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Original Article**A study on prescribing pattern of drugs in patients with rheumatic heart disease at tertiary care hospital**

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Abstract**Introduction**

Rheumatic heart disease (RHD) is a common cardiac problem. Medical therapy is directed toward secondary prophylaxis and supportive treatment for heart failure (HF), rhythm disorder and anticoagulation to prevent thromboembolism. Drug utilization patterns thus provide a favorable feedback to physicians and help to modify treatment strategies.

Materials and Methods

This is a cross sectional study on 140 patients with RHD who received care at Nobel Medical College Teaching Hospital from October 2017 to September 2018. A semi structured questionnaire was administered to record the demographic characteristics, co-morbid conditions and use of different drugs.

Results

Mean age was 50.09 ± 10.99 years. RHD was more common in females (75.7%). Penicillin prophylaxis was prescribed for 38 (27.1%) patients. Out of which, 22.8% were on daily oral penicillin and 4.2% were receiving three weekly benzathine benzylpenicillin. Beta blockers were the most frequently used drug for heart rate control for patients (51.4%) with both atrial fibrillation (AF) and/or symptomatic mitral stenosis (MS). Digoxin was used in 10% and calcium channel blockers were used in 3.5% of patients who have AF. Different diuretics were used in 88.5% of patients with features of systemic or pulmonary congestion. Out of 20 cases of AF, eleven (55%) were receiving aspirin and nine (45%) were on oral anticoagulants. Out of nine patients receiving warfarin, only four (20%) had therapeutic international normalized ratio (INR).

Conclusions

This study focuses on prescription pattern of drugs for different indications in patients with RHD. There is a need for improved use of secondary prophylaxis to prevent recurrence of RF and antithrombotic in patients with AF.

Key words: *Drugs, Prescription pattern, Rheumatic heart disease*

Introduction

According to WHO, at least 15.6 million people worldwide have RHD. Of the 5,00,000 individuals who acquire RF every year, 3,00,000 go on to develop RHD and 233,000 deaths annually are attributed to RF or RHD [1]. Various studies have been

published on prevalence of RHD in Nepal. All these studies have shown the prevalence of RHD among school children to be between 0.9-1.35 per thousand [2, 3, and 4]. Only an echocardiography based study done in eastern part of Nepal by Shrestha NR, et al showed the prevalence

of RHD 10.2 per thousand indicating that population prevalence of RHD increases when echocardiography is used for screening [5].

RHD is one of the common types of structural heart disease and carry a significant morbidity and mortality in developing countries. Medical therapy in RHD includes measures to prevent RF and thus RHD. In patients who develop RHD, therapy is directed toward eliminating the group A streptococcal pharyngitis, suppressing inflammation and providing supportive treatment for HF, rhythm disorder and anticoagulation in selected cases to prevent thromboembolism.

Periodic evaluation of drug use patterns in hospital setting can be of help to monitor and supervise the drug use behaviors. Drug utilization studies thus provide a favorable feedback to treating physicians and help to modify treatment strategies, identify and correct the shortcomings if any, thus providing a rational and cost effective therapy to the patients. This study was conducted in patients with RHD to highlight these facts.

Material and Methods

This was a descriptive cross-sectional study conducted from October 2017 to September 2018. The diagnosis of RHD was made on the basis of clinical history, examination and echocardiography. A total of 140 patients of RHD were enrolled consecutively who received care at cardiology clinic of Nobel Medical College Teaching Hospital. A semi structured questionnaire was administered to record the demographic characteristics, co-morbid conditions and use of different drugs. Physical examination was performed to note vital signs and abnormal cardiac and neurological findings. Electrocardiography and echocardiography were done to define electrical and structural heart abnormalities respectively. Biochemical parameters were requested to look for blood hemoglobin, renal

function and INR if clinically indicated. Collected data were entered in microsoft excel. Mean, standard deviation and IQR (Interquartile range) were calculated for descriptive statistics. Tabular presentation was made where necessary.

