ORIGINAL RESEARCH

Adherence to Secondary Prophylaxis and Risk Factors Among Patients with Rheumatic Heart Disease at Public Hospitals in Addis Ababa, Ethiopia, 2021–2022

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Background: Rheumatic heart disease is a preventable cardiovascular disease that affects over forty million people worldwide. Poor adherence to secondary prophylaxis increases the risk of recurrent acute rheumatic fever. Studies on adherence to secondary prophylaxis in Ethiopia are scarce. Thus, this study aimed to determine adherence to secondary prophylaxis and risk factors among patients with rheumatic heart disease.

Methods: Facility-based cross-sectional study design was employed to conduct this study from December 25/2021 to January 22/2022. The study was performed among rheumatic heart disease patients in randomly selected four public hospitals in Addis Ababa. Data were collected through face-to-face interviews using a structured questionnaire from follow-up patients after using a pre-tested questionnaire. Data were entered into EPI info version 7.2 and exported to SPSS version 26 for analysis. Multivariable logistic regression analysis was performed using variables with a p-value of less than 0.25 in bi-variable logistic regression analysis. Adjusted Odds Ratio (AOR) with a 95% confidence interval was estimated to determine the strength of association with poor adherence. Statistical significance multivariable logistic regression analysis was declared when the p-value is <0.05.

Results: Three hundred and eighty-one study participants completed the study with a response rate of 95%. The mean age of the respondents was 26.45 ±10.5 years. The overall poor level of adherence was 29.1% (95% CI: 24.7–33.8%). Rural residency (AOR = 2.637, 95% CI: 1.068–6.513), living with > family members (AOR = 2.879, 1.282–6.465), living more than 30 km from health clinic (AOR = 3.247, 95% CI: 1.051–10.033), lack of penicillin V (AOR = 6.772, 95% CI: 3.234–14.177) and fear of catching Covid-19 (AOR = 0.04, 95% CI: 0.014–0.114) were independently associated with risk factors for poor adherence.

Conclusion: Considerable proportion of patients with rheumatic heart disease in Addis Ababa had a poor level of adherence to secondary prophylaxis. Stakeholder's better supply penicillin regularly and administers them at primary health-care facilities.

Keywords: rheumatic heart disease, secondary prophylaxis, adherence

Introduction

Acute rheumatic fever (ARF) results from an autoimmune response to pharyngitis caused by a group of streptococcus (GAS) bacterial infections. It involves the joints, brain, skin, and heart muscles. Long-term damage to cardiac valves caused by a single severe episode or multiple recurrent episodes of ARF is known as rheumatic heart disease (RHD).[1] Rheumatic fever mostly affects children and adolescents in low- and middle-income countries, especially in areas where

poverty is widespread and access to health services is limited. People living in overcrowded and poor conditions, including in Ethiopia, are at risk of developing this disease.[2,3]

The most effective treatment for preventing further infection is benzantine penicillin G (BPG), which is administered via intramuscular injection every month. Alternatively, daily oral penicillin V can be given to a selected number of patients if compliance is guaranteed.[2,4] Secondary prophylaxis is the continuous administration of penicillin to patients with a previous attack of acute rheumatic fever or well-documented RHD. The rational use of secondary prophylaxis is a critical cost-effective intervention for preventing morbidity and mortality related to ARF and RHD. Patients with RHD are expected to receive at least 80% of the annual prescribed injections. Otherwise, there is a higher risk of recurrent ARF and complications.[5] Adherence is the extent to which a person's behavior in taking medication corresponds with the recommendations agreed upon by health-care providers.[6] A patient is classified under good adherence when he/she takes was ≥80% of secondary prophylaxis for RHD (if injected more than nine times per year). Whereas, poor adherence is considered when the patient missed secondary prophylaxis for RHD at least three times per year.[7]

In 2019, an estimated 40.5 million cases of RHD were reported causing 306,000 deaths annually.[8] The burden of the problem decreased significantly in the developed world. However, the morbidity and mortality in developing countries due to limited access to cardiac surgery and the cost related to surgical intervention remains high.[9] Africa, Southeast Asia, and the Western Pacific regions are the primary victims accounting for 84% of all cases and 80% of estimated deaths in 2015. Socioeconomic and environmental factors such as poor housing, undernutrition, overcrowding, and poverty are contributors to the incidence, magnitude, and severity of ARF and RHD.[10] The prevalence of RHD in East Africa is 17.9 cases per 1000 school children.[11]

