of the effectiveness of rapid diagnosis of streptococcal pharyngitis, primary prevention through public education to increase the awareness of the people on the importance of timely and adequate treatment of acute streptococcal pharyngitis, and effort to empower children and the community to seek treatment with appropriate antibiotics.

In May 2012, the United Nations and the World Health Assembly agreed to adopt a global target to reduce premature non-communicable diseases (NCDs) mortality by 25% by 2025.³⁵ RHD is a disease where this may be achievable because there are relatively inexpensive, proven, and effective control strategies that can lead to decrease in deaths, especially in young people.³⁶

The World Heart Federation Working Group on RF and RHD was established in 2011 to achieve its goals in the control of RF and RHD.³⁷ Unlike other NCDs, RHD is preventable. As such, research on ARF and RHD, and the incorporation of RHD into the national NCD prevention programmes should be top priorities. With these concerted efforts, Malaysia may be able to achieve the United Nations and the World Health Assembly's target of reducing premature NCD mortality by 25% by 2025, especially amongst poor women and children who are most affected with RHD.

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