

Treatment adherence and its determinants among the rheumatic fever/rheumatic heart disease patients during COVID 19 pandemic – A cross sectional study from Chandigarh, India

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ABSTRACT

Background: Rheumatic heart disease/Rheumatic fever is a non-communicable disease being a major neglected health problem. Recurrent attacks of rheumatic fever can have catastrophic outcomes, therefore regular administration of antibiotics is recommended. During COVID 19 pandemic, people were afraid to approach hospitals hence the compliance and follow up of patients were affected. This study had planned to assess the treatment adherence of patients diagnosed with rheumatic fever/rheumatic heart disease during COVID 19 pandemic and to describe the socio demographic factors, clinical characteristics. This study also determines the factors associated with the treatment adherence. **Methods:** A cross sectional study was conducted among Rheumatic Fever/Rheumatic Heart Disease patients, attending Outpatient department at tertiary care hospital during COVID 19 pandemic. Mean score with confidence interval was calculated for quantitative data. *P* value less than 0.05 is significant. **Results:** The Mean (SD) age of the study participants was 41 ± 14.17 years. Treatment adherence was found to be 94.5 percent among Rheumatic Fever/Rheumatic Heart Disease patients during COVID 19 pandemic. 89.5% of injection benzathine penicillin users had an adherence rate above 80 percent. It was found that the presence of comorbidities (Diabetes/Hypertension/both Diabetes and Hypertension) had a statistically significant association with treatment adherence. **Conclusions:** Rheumatic Heart Disease is a disease of young and middle-age population affecting predominantly females. The overall adherence rate among Rheumatic Fever/Rheumatic Heart Disease patients was high. High time to maintain hospital-based registry to have follow up of patients.

Keywords: COVID-19, rheumatic heart disease/rheumatic fever, treatment adherence

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Received: 08-06-2023

Revised: 21-07-2023

Accepted: 09-08-2023

Published: 21-12-2023

Access this article online

Quick Response Code:



Website:
<http://journals.lww.com/JFMPC>

DOI:
10.4103/jfmpe.jfmpe_941_23

Introduction

Rheumatic fever/Rheumatic heart disease is a noncommunicable disease which remains a major neglected public health problem in India.^[1] Acute rheumatic fever (ARF) is an autoimmune sequelae

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How to cite this article: Ilanchoorian D, Thakur JS, Vijayvergiya R, Jindal AK, Gandhi A, Sagar V. Treatment adherence and its determinants among the rheumatic fever/rheumatic heart disease patients during COVID 19 pandemic – A cross sectional study from Chandigarh, India. *J Family Med Prim Care* 2023;12:3254-61.

caused by Group A streptococcus pharyngitis.^[2] ARF primarily affects the heart, joints, and central nervous system.^[3] Rheumatic heart disease (RHD) is a result of the damage to heart valves as an immunologic sequel to group A streptococcal infections. Rheumatic heart disease predominantly affects children and the younger age groups.^[4] RHD is also the commonest heart disease detected during pregnancy.^[1] Early diagnosis, including echocardiographic screening, holds a promise for both raising awareness and developing preventive strategies that decrease the need for intervention.^[5]

Worldwide, there are over 15 million cases of RHD with 282,000 new cases occurring annually. Two percent of all deaths from cardiovascular disease is due to RHD.^[1] Although overall prevalence has decreased in India over 3–4 decades, it continues to be a major health problem. In India, the prevalence of RHD is around 5–7 per thousand population in 5–15 years of age and about 1 million across all age groups. RHD persists in almost all WHO regions. In the South-East Asia region, India accounts for the largest contribution of about 27% of all cases globally.^[6] Still, RHD is a leading cause of cardiovascular morbidity and mortality among children and young adults of low and middle-income countries.^[7] The World Heart Federation has set a target to bring about a 25% reduction in premature deaths from rheumatic fever and RHD among individuals under the age of 25 years by the year 2025.^[8]