Results

Mean age was 50.09 (range 22-80) years. The number of RHD was more in females (75.7%) as compared to males (24.2%). Among all patients, 10 (7.1%) were current smoker and 9 (6.4%) were significant alcohol consumer. Mean hemoglobin (Hb) was 12.5 ± 2.02 gm/dl. Mean body mass index (BMI) was 21.42 ± 3.98 kg/m². Mean estimated glomerular filtration rate (eGFR) was 69.48 ± 19.8 ml/min with majority 121 (86.4%) had reduced eGFR of <90 ml/min. Table 1 shows baseline characteristics of the study population.

Penicillin prophylaxis was prescribed for 38 (27.1%) patients. Out of which, 22.8% were on daily oral penicillin and 4.2% were receiving three weekly intramuscular injection of benzathine benzylpenicillin. Beta blockers were the most frequently used drug for heart rate control for patients (51.4%) with both AF and/or symptomatic moderate to severe mitral stenosis. Digoxin was used in 10% and calcium channel blockers were used in 3.5% of patients who had AF. Different diuretic agents were used in 88.5% of patients who had clinical features of systemic or pulmonary congestion. Out of 20 cases of AF, three (15%) had evidence of stroke. Eleven (55%) were receiving aspirin and nine (45%) patients were on warfarin for prevention of stroke and thromboembolism. Out of nine patients receiving warfarin, only four (20%) had therapeutic INR at the time of enrollment. Mitral valve was the most commonly affected valve (82.1%) followed by aortic valve (10%). Both mitral and aortic valves were involved in 7.8 %

patients. Primary TV was involved in 2.8% and secondary TR was present in 52.1% cases.

Table 1. Baseline characteristics of patients with rheumatic heart disease (n = 140)

Characteristics	n
Male: female	34:106
Mean age in years (SD)	50.09 ± 10.99
Mean body mass index in kg/m ² (SD)	21.42 ± 3.98
Mean systolic blood pressure in mmHg (SD)	107.09 ± 13.06
Mean diastolic blood pressure in mmHg (SD)	72.0 ± 9.34
Mean hemoglobin in gm/dl (SD)	12.5 ± 2.02
Mean eGFR (ml/min)	69.48 ± 19.88
Mean heart rate (BPM)	93.74 ± 21.83
≤ 100	95 (67.8%)
> 100	45 (32.1%)
Sinus rhythm	120 (85.7%)
Atrial Fibrillation	20 (14.2%)
Mean LVEF (%)	53.1 ± 8.32
LA diameter in mm (SD)	52.8 ± 7.13
Pulmonary artery hypertension	73 (52.1%)
Smoker	10 (7.1%)
Alcohol use	9 (6.4%)
Hypertension	3 (2.1%)
Diabetes Mellitus	2 (1.4%)
Coronary artery disease	2 (1.42%)

SD: Standard deviation; eGFR: Estimated glomerular filtration rate; BPM: Beat per minute; LVEF: Left ventricular ejection fraction; LA: Left atrium

Table 2. Patterns of drugs used in patients with rheumatic heart disease (n = 140)

Antithrombotics	
None	120 (85.7%)
Aspirin	11 (7.8%)
Warfarin	9 (6.4%)
For rate control	
Beta blockers	72 (51.4%)
Digoxin	14 (10%)
Calcium channels blockers	5 (3.5%)
Diuretics	124 (88.5%)
Loop	101 (72.1%)
Spironolactone	23 (16.4%)

Amiloride	38 (27.1%)
Penicillin prophylaxis	32 (22.8%)
Oral penicillin	6 (4.2%)
Benzathine benzylPenicillin (i.m.)	

Table 3. Use of antithrombotic treatment in rheumatic heart disease with atrial fibrillation (n = 20).