Global adherence to treatment of chronic diseases including RHD in developed countries is only 50%, particularly affecting the poor population.[6,7] Due to poor levels of adherence to secondary prophylaxis in patients with RHD continues to report high rates (7%) of an advanced stage of heart valve injury.[12] Poor adherence to secondary prophylaxis increases ARF recurrence, worsens RHD, and rapidly leads to hospitalization and surgical intervention.[13] In the Gambia, poor adherence to secondary prophylaxis leads to recurrence of ARF by 53.3%, worsening of RHD by 25%, and leading to progression to chronic valvular heart disease and increased surgery by 9.9%.[14] Only one per cent of the world's cardiothoracic surgeons are found in Africa with limited surgical intervention settings. Thus, most patients with chronic valvular heart disease die without undergoing cardiac surgery.[15] Besides, poor adherence is associated with socioeconomic status, condition-related factors, patient-related factors, therapy-related factors, and health system-related factors.[5,6,16,17]

In Ethiopia, studies on adherence to secondary prophylaxis and associated factors are limited. There is only one study conducted among 145 adult patients in a single institution in Addis Ababa among them 30.3% were poor adherence and 37% were from Jimma zonal hospitals. The most common secondary prophylaxis medication in Ethiopia.[16] This compromises the generalizability of the findings. In addition, all possible factors associated with poor adherence are not uncovered in Ethiopia. Therefore, this study aimed to determine the level of adherence to secondary prophylaxis and risk factors in patients with RHD at selected public hospitals in Addis Ababa, Ethiopia.

Methods and Materials
Study Area and Period
The study was conducted in Addis Ababa public hospitals. Addis Ababa is the capital city of Ethiopia. It is also the largest city in the country with a total population of 3,384,569 as reported by the 2007 census.[18] There are 12 public hospitals in Addis Ababa to provide cardiac follow-up. Four hospitals were selected using a simple random sampling method, which was Tirunesh Beijing hospital, Zewditu memorial hospital, Yekatit 12 hospital, and Saint Peter Specialized hospital. This included 1883 total RHD patients from the District Health Information Software 2 (DHIS 2) registration who were diagnosed before one year and 917 RHD patients appointed from appointment sheets during the study period. The study was conducted from December 25/2021 to January 22/2022.

Study Design and Population
A cross-sectional study was conducted to assess the level of adherence to secondary prophylaxis and the risk factors among patients with RHD at public hospitals in AA, Ethiopia. All registered patients at RHD clinic in Addis Ababa

public hospitals were the source population and all registered patients at RHD in selected public hospitals of Addis Ababa were the study population. A selected RHD patient who was interviewed at the RHD clinic during the collection period at a selected public hospital in Addis Ababa was the study unit.

Inclusion and Exclusion Criteria

Patients with RHD who were diagnosed at least one year before the study period were included. However, patients who were critically ill and had no attendants were excluded.

Sample Size Determination and Sampling Procedure

The required sample size was calculated using the single population proportion formula since there was a previous study in Jimma zone hospitals. Poor adherence to secondary prophylaxis was 37%[9] and desired precision of 5% and 95% confidence intervals were used for the calculation; the sample size was 358. With a 10% non-response rate, the final sample size was 394.

Sample Size Determination for the Second Objective

By using the double population proportion formula, the following sample size calculation was used for each independent variable by open epi info software 95% CI with 5% margin of error, 80% power, and 1 ratio of exposed to non-exposed outcomes. Three hundred and sixty-four is the largest sample size among others; so, by adding a 10% non-response rate it becomes 400 which is higher than 394; therefore, the final sample size of the study was 400.

Simple random sampling was used to select four hospitals. Next, the calculated sample size (400) was distributed to four hospitals using probability proportional to the size and the numbers of RHD patients required for the study in four hospitals were determined (Figure 1).

Therefore, 400 study participants were sampled from respective Hospitals by a simple random sampling method from a RHD clinic sheet using the patient's medical registration number sampling frame.

Data Collection and Procedures

The questionnaire was adapted through reviewing different literature and previous similar studies.[5,6,16] The questionnaire was translated to the local language Amharic and data were collected by face-to-face interviews with patients or their attendants/guardians for pediatric patients who came for follow-up during the study period. Medical data were reviewed from patient records. Eight data collectors and one supervisor were recruited among health-care providers who work in cardiac chronic outpatient departments.

Data Quality Control and Management

One day of training for 8 nurses and one physician was given on data collection methods and a pretest was done using 5% of 60 RHD patients at Alert hospital. The purpose of the pre-test was to ascertain patients 'understanding of the items asked and the appropriateness of responses and time required to fill out the questionnaire. A reliability estimate was conducted and Cronbach's alpha was 0.83 for adherence factors to secondary prophylaxis measurement tools. Daily supervision was conducted by the supervisor and principal investigator during data collection and data were checked for completeness on daily basis.