Secondary prophylaxis with regular intramuscular injection of benzathine penicillin G (BPG) is a key component of ARF and RHD control programs. The World Health Organization (WHO) recommends 3–4 weekly BPG continued for a duration dependent on factors including age, time since the last episode, risk of streptococcal infections in the area, and presence of RHD. According to WHO guidelines, secondary prophylaxis should continue for at least 5 years after the last episode of ARF or until the age of 18 years (whichever is longer) and for a greater length of time in case of carditis or RHD. However, it varies with local authorities who give slightly varying recommendations for the frequency and duration of BPG injections.^[9] The individual must believe that the efficacy of treatment is associated with adherence.^[10] A significant risk factor for the recurrence of ARF is noncompliance to the secondary prophylaxis. Regular BPG injection is vital to prevent disease morbidity and cardiac sequelae in affected ARF and RHD patients. Poor uptake remains a challenge to ARF/RHD control programs.

The data on incidence and prevalence on a nationally represented sample are lacking. The documented prevalence of RHD is varied in different Indian studies, because of the inclusion of different populations at different point of times and usage of different screening methods for the diagnosis. Majority of them are individual investigator-led survey studies, performed in school children of urban and some rural areas.

There is a need for establishing a population-based surveillance system in the country for monitoring trends, management

practices, and outcomes to formulate informed guidelines for initiating interventions for prevention and control of RHD.^[11] The registry will give the required database of patients regarding their treatment, mortality and comorbidities, and for good follow-up of the patients. It is useful for recording prophylaxis delivery, the recall of patients who are due for, or miss doses of, BPG, and informing health education and health promotion programs. Reliable data on treatment practices and patient compliance with secondary prophylaxis and oral anticoagulation regimens will help policymakers in developing countries in formulating strategies to improve adherence to important treatments, thereby improving patient outcomes. There is no structured program at a national level for prevention and control of RF/RHD.^[12]

India imposed a Nationwide lockdown from March 24, 2020, to contain the COVID-19 crisis.^[13] People were asked to stay back in their houses and public movement was restricted except for emergencies and essential services. This has reduced the accessibility of millions to non-COVID health-care services.

There is no specific study regarding the treatment adherence for RF/RHD patients during COVID-19 pandemic. We conducted a study to know about treatment adherence and characteristic features among RF/RHD patients attending cardiology/pediatric rheumatology clinic at tertiary care hospital during the COVID-19 pandemic.

Materials and Methods

This was a cross-sectional study conducted from December 1, 2020, to May 31, 2021, including patients of any age group with rheumatic fever/RHD attending the outpatient clinic at the department of cardiology, advanced cardiac center, and pediatric rheumatology clinic at the department of pediatrics, advanced pediatrics center, of a tertiary care hospital in Chandigarh. Patients with primary diagnosis of valvular disease other than RHD (e.g., infective endocarditis, congenital, posttraumatic, dystrophic, and degenerative lesions, cardiomyopathy, and ischemic or inflammatory diseases) and those who did not give consent were excluded.

Sample size estimation and sampling technique

A sample size of 110 was calculated using $4 \times pq/L^2$ formula by using prevalence from previous study as 53%^[11] and absolute precision of 10% and 80% power. A nonresponse rate of 10% was added to produce the final sample size of 110. All the eligible patients presenting to cardiology OPD (ACC) and pediatric rheumatology clinic (APC), of tertiary care hospital during the period of December 1, 2020, to May 31, 2021, were enrolled until the sample size was achieved with inclusion and exclusion criteria.

The main outcomes of interest were treatment adherence during COVID-19 pandemic from December 1, 2020, to May 31, 2021, sociodemographic, clinical features, and factors associated with nonadherence to treatment among study participants.