No. of patients with AF	20
No. of patients with AF and stroke	3 (15%)
No. of patients on Aspirin	11 (55%)
No. of patients on warfarin	9 (45%)
No. of patients on warfarin with therapeutic INR (2.0-3.0)	4 (20%)

AF: Atrial fibrillation; INR: International normalized ratio

Table 4. Patterns of valve involvement in patients with rheumatic heart disease (n = 140)

Valves	n
Mitral valve	115 (82.1%)
Aortic valve	14 (10%)
Mitral + Aortic valve	11(7.8%)
Tricuspid Valve (primary)	4 (2.8%)
Tricuspid Valve (Secondary)	73 (52.1%)

Discussion

RHD is a significant complication of RF. Although, RF is equally common in both males and females, RHD tends to be more common in females [6, 7]. In our study, female cases of RHD (75.7%) were more compared to males. It is unclear whether this difference in RHD prevalence is due to greater susceptibility to autoimmune responses following *S. pyogenes* infection or other social factors [8]. People who have suffered RF are more likely to have recurrent episodes and may cause further damage to the cardiac valves. Thus, RHD steadily worsens in people who have multiple episodes of ARF [9]. Primary Prevention is defined as treatment of group A streptococcal sore throat [10] and is indicated only when there is evidence of group A streptococcal infection [11]. Secondary prophylaxis is indicated to

patients with a previous attack of RF or documented RHD. The purpose is to prevent colonization or infection of throat with group A beta-hemolytic streptococci and development of recurrence of RF. In our study, secondary prophylaxis was given in only 27.1% of cases. Although intramuscular injection of benzathine benzylpenicillin every three weeks is advised as the most effective therapy for prevention of recurrent attacks of RF [9], only 4.2% of our patients were receiving benzathine benzylpenicillin. There are a number of interrelated factors associated with underutilization of secondary prophylaxis. RHD remain more prevalent in underprivileged settings. Poor access to health care facility, lack of family support, fear of anaphylaxis, need for long term painful injection etc. could be some reasons for low adherence of treatment and underutilization [11].

The most common cardiac manifestations of RHD are MS followed by aortic valve involvement [12]. In our patients, 82.1% had mitral valve involvement followed by aortic valve (10%) involvement either in the form of regurgitation or stenosis. MS is a slow and progressive condition, takes over decades, usually manifesting in the third to sixth decade of life [13]. Over time, decrease in stroke volume can cause reflex tachycardia which may contribute to an elevated left atrial pressure. The onset of AF secondary to the stenosis may precipitate acute pulmonary edema.

The only medical therapies indicated for these patients are secondary prevention of repeat carditis [14]. Beta blockers can be helpful for symptomatic patients who have tachycardia and /or AF [15]. In our study, 51.4% patients of moderate to severe MS with or without AF were on beta blocker therapy.

Medical management for RHD is provided based on the presence or absence of cardiac symptoms. Most patients with mild

to moderate valvular disease remain asymptomatic for years. There is no role for medical therapy in patients with severe mitral or aortic regurgitation and preserved LV function [16]. Patients who are symptomatic or have decreased LV function should be referred for surgery. If surgical intervention is unavailable or contraindicated, medical therapy for systolic dysfunction is considered a reasonable course of treatment to manage symptoms. Diuretics are used judiciously in patients with evidence of systemic or pulmonary congestion.

Anticoagulants should be administered in the setting of AF or LA thrombus or prior embolic event [15]. In our study, out of 20 cases of MS with AF, 45% patients were on oral anticoagulants and only 20% achieved therapeutic INR at the time of enrollment indicating marked underuse of anticoagulation. A study done in rural part of Nepal showed the marked underuse of anticoagulants, only 22.7% patients with RHD and AF obtained oral anticoagulants [17]. The reasons for under-treatment could be due to include lack of knowledge about treatment guidelines, perceived potential contraindications, fear of bleeding, poor drug compliance, cost and inconvenience of monitoring.

Balloon valvuloplasty is performed if the valve anatomy is favorable and there is no significant mitral regurgitation [15]. Patients who have non-calcified, relatively mobile valves and lack severe leaflet thickening or subvalvular pathology are most likely to have good early and late outcome [18].

Conclusions

The progression of RHD, beginning with *S. pyogenes* infection followed by RF and subsequent cardiac valve damage offers opportunities for the prevention. Improvement in the use of secondary prophylaxis may halt the progression of disease. This study focuses on prescription

pattern of drugs for different indications in patients with RHD. There is a need for improved use of secondary prophylaxis to prevent recurrence of RF and anticoagulants for prevention of stroke in patients with AF.

Ethical Clearance

The study was approved by IERB of Nobel Medical College Teaching Hospital prior to beginning of the study.