Data Analysis Procedure

After the data collection is completed, the data were checked for properly collected and recorded, coded, entered, and cleaned into EPI Info version (7.2) and exported to package for social science (SPSS) window version 26 for analysis. Descriptive statistics with including frequency, proportion, and mean of variables were used for reporting the descriptive results. Variables with a p-value <0.25 in the bi-variable logistic regression analysis were fitted to multiple logistic regression analysis. In the multivariate logistic regression model, fitness was tested using the Hosmer-Lemeshow goodness-of-fit. Adjusted odds ratio (AOR) with a 95% confidence interval was estimated to assess the strength of the
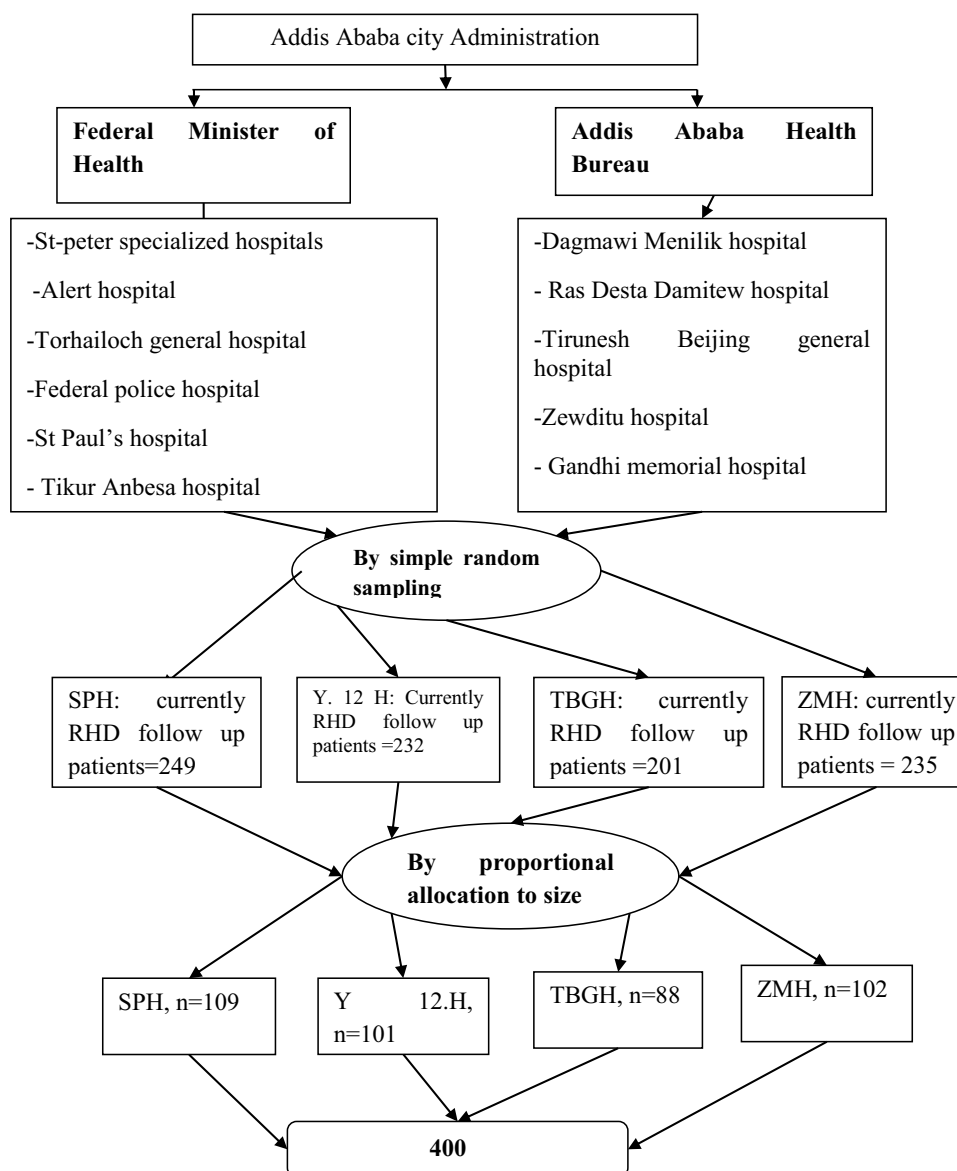
Figure 1 The schemes presentation of sampling procedure to select study participants from Addis Ababa governmental hospitals, 2022.

association with poor adherence to secondary prophylaxis. A p-value less than 0.05 was considered significant. Finally, the processed data will be presented by creating frequency, and percentages with tables, text, and graphs.

Ethical Consideration

Before data collection, ethical clearance was obtained from St. Paul's hospital millennium Medical College Institutional Review Board. A permission letter to conduct the study was secured from the Addis Ababa Regional Health Office, and selected hospitals. Informed consent was obtained from respondents and institutions to execute data collection procedures. Covid 19 protocol and safety were maintained. Information was kept anonymous and confidential.