Data collection

The patients were briefed about the study using Patient Information Sheet. OPDs were conducted through teleconsultation due to ongoing COVID-19 pandemic. Only a few necessary patients were called for physical OPD. Patients were enrolled and enquired at the time of OPD visit (Physical/Tele). The consent and assent were obtained from parents and children before enrolling the patients in the study. Sociodemographic characteristics, clinical details, echocardiographic findings, medications prescribed along with current status of the patient, and their adherence to medication during COVID-19 pandemic were obtained using questionnaire by face-to-face and telephonic interviews during the study period. The socioeconomic condition was assessed by the Modified B.G. Prasad Scale (2020).

A predesigned, pretested, semistructured, mono-lingual (English) questionnaire was used to collect the data from the study participants. The questionnaire was pretested in 10% of the study participants and all necessary amendments were made before using it for data collection. The rate of adherence to monthly BPG injection was determined by calculating the percentage of administered doses based on the following formula.^[19]

$$\text{Adherence rate} = \frac{\text{Number of BPG doses actually administered to specific patient}}{\text{Number of BPG doses expected for that specific patient}} \times 100$$

Data analysis

Epicollect 5 software was used to collect the quantitative data and analysis was done using SPSS version 21. Continuous variables were expressed in mean \pm SD or median \pm IQR; and categorical variables were represented as proportions. Binary logistic regression analysis was used to identify the determinants of adherence. *P* value less than 0.05 was considered statistically significant.

Operational definitions

Adherence to monthly BPG

Patients were considered as adherent and non-adherent to monthly BPG prophylaxis if they received $\geq 80\%$ and $< 80\%$ of their monthly prescribed doses of BPG, respectively.^[19]

Results

Overall, 110 rheumatic fever/RHD patients during the study period were recruited from both cardiology OPD and pediatric rheumatology clinic.

Sociodemographic characteristics of participants

The mean (SD) age of the study participants was 41 years. Out of the study participants, majority were females (65.5%).

The minimum age was 11 years and maximum age was 66 years. Majority of the RF/RHD patients attending the

study setting were from Punjab (39.1%). More than half of the participants (59.1%) belonged to joint family and majority of the participants (48.6%) belonged to class I Modified B.G. Prasad's Scale (2020) based upon per capita monthly income. The sociodemographic characteristics of the study participants are enumerated in Table 1.

Clinical characteristics of participants

Among 110 participants, 4 (3.6%) participants had ARF, while 106 (96.4%) had established RHD. Among 110 participants, all were diagnosed as rheumatic fever/RHD by echocardiography (100%).

Duration from diagnosis was ≤ 10 years in 68.2% of participants. Among 110 participants, 27.9% participants were waiting for

Table 1: Sociodemographic details of the participants attending cardiology/pediatric rheumatology clinic (n=110)

| Variables | Frequency | % |
|---------------------------------------|-----------|-------|
| <i>n</i> | 110 | 100.0 |
| Gender | | |
| Female | 72 | 65.5 |
| Male | 38 | 34.5 |
| Age | | |
| More than 18 years | 100 | 90.9 |
| 0–18 years | 10 | 9.1 |
| Place of residency | | |
| Punjab | 43 | 39 |
| Haryana | 24 | 21.8 |
| Himachal Pradesh | 14 | 12.7 |
| Chandigarh | 9 | 8.2 |
| Uttar Pradesh | 9 | 8.2 |
| Jammu and Kashmir | 6 | 5.5 |
| Bihar | 5 | 4.5 |
| Marital status | | |
| Married | 92 | 83.6 |
| Unmarried | 18 | 16.4 |
| Type of family | | |
| Joint | 65 | 59.1 |
| Nuclear | 45 | 40.9 |
| Number of family members | | |
| 5–8 | 70 | 63.6 |
| 1–4 | 22 | 20 |
| 9–13 | 18 | 16.4 |
| Education | | |
| Primary | 37 | 33.3 |
| Higher secondary | 25 | 22.5 |
| Graduate | 24 | 21.6 |
| Secondary | 13 | 11.7 |
| Uneducated | 11 | 9.9 |
| Socioeconomic class (BG Prasad Scale) | | |
| I | 54 | 48.6 |
| II | 26 | 23.4 |
| III | 27 | 24.3 |
| IV | 0 | 0 |
| V | 3 | 2.7 |

their valve surgery and 14.4% participants had valve surgery already done. Among 110 participants, 3 participants (2.7%) had a history of COVID-19-positive status. Clinical characteristics of the study participants are enumerated in Table 2.