Competing interests

None declared

References

- [1] Carapetis JR, Steer AC, Mulholland EK, Weber M. The global burden of group A streptococcal diseases. *The Lancet Infectious Diseases*. 5 (2005) 685–94.
- [2] Prajapati D, Sharma D, Regmi PR et al. Epidemiological survey on Rheumatic fever, Rheumatic heart Disease and Congenital Heart Disease among school children in Kathmandu Valley of Nepal. *Nepalese heart Journal*. 1 (2013) 1-5.
- [3] Regmi PR, Pandey MR. Prevalence of rheumatic fever and rheumatic heart disease in school children of Kathmandu city. *Indian heart J*. 49 (1997) 518-41.
- [4] KC MB, Sharma D, Shrestha MP et al. Prevalence of Rheumatic and Congenital heart Disease in school children of Kathmandu Valley in Nepal. *Indian heart J*. 55 (2002) 615-18.
- [5] Shrestha NR, Karki P, Mahto R, Gurung K, Pandey N, et al. Prevalence of subclinical Rheumatic heart disease in Eastern Nepal: A school based cross sectional study. *JAMA Cardiol*. 1(2016) 89-96.
- [6] Lawrence JG, Carapetis JR, Griffiths K, Edwards K, Condon JR. Acute rheumatic fever and rheumatic heart disease: incidence and progression in the Northern Territory of Australia, 1997 to 2010. *Circulation*. 128 (2013) 1492–1501.
- [7] Parnaby MG, Carapetis JR. Rheumatic fever in indigenous Australian children. *Journal of Paediatrics and Child Health*. 46 (2010) 527–33.
- [8] Carapetis JR, Beaton A, Cunningham MW, Guilherme L, Karthikeyan G, Mayosi BM, et al. Acute rheumatic fever and rheumatic heart disease. *Nature Reviews Disease Primers*. 2 (2016) 15084.
- [9] WHO Expert Consultation on Rheumatic Fever and Rheumatic Heart Disease. Rheumatic fever and rheumatic heart disease: report of a WHO Expert Consultation, 29 October - 1 November 2001. Geneva; 2004.
- [10] Carapetis JR, McDonald M, Wilson NJ. Acute rheumatic fever. *Lancet*. 366 (2005)155–68.
- [11] Harrington Z, Thomas DP, Currie BJ, Bulkanhawuy J. Challenging perceptions of non-compliance with rheumatic fever prophylaxis in a remote Aboriginal community. *Med. J. Aust*. 184(2006) 514–17.
- [12] Manjunath CN, Srinivas P, Ravindranath KS and Dhanalakshmi C. Incidence and patterns of valvular heart disease in tertiary care high volume cardiac center: A single center experience. *Indian Heart J*. 66 (2014) 320–26.
- [13] Horstkotte D, Niehues R and Strauer BE. Pathomorphological aspects, aetiology and natural history of acquired mitral valve stenosis. *European Heart Journal*. 12 (1991) 55-60.
- [14] Gerber MA, Baltimore RS, Eaton CB, et al. Prevention of Rheumatic Fever and Diagnosis and Treatment of Acute Streptococcal Pharyngitis. A Scientific Statement from the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee of the Council on Cardiovascular Disease in the Young, the Interdisciplinary Council on Functional Genomics and Translational Biology, and the Interdisciplinary Council on Quality of Care and Outcomes Research. *Circulation*. 2009
- [15] Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP, Guyton RA, et al. 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: Executive Summary: A Report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. 2014.
- [16] Borer JS, Bonow RO. Contemporary approach to aortic and mitral regurgitation. *Circulation*. 108 (2003) 2432–38.
- [17] Dhungana SP, Sherpa K. Antithrombotic agents and Risk Profile of Patients with Atrial Fibrillation from Rural Part of Nepal. *Journal of Institute of Medicine*. 37 (2015) 16-21.
- [18] Wilkins GT, Weyman AE, Abascal VM, Block PC, Palacios IF. Percutaneous balloon dilatation of the mitral valve: an analysis of echocardiographic variables related to outcome and the mechanism of dilatation. *British Heart Journal*. 60 (1988) 299–308.