Challenges with international normalised ratio control in paediatric patients with rheumatic heart valve replacement surgery in the Eastern Cape Province, South Africa

ZM Makrexeni

Faculty of Medicine and Health Sciences, Walter Sisulu University, South Africa

Address for correspondence:
Sisson Street, Fortgale, Mthatha

Email:
mmmaso30@gmail.com

ZM Makrexeni https://orcid.org/0009-0007-3903-5891
DOI: https://doi.org/10.24170/22-3-7428

ABSTRACT

Introduction: Rheumatic heart disease (RHD) is a preventable chronic condition that affects the heart valves. The incidence of acute rheumatic fever (ARF) and RHD has waned in Western countries; however, this is not the case in developing countries. Poor access to healthcare and a lack of adherence to international normalised ratio (INR) monitoring in RHD contribute to thromboembolic complications.

Methods: Records of patients from the Eastern Cape municipal districts with RHD were reviewed over 10 years. Patients who underwent rheumatic valve replacement surgery were isolated and analysed for their INR control.

Results: A total of 30 patients with RHD were reviewed. All patients presented with severe RHD. Of the 30 patients, 20 had mitral valve replacement surgery, and 6 had mitral valve repair surgery. The 6 patients who had mitral valve repair surgery eventually required mitral valve replacement. Those who had mitral valve replacement surgery were started on anticoagulation (warfarin) post-operatively. Two patients died due to mitral valve thrombosis. Four patients were subsequently admitted for anticoagulation due to a thrombosed prosthetic mitral valve. Most of the patients were struggling to maintain a therapeutic range INR with values ranging from 1.1 to 2, and up to 8–10 on rare occasions.

Conclusion: Most chronic RHD patients underwent mitral valve replacement surgery with a prosthetic valve. Most patients who were started on warfarin struggled to maintain a therapeutic range INR post-operatively due to poor healthcare access and adherence.

Keywords: acute rheumatic fever, rheumatic heart disease, valve replacement surgery, international normalised ratio, disease outcomes

SA Heart® 2025;22:151-154

INTRODUCTION

ARF is a post-infectious, non-suppurative sequel of pharyngeal infection with group A beta-haemolytic *Streptococcus*.[1] More than one-third of affected patients develop carditis, followed by progressive and permanent valvular heart disease, particularly mitral valve and aortic valve regurgitation and/or stenosis.[2] The burden of RHD in developed countries declined drastically at the end of the 20th century, largely due to reduced overcrowding and improved sanitation and living conditions.[3-4]

In South Africa, RHD cases declined somewhat since the dawn of democracy in 1994, which was attributed to improved healthcare access.[5] The earlier improvements in South Africa since 1994 were only demonstrated in certain parts of the country, not its entirety. The previously disadvantaged communities remained poor under the new government of democracy, and, as such, the prevalence of RHD never improved.[6] The former Transkei region of the Eastern Cape Province remains poor and is overburdened with cases of chronic RHD.

Surgery is indicated for patients with RHD presenting with symptomatic valvular dysfunction.[7] The surgical options for RHD include closed mitral valvotomy, mitral valve repair, or replacement with a mechanical, bioprosthetic, or autograft valve. Aortic valve disease is usually treated with valve repair or replacement with a mechanical, homograft, or pulmonary autograft valve.[7] The choice of therapy for young patients is influenced by many factors, such as socio-economic status, access to healthcare, availability of prophylaxis for ARF, and anticoagulation therapy. In these situations, the importance of repair, especially of the mitral valve, is unquestionable.[8]

Global survival and survival-free rates from prosthetic valve complications are lower after valve replacement, with either mechanical or biological prostheses, because of higher rates of thromboembolism with mechanical valves and the faster degenerative process with biological prostheses.[8] Mitral valve repair surgery is preferred in children over valve replacement

surgery; however, the durability of repair of the rheumatic mitral valve is generally poorer than in nonrheumatic valves.[9]

In RHD-endemic regions with limited access to surgery and emerging surgical programmes, the most important considerations may be the risk of needing reoperation, given the limited resources (and low probability of obtaining a second operation) and the surgical team's expertise in valve replacement rather than repair. Consequently, valve replacement is often the practice of choice in many settings, despite the need for lifetime anticoagulation.[9]

For most young patients who undergo replacement valve therapy with mechanical prostheses, reliable anticoagulation management is often unattainable under the prevailing socio-economic circumstances.[10] Cases of patients with clotted valves presenting for emergency surgery due to poor compliance with anticoagulation control are frequent, with INR ranges below the recommended therapeutic ranges (2.5–3.5).