Participants had single as well as multiple valve involvement. Mitral valve involvement such as mitral stenosis and mitral regurgitation was seen in 76 (69.1%) and 71 (64.5%) participants, respectively. Aortic valve involvement was seen in 21 (19.1%) participants. In tricuspid valve involvement, tricuspid regurgitation was commonly found in 31 (28.2%) participants. Among 110 patients, 25 (22.7%) were on secondary prophylaxis, in which only 19 (17.3%) patients were on injection benzathine penicillin, 2 (1.8%) were on oral penicillin, and 4 (3.6%) were on erythromycin. Remaining 85 (77.3%) were only receiving other medicines like beta-blockers, diuretics, and anticoagulants. Majority of the participants were in overweight category (47.3%); 40.9% participants were in the normal range of BMI; and 10.0% and 1.8% participants were obese and underweight, respectively.

Treatment adherence of diagnosed RF/RHD patients

The treatment adherence rate of the patients in our study was 94.5% (104/110). Among six patients (5.5%) who were not adherent, two were on injection benzathine penicillin, one was

on oral erythromycin, and three were on other medications such as oral anticoagulants and beta-blockers. Among 19 patients who were taking injection BPG, 17 (89.5%) were adherent, with the adherence rate above 80%, and 2 (10.5%) were nonadherent, with the adherence rate below 80%. The stated reason for missing the medication during COVID-19 pandemic was: fear of going to hospital (1), forgot taking the medication (2), nonavailability of injection BPG (2), and no specific reason (1).

Association between the sociodemography and treatment adherence

There was no significant association found between sociodemographic factors and treatment adherence [Table 3].

It was found that the presence of comorbidities (diabetes/hypertension/both diabetes and hypertension) had a statistically significant association with treatment adherence. Other factors like age, gender, place of residence, current disease status, and COVID status did not have statistically significant association with adherence to treatment in the diagnosed rheumatic fever/RHD patients during COVID-19 pandemic [Tables 3 and 4].

The estimates of binary logistic regression show that presence of comorbidities (diabetes mellitus with hypertension) is a strong predictor for nonadherence to treatment among RF/RHD patients (OR = 46.39, 95% CI). Binary logistic regression shows that nonadherence to treatment was found to be 46.39 times higher in patients with diabetes and hypertension compared with those without these comorbidities.

Table 2: Clinical characteristics of rheumatic fever/rheumatic heart disease patients attending the cardiology/pediatric rheumatology clinic

| Variables | Frequency (n=110) | Percentage (100) |
|---|-------------------|------------------|
| Diagnosis | | |
| ARF* | 4 | 3.6 |
| RHD* | 106 | 96.4 |
| Documented past RF | 0 | 0 |
| Mode of diagnosis | | |
| Auscultation | 0 | 0 |
| Echocardiography | 110 | 100 |
| Duration since diagnosis of RHD (years) | | |
| >10 years | 75 | 68.2 |
| ≤10 years | 35 | 31.8 |
| Comorbidities | | |
| No comorbidities | 103 | 93.6 |
| DM* | 2 | 1.8 |
| HTN* | 2 | 1.8 |
| DM + HTN | 2 | 1.8 |
| Asthma | 1 | 0.9 |
| COVID-19 status | 3 | 2.7 |
| Current status of the patient | | |
| Stable | 84 | 75.7 |
| Waiting for valve surgery | 31 | 27.9 |
| Valve surgery done | 16 | 14.4 |
| NYHA *Grade 2 | 13 | 11.7 |
| Heart failure | 1 | 0.9 |

*ARF=Acute rheumatic fever, RHD=rheumatic heart disease, DM=diabetes mellitus, HTN=hypertension, NYHA=New York heart association

Discussion

The outcomes of the study were treatment adherence and profile of RF/RHD patients attending a tertiary care center. Treatment adherence monitoring for RF/RHD has been done in pre-COVID times but COVID pandemic situation has put forward another level of challenge as far as treatment adherence is concerned. This study explored the treatment adherence of the diagnosed RF/RHD patients during COVID-19 pandemic and their sociodemographic and clinical characteristics along with factors associated with adherence.

Treatment adherence is of utmost importance in prevention of recurrence of RF/RHD. The study findings suggest that a treatment adherence to all medications during COVID-19 pandemic among RF/RHD patients was 94.5%. A study in Bangladesh conducted during 2017 found 50% mean treatment adherence to medications among RF/RHD patients.^[14] In our study, adherence rate to injection benzathine penicillin was calculated separately with a formula and found that 89.5% (17 of 19 participants) had an adherence rate above 80%. This compares well (92%)^[15] with previous Indian studies and also Ethiopian study which had an overall adherence rate of 80.6%.^[16] Studies conducted in other rural areas of Northern India recorded higher

Table 3: Sociodemographic factors associated with treatment adherence of medications in diagnosed rheumatic fever/ rheumatic heart disease patients during COVID-19 pandemic

| Variables | | Total n (%) | Adherent n (%) | Nonadherent n (%) | Chi-square value | P |
|--------------------|-------------------|----------------|-------------------|----------------------|------------------|-------|
| Age | Less than 18 | 10 (9.1) | 9 (8.2) | 1 (0.9) | 0.754 | 0.385 |
| | More than 18 | 100 (90.9) | 96 (87.3) | 4 (3.6) | | |
| Gender | Male | 38 (34.5) | 35 (31.8) | 3 (2.7) | 1.501 | 0.338 |
| | Female | 72 (65.5) | 70 (63.6) | 2 (1.8) | | |
| Marital status | Married | 92 (83.6) | 88 (80.0) | 4 (3.6) | 0.51 | 1.0 |
| | Unmarried | 18 (16.4) | 17 (15.5) | 1 (0.9) | | |
| Place of residence | | | | | 4.29 | 0.6 |
| | Punjab | 43 (39.1) | 39 (35.5) | 4 (3.6) | | |
| | Chandigarh | 9 (8.2) | 9 (8.2) | 0 (0.0) | | |
| | Haryana | 24 (21.8) | 23 (20.9) | 1 (0.9) | | |
| | Himachal Pradesh | 14 (12.7) | 14 (12.7) | 0 (0.0) | | |
| | Jammu and Kashmir | 6 (5.5) | 6 (5.5) | 0 (0.0) | | |
| | Uttar Pradesh | 9 (4.5) | 5 (4.5) | 0 (0.0) | | |
| | Bihar | 5 (4.5) | 5 (4.5) | 0 (0.0) | | |
| Education | | | | | | |
| | Uneducated | 11 (10.0) | 10 (9.1) | 1 (0.9) | | |
| | Primary | 37 (33.6) | 36 (32.7) | 1 (0.9) | | |
| | Secondary | 13 (11.8) | 13 (11.8) | 0 (0.0) | | |
| | Higher secondary | 25 (22.7) | 24 (21.8) | 1 (0.9) | | |
| | Graduate | 24 (21.8) | 22 (20.0) | 2 (1.8) | | |
| B.G Prasad Scale | | | | | 0.34 | 0.95 |
| | Class I | 54 (49.1) | 51 (46.4) | 3 (2.7) | | |
| | Class II | 26 (23.6) | 25 (22.7) | 1 (0.9) | | |
| | Class III | 27 (24.5) | 26 (23.6) | 1 (0.9) | | |
| | Class V | 3 (2.7) | 3 (2.7) | 0 (0.0) | | |
| Type of family | | | | | 0.94 | 0.647 |
| | Nuclear | 45 (40.9) | 44 (40.0) | 1 (0.9) | | |
| | Joint | 65 (59.1) | 61 (55.5) | 4 (3.6) | | |