Without trivialising the seriousness of bleeding complications associated with over-anticoagulation, under-coagulation in low- to middle-income countries far exceeds the former.[11] In two African studies involving patients with RHD who underwent mechanical valve replacement, most thromboembolic complications, including clotting of the valves, occurred at an INR < 2.[11]

Risk factors for poor adherence to warfarin are young patient age, lack of formal education, unemployment, and limited access to an immediate healthcare facility.[12] Unfortunately, these factors are simultaneously the hallmark features of RHD, for which a significant association with low socio-economic circumstances exist.[13]

Our setting, the former Transkei region of the Eastern Cape, is considered one of the poorest provinces in South Africa, characterised by high levels of unemployment and illiteracy.[14] We only have access to 1 cardiothoracic surgeon who performs part-time sessions at the state hospital.[15] We are only able to do 1–2 cases per week, an average of 3–4 cases per month. These cases are prioritised according to which one is deemed an emergency or urgent case at the time.[15] RHD tends to fall behind congenital heart diseases, which are usually more urgent. Therefore, RHD patients tend to suffer the most.

METHODS

This was a retrospective review of paediatric patients treated for rheumatic valvular heart disease at a tertiary hospital in the Eastern Cape Province over 10 years. Demographic data, such as age, sex, and place of origin, were analysed. Patient presentation and type of rheumatic valve disease were analysed. Follow-up echocardiograms were recoded, which were performed immediately post-operatively, at 1 month, 6 months, and 1 year. All patients with prosthetic mitral valves were started on warfarin post-operatively. INR was monitored monthly in all patients on warfarin, depending on the INR control. The INR therapeutic target range was 2.5–3.5. The INR data were collected from the National Health Laboratory Service (NHLS).

Statistical analysis and ethical clearance

Variables were reported as a mean (standard deviation) or median (interquartile range). Nominal variables were compared using the t-test. Ethical clearance was obtained from the chief executive officer of Dora Nginza Hospital and the Health Research Ethics and Biosafety Committee of Walter Sisulu University.

RESULTS

A total of 30 patients were treated for chronic rheumatic valve disease at a tertiary hospital over 10 years. There were 19 males (63%) and 11 females (36.6%) (Figure 1). Most patients (n = 19, 63%) were from the former Transkei region (OR Tambo District Municipality). The average distance travelled from home to the tertiary hospital was 200 km. The remaining patients were from the Nelson Mandela Bay Metro and Sarah Baartman municipalities. All the patients were between the ages of 5 and 15 at the time of presentation and operation.

Most patients (n = 28) presented with severe mitral valve regurgitation, and only 2 with mixed mitral valve disease. A few patients presented with severe mitral valve regurgitation and mild aortic regurgitation, which did not require any aortic valve repair or replacement.

Most patients (n = 24, 80%) had mitral valve replacement surgery with mechanical prostheses. The rest of the patients initially had mitral valve repair but later required redo surgery for mitral valve replacement due to severe mitral regurgitation post-operatively (Figure 2).

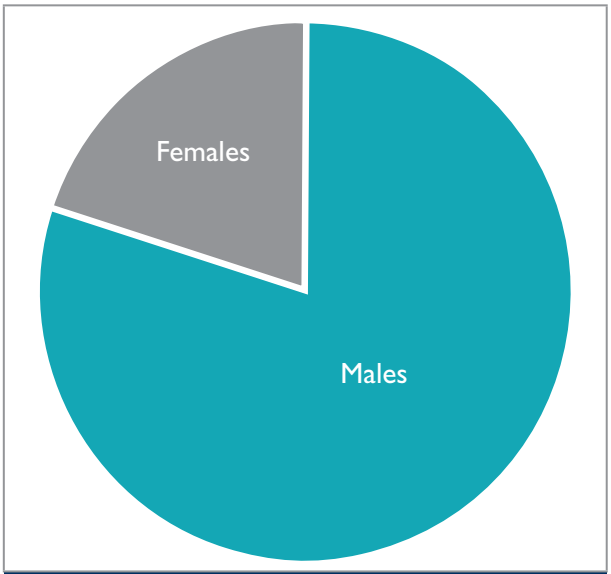

FIGURE 1: Total of 30 patients; 24 males and 6 females.