compliance rate of more than 90%,^[15] whereas compliance rate to secondary prophylaxis in Bihar study was only 53%,^[11] which was comparable to a study conducted in Jamaica (48.7%),^[10] and 54% in African study.^[17] In an aboriginal community in Australia, 59% of patients were found to be adherent by Harrington, who had received more than 75% of their prescribed injections.^[18] The variability in levels of adherence may reflect the different systems in which these studies were done, duration of follow-up, individual study design, and different factors that might influence adherence.

Analyzing the association of patient factors with adherence levels provides insight into those groups at particular risk of recurrence through poor adherence. Only one factor was having significance with treatment adherence that was present with both diabetes and hypertension comorbidity. It has been described in other studies that patients with comorbidities, such as diabetes, hypertension, and other chronic diseases, were more likely to be poorly adherent to medications. Sociodemographic factors were not having a significant association with adherence. There are similar studies by Stewart in Australia^[19] and Musoke in Africa^[17] which found no significant demographic factors associated with adherence. A cross-sectional study conducted in Bangladesh concluded that risk factors like gender, marital

status, education, family size, and duration of diagnosis were significantly associated with RHD.^[14]

The commonest reason reported for missing the medication was forgetting to take medicines and non-availability of injection benzathine penicillin (33.3%). This was closely followed by fear of going to hospital (16.7%) and no specific reasons (16.7%). There are similar reports in a study where forgetting was a major reason for missing injections. A study in Bangladesh had 70% of participants who reported forgetting to take their medicine as the cause for missing.^[14] A study by Prasad conducted in Bihar found that majority had no specific reason for being non-compliant to medication.^[11] Beside this, a study in Fiji reported lack of awareness, feeling well, access, and transport cost as determinants of missing the doses. They recommended reminder strategies, particularly phone-based reminders which were considered helpful by 94% of participants to improve the adherence.^[20] This could be due to ignorance of the disease, which could be dealt with counseling of patients and their relatives, regarding the importance of secondary prophylaxis. Many patients missed injections as they felt healthy or did not understand why injections were needed which was one of the reasons in Engelman D *et al.* study.^[20] Another important factor playing a very important

Table 4: Clinical factors associated with treatment adherence of medications in diagnosed rheumatic fever/rheumatic heart disease patients during COVID-19 pandemic

| Variables | | Total n (%) | Adherent n (%) | Non-adherent n (%) | 8 | P |
|----------------------|---------------------------|-------------|----------------|--------------------|----------|----------|
| BMI | | | | | 7.13 | 0.06 |
| | Underweight | 2 (1.8) | 2 (1.8) | 0 (0.0) | | |
| | Normal | 45 (40.9) | 45 (40.9) | 0 (0.0) | | |
| | Overweight | 52 (47.3) | 49 (44.5) | 3 (2.7) | | |
| | Obese | 11 (10.0) | 9 (8.2) | 2 (1.8) | | |
| Diagnosis | ARF | 4 (3.6) | 3 (2.7) | 1 (0.9) | 4.00 | 0.17 |
| | RHD | 106 (96.4) | 102 (92.7) | 4 (3.6) | | |
| Valvular involvement | Mitral stenosis | 76 (69.1) | 73 (66.4) | 3 (2.7) | 0.20 | 0.64 |
| | Mitral regurgitation | 71 (64.5) | 66 (60.0) | 5 (4.5) | 2.87 | 0.15 |
| | Tricuspid regurgitation | 31 (28.2) | 29 (26.4) | 2 (1.8) | 0.36 | 0.61 |
| | Aortic stenosis | 4 (3.6) | 3 (2.7) | 1 (0.9) | 4.00 | 0.17 |
| | Aortic regurgitation | 17 (15.5) | 16 (14.5) | 1 (0.9) | 0.08 | 0.57 |
| Treatment received | IM penicillin | 19 (17.3) | 17 (15.5) | 2 (1.8) | 6.46 | 0.09 |
| | Oral penicillin | 2 (1.8) | 2 (1.8) | 0 (0.0) | | |
| | Erythromycin | 4 (3.6) | 3 (2.7) | 1 (0.9) | | |
| | Other | 85 (77.3) | 83 (75.5) | 2 (1.8) | | |
| Comorbidities | Diabetes mellitus | 2 (1.8) | 2 (1.8) | 0 (0.0) | 9.86 | 0.04 |
| | Hypertension | 2 (1.8) | 2 (1.8) | 0 (0.0) | | |
| | DM + HTN | 2 (1.8) | 2 (1.8) | 0 (0.0) | | |
| | Asthma | 1 (0.9) | 1 (0.9) | 0 (0.0) | | |
| | No comorbidities | 103 (93.6) | 99 (90.0) | 4 (3.6) | | |
| COVID-19 status | | 105 (95.5) | 3 (2.7) | 102 (92.7) | 0.147 | 1.00 |
| Current status | Stable | 84 (76.4) | 79 (71.8) | 5 (4.5) | 1.621 | 0.33 |
| | Heart failure | 1 (0.9) | 1 (0.9) | 0 (0.0) | 0.04 | 1.00 |
| | NYHA grade | 13 (11.8) | 13 (11.8) | 0 (0.0) | 0.702 | 1.00 |
| | Waiting for valve surgery | 31 (28.2) | 30 (27.3) | 1 (0.9) | 0.17 | 1.00 |
| | Valve surgery done | 16 (14.5) | 16 (14.5) | 0 (0.0) | 0.89 | 1.00 |
| Treatment duration | Less than 10 years | 75 (68.2) | 72 (65.5) | 3 (2.7) | 0.16 | 0.65 |
| | More than 10 years | 35 (31.8) | 33 (30.0) | 2 (1.8) | | |

role in treatment adherence is the availability of injection benzathine penicillin. Availability of penicillin is a burning issue in most of the states in India.^[12] RHD is a significant health problem in our country. Prasad *A et al.* suggested in their study that government health care can provide regular secondary prophylaxis free of cost.^[11] Regular BPG injection is vital to prevent disease morbidity and cardiac sequelae in affected ARF and RHD patients. In our study, 25 patients were on secondary prophylaxis, in which 19 were on benzathine penicillin, 2 were on oral penicillin, and 4 were on erythromycin. Remaining were receiving other medications. Similarly, study conducted by Mehta *A et al.* found that 436 patients were prescribed with injection benzathine penicillin, 11 were prescribed with oral erythromycin tablets, and 4 were on oral penicillin V tablets for secondary prophylaxis.^[7]

Though India contributes to nearly 25–50% of the global burden, very few studies have addressed the pattern of the disease involvement among patients with RHD in India. A multinational REMEDY (Global RHD Registry) registry with 3,343 participants enrolled from 25 sites in 12 African countries, Yemen, and India discussed the characteristics, complications, and treatment gaps in patients of RHD, but the registry had a small cohort.^[8] More recently, study was

conducted in Shimla with HP-RHD (Himachal Pradesh Rheumatic Heart Disease) registry to know about the clinical characteristics, complications, and treatment practices among 2,005 enrolled patients.^[21]

This study highlights multiple findings. First, the patients with RF/RHD were middle aged (mean age [SD] 41 ± 14.17 years), largely female (65.5%) with class I socioeconomic status (48.6%) based on per capita monthly income, and 33.3% had completed primary level schooling. Majority of the patients were from Punjab (39.1%) and 59.1% belong to the joint family. This is one of the risk factors in RF/RHD patients as proved in study done in Australia where crowding was the most assessed factor^[22] and RF/RHD continues to be a public health problem in Punjab, India.^[23] Female population is affected largely which is similar to other studies showing 66.2%^[24] and in VALVAFRIC study (59.7%).^[25] In an Indian study, 6-year results obtained from HP-RHD registry also stated that RHD affected predominantly female subjects (72.3%).^[21] Second, majority were diagnosed with RHD (96.4%) while patients with ARF were around 3.6%. Differential patterns of valvular involvement were seen, in which majority of the patients had mitral valve involvement with mitral stenosis (69.1%) being the commonest. This is similar to the study conducted in Shimla by Negi which stated mitral valve was