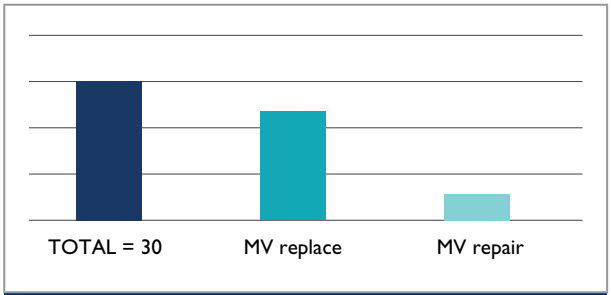

FIGURE 2: Total of 30 surgical operations; 24 MV replacement, 6 MV repair.
MV: mitral valve

All the patients with mitral valve replacement were started on anticoagulation therapy with warfarin and were followed up for INR monitoring. Two patients died due to mitral valve thrombosis because of poor anticoagulation adherence. Four patients were admitted to the hospital for intensive anticoagulation for a thrombosed prosthetic valve due to poor anticoagulation adherence. These patients were started on enoxaparin sodium and warfarin in the ward until proper thrombolysis. This was the only option due to the unavailability of cardiothoracic surgical services.

The rest of the patients are currently on anticoagulation with poorly controlled INRs fluctuating between 1 and 2. Most patients (n = 20) have an INR average < 2. The rest of the patients fluctuate between an INR of 2 and 3, and > 3. Only 1 patient was admitted with warfarin toxicity and bleeding.

There are no INR clinics at the district hospitals, and some do not have an on-site laboratory to perform the INR. Therefore, patients must travel for 2 days to access an INR and have their medication adjusted accordingly. Some of the delays in getting the INR contribute to poor control.

DISCUSSION

During the study period, only 30 patients underwent rheumatic valve surgery. There is a long waiting list for some of the patients due for surgery who must wait because of the lack of paediatric cardiothoracic surgeons in the province. Approximately 30 more patients with severe rheumatic valve disease are awaiting surgery.[16] This means, on average, we have only operated on 3 patients per annum. National waiting lists for paediatric cardiac surgery are currently estimated in excess of 3 000 patients, including congenital heart disease and rheumatic valve disease.

There was a male predominance among the patients operated on. Most of these patients were from the former Transkei region of the Eastern Cape, one of the poorest provinces in the country.[14] These patients would travel approximately 200 km from their local district hospitals, which would take an ambulance about 3 hours to reach a tertiary hospital with paediatric cardiologists. After they have been assessed and considered due for surgery, they are referred to another centre with a cardiothoracic surgeon, approximately 520 km away. There is only 1 part-time cardiothoracic surgeon for the entire Eastern Cape Province. On average, it takes 6–8 hours or more for patients to reach a centre with a surgeon to undergo surgery.[11,17]

Regarding clinical presentation, most patients had severe mitral regurgitation, with a few cases of mixed mitral valve and aortic valve regurgitation. As such, most patients had mitral valve replacement and repair surgery with no aortic valve surgery.[6] Most of the patients had mitral valve replacement surgery instead of mitral valve repair, which is the preferred surgical option in children with RHD.[7,10] Mitral valve repair surgery has the advantage of not requiring anticoagulation post-operatively, thus avoiding the complications of under- or over-anticoagulation.[7]

Due to several reasons, most patients had valve replacement surgery instead of valve repair, which is the preferred surgical option, as a result of the shortage of surgeons, limited skill with rheumatic valve surgery, a long waiting list for paediatric cardiac surgery, and the possibility of redo being required later on in life for patients with valve repair.[7,8,10,16] Patients who initially underwent mitral valve repair eventually required mitral valve replacement due to severe residual mitral valve regurgitation post-repair.[8,9]

All patients ultimately received anticoagulation, including those who initially underwent mitral repair surgery. Most patients travel far to access a specialist and other services, such as laboratory testing.[12,17] The lack of skilled healthcare workers and the unavailability of anticoagulants at their district hospitals and clinics have resulted in patients not receiving their warfarin as prescribed or their INR not being optimised.[12] Consequently, their INR control was challenging.

Approximately 80% of the patients had an INR average < 2, which is suboptimal. These patients are at risk of valves being blocked by clots.[12] The other risk was warfarin toxicity because they had to take high doses of anticoagulation to try to achieve INR therapeutic ranges (2.5–3.5). Of the patients on warfarin, 4 were admitted for a thrombosed prosthetic mitral valve, and 2 patients died due to thrombosis of the mitral valves.[10]

One of the biggest challenges of INR control is the limited access to medical healthcare services and the scarcity of INR clinics at district hospitals. Due to the unavailability of surgery and long waiting lists for theatre, patients with thrombosed valves were admitted on high-dose anticoagulation and dual anticoagulation therapy to try to dissolve the clots.[18] The 4 patients were picked up early and were treated successfully without any surgery. The two other patients died before their INR could be controlled.

Unfortunately, there are no plans in place by the government to address the situation. Poor patients continue to suffer from a lack of healthcare services and shortages of human resources.