the commonest affected valve (83.3%)^[21] and more recent study by Prasad stated mitral valve to be the most commonest (98% of cases).^[11] Third, 75.7% were stable in the current status of the patients, 27.9% were waiting for valve surgery, and 14.4% patients already had valve surgery done.

RHD is a sequelae of rheumatic carditis resulting from immune-inflammatory injury to cardiac valves triggered by Group A beta hemolytic streptococcal acute pharyngitis.^[26] This contributes to the cardiovascular-related loss of disability-adjusted life years in children.^[8] In this study, mean age was similar to study by Negi (median age: 40 years)^[27] but its 12 years more than reported in the REMEDY registry^[8] and Bihar study by Prasad (median age: 13 years).^[11] This could be an indicator of the declining prevalence of RF/RHD in our part of the world; however, more studies are required and we cannot come to conclusion with our study because of the small sample size. The COVID-19 status among the study participants was seen in 2.7% in our study.

Strengths and limitations

This was the first study to assess the treatment adherence, clinical characteristics, and factors of treatment adherence of RF/RHD patients during the COVID-19 pandemic in India. We had assessed adherence for all the medicines and calculated adherence rate for injection benzathine penicillin among them. Our study is not without limitations. Foremost, temporal association cannot be established. The results of the study cannot be generalized since it has inherent selection bias due to the patients being from a single-center, hospital-based study. There can also be recall bias among participants.

Conclusion

RHD is a disease of young and middle-age population affecting predominantly females. The overall adherence rate among RF/RHD patients was high (94%). The current status of the patients in majority was stable (75.7%) and 93.6% had no other comorbidities. Higher number of participants (89.5%) had an adherence rate above 80% among injection BPG users. Availability of the injection benzathine penicillin should be ensured since it was quoted as one of the main reasons for missing the medication. RF/RHD patients with comorbidities must be closely followed-up, and a reminder system may be introduced in the current settings for improving the compliance.

Recommendations

The availability of injection benzathine penicillin should be noted. Awareness campaigns about RHD/rheumatic fever should be conducted. It is high time to maintain a hospital-based registry to have a record in the hospital so that it will be easy to assess the follow-up and treatment adherence of the patients. Sustainability is very essential for the registry. This has been discussed with PIO of Chandigarh registry and is already considered to be included

in the registry program for assessing long-term compliance and encouraging patients to enroll.

List of abbreviations

| Abbreviation | Definition |
|--------------|--|
| ACC | Advanced cardiac center |
| APC | Advanced pediatrics center |
| ARF | Acute rheumatic fever |
| BMI | Body mass index |
| BPG | Benzathine penicillin G |
| DM | Diabetes mellitus |
| GAS | Group A streptococcus |
| HLA | Human leucocyte antigen |
| HP-RHD | Himachal Pradesh Rheumatic Heart Disease |
| HTN | Hypertension |
| NYHA | New York heart association |
| OPD | Outpatient department |
| PI | Principal investigator |
| PIS | Patient information sheet |
| REMEDY | Global rheumatic heart disease registry |
| RF | Rheumatic fever |
| RHD | Rheumatic heart disease |
| TGF | Transforming growth factor |

Ethical policy and institutional review board statement

Ethical clearance was obtained from the Institute Ethics Committee (Ref No: NK/7086/MD/254).

Patient declaration of consent statement

The consent form had two parts: information for the participants (PIS) and the informed consent form. For the age group of >7 years, the assent form was taken. As the interview was conducted telephonically, the consent from the participant was taken verbally.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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