Recommendations

Paediatric cardiac surgical services require a multistakeholder collaboration for success, involving paediatric cardiologists, paediatric cardiothoracic surgeons, the Department of Health, the Colleges of Medicine of South Africa, the Health Professions Council of South Africa, the South African Medical Association, and civil society groups. A collaborative approach is recommended to find solutions to these challenges.

CONCLUSION

Most patients with chronic rheumatic valve disease underwent mitral valve replacement surgery with a prosthetic valve that required anticoagulation post-operatively. Most patients who were started on warfarin had subtherapeutic INR due to poor healthcare access and compliance.

Conflict of interest: none declared.

REFERENCES

1. Carapetis JR, Sreer AC, Mulholland EK, Weber M. The global burden of group A streptococcal diseases. Lancet Infect Dis 2005;5(110):685-694.
2. Marijon E, Mirabel M, Celermajer DS, Jouven X. Rheumatic heart disease. Lancet 2012;379(9819):953-964.
3. Gordis L. The virtual disappearance of rheumatic fever in the United States: Lessons in the rise and fall of the disease. T. Duckett Jones memorial lecture. Circulation 1985;72(6):1155-1162.
4. Essop MR, Nkomo VT. Rheumatic and nonrheumatic valvular heart disease: Epidemiology, management, and prevention in Africa. Circulation 2005;112(23):3584-3591.
5. Cilliers AM. Rheumatic fever and rheumatic heart disease in Gauteng on the decline: Experience at Chris Hani Baragwanath Hospital, Johannesburg, South Africa. S Afr Med J 2014;104(9):632-634.
6. Makrexeni ZM, Pepeta L. Clinical presentation and outcomes of patients with acute rheumatic fever and rheumatic heart disease seen at a tertiary hospital setting in Port Elizabeth, South Africa. Cardiovasc J Afr 2017;28(4):248-250.
7. Kumar AS. Surgical options in rheumatic heart disease: An Indian surgeon's perspective. Asian Cardiovasc Thorac Ann 2019;28(7):371-373.
8. Moorthy PSK, Sivalingam S, Dillon J, Kong PK, Yakub MA. Is it worth repairing rheumatic mitral valve disease in children? Long-term outcomes of an aggressive approach to rheumatic mitral valve repair compared to mitral valve replacement in young patients. Interact Cardiovasc Thorac Surg 2019;28(2):191-198.
9. Antunes MJ. Repair of rheumatic mitral valve disease: The controversy goes on! Heart 2018;104(10):796-797.
10. Zille P, Human P, Pennel T. Mechanical valve replacement for patients with rheumatic heart disease: The reality of INR control in Africa and beyond. Front Cardiovasc Med 2024;11:1347838.
11. Ntlokotsi S, Moshesh MF, Mntla P, Towobola OA, Mogale MA. Optimum INR intensity and therapeutic INR control in patients with mechanical heart valve prosthesis on warfarin oral anticoagulation at Dr George Mukhari academic hospital: a three-year retrospective study. S Afr Fam Pract 2018;60(6):192-196.
12. Mangnall LJT, Sibbritt D, Al-Sheyab N, Gallagher RD. Predictors of warfarin non-adherence in younger adults after valve replacement surgery in the South Pacific. Heart Asia 2016;8(2):18-23.
13. Zühlke L, Karthikeyan G, Engel ME, et al. Clinical outcomes in 3343 children and adults with rheumatic heart disease from 14 low- and middle-income countries: Two-year follow-up of the Global Rheumatic Heart Disease Registry (the REMEDY Study). Circulation 2016;134(19):1456-66.
14. Westaway A. Rural poverty in the Eastern Cape Province: Legacy of apartheid or consequence of contemporary segregationism? Development Southern Africa 2012;29(1):115-125.
15. Awuah WA, Adebusoye FT, Wellington J, et al. A reflection of Africa's cardiac surgery capacity to manage congenital heart disease: A perspective. Ann Med Surg (Lond) 2023;85(8):4174-4181.
16. Hoosen EMG, Cilliers AM, Hugo-Hamman CT, et al. Audit of paediatric cardiac services in South Africa. SA Heart J. 2010;7(1).
17. Welke KF, Pasquali SK, Lin P, et al. Hospital distribution and patient travel patterns for congenital cardiac surgery in the United States. Ann Thorac Surg 2019;107(2):574-581.
18. Bonou M, Lampropoulos K, Barbetseas J. Prosthetic heart valve obstruction: thrombolysis or surgical treatment? Eur Heart J Acute Cardiovasc Care 2012;1(2):122-127.