Results

Socio-Demographic Characteristics

This study included 381 patients with rheumatic heart disease (RHD) who attended a follow-up cardiac clinic with a response rate of 95%. The mean age of the respondents was 26.45 (±10.5 years). Among the participants, 228 (59.8%)

were females and 305 (80.1%) were urban residents. Regarding the marital status of the respondents, 192 (50.4%) were single, and 171 (44.9%) were married. The majority of patients attended elementary (1–8) education (34.9%). Unemployment accounted for 228 (59.8%) followed by non-governmental (driver, merchant, private) 101 (26.5%). The majority of respondents travelled 1–5 km to get a BPG injection at health facility 216 (56.7%) and public transportation 241 (63.3%) was mostly used to travel to the health facility (Table 1).

Table 1 Socio-Demographic Characteristics of the Patients with RHD at Selected Governmental Hospitals, in Addis Ababa, Ethiopia, 2022 (n = 381)

Variables		Number (n=381)	Percent (%)
Age category	<15 years	62	16.3
	15–24 years	109	28.6
	>24 years	210	55.1
Sex	Males	153	40.2
	Females	228	59.8
Marital status	Single	192	50.4
	Married	171	44.9
	Divorced	10	2.6
	Widowed	8	2.1
Educational status	Non-formal	29	7.6
	Primary	133	34.9
	Secondary	108	28.3
	Higher	111	29.1
Occupation	Student	130	34.1
	Gov't employer	52	13.6
	Non-governmental	149	39.2
	Unemployment	50	13.1
Address	Urban	305	80.1
	Rural	76	19.9
Family size	≤5	292	76.6
	>5	89	23.4
Distance from health facility for BPG injection (KM)	≤30	337	88.5
	>30	44	11.5
Transportation used went to facilities for BPG injection	Public (bus, taxi)	241	63.3
	Private car	27	7.1
	Walking on feet	86	22.6
	Others (mule, horse)	27	7.1
Health insurance	Yes	156	40.9
	No	225	59.1

Clinical Characteristics of Participants

In this study, the majority 285 (74.8%) of the participants were diagnosed with RHD in the past ten years with a mean of 7.5±5.9. Most patients claim their disease condition was moderate by echocardiography evaluation from patients' chart and sixty-two (16.3%) had a history of co-morbidities (ie, hypertension, Diabetics, Asthma). Most of the participants were aware that sore throat can be caused by bacteria 240 (63%), 254 (66.7%) knew sore throat can be associated with

RHD and two-hundred sixty participants perceived that BPG can prevent recurrence and worsening of RHD. The mean waiting time for injection from a health facility was 27.9 ±19.3 minutes (Table 2).

Table 2 Clinical Characteristics and Awareness Regarding RHD Among Respondents at Selected Governmental Hospitals, Addis Ababa, Ethiopia 2022 (n = 381)

Variables		Number (n=381)	Percent (%)
Duration of RHD diagnosis	≤10 years	285	74.8
	11–20 years	86	22.6
	>20 years	10	2.6
Duration since prophylaxis started time for RHD	≤5 years	211	55.4
	>5 years	170	44.6
Interval appointment for RHD	One month	186	48.8
	Two months	45	11.8
	Three months	106	27.8
	> three months	44	11.5
Co-morbidities	Hypertension	16	25.8
	Diabetes-mellitus	14	22.6
	Stroke	13	21
	Epilepsy	6	9.6
	Others	13	21
No admission in the last 1 year	Once	83	79.8
	Two and above	21	20.2
The severity of the RHD	Mild	101	26.5
	Moderate	183	48
	Severe	97	25.5
Good progress in the disease	Yes	274	71.9
	Not	107	28.1
Drugs taking	< 3	187	49.1
	≥3	194	50.9
Average waiting time for injection of BPG at the health facility	<20 minute	202	53
	20–40 minute	104	27.3
	41–60 minute	71	18.6
	>60 minute	4	1.0

Adherence to Secondary Prophylaxis for RHD Patients

All participants reported that health professionals prescribed secondary prophylaxis drugs and 100% has been on BPG injection from patient's card and almost 98.7% of participants had injection card for BPG. Most of 218 (57.2%) did not miss a monthly injection, 53 (13.9%) patients missed one to two injections, and 111 (29.1%) missed three and more than three injections. Two hundred seventy (70.9%) of the participants had good adherence whereas the left had poor adherence to BPG prophylaxis. One hundred and three (27.0%) did nothing followed by 50 (13.1%) waiting until the next appointment when they missed the injection and seven (1.8%) went a few days later and 4 (1.0%) others (ie, took alternative medication (herbal), non-functioned the health facilities due to instability, having pregnancy) when they missed monthly injections (Figure 2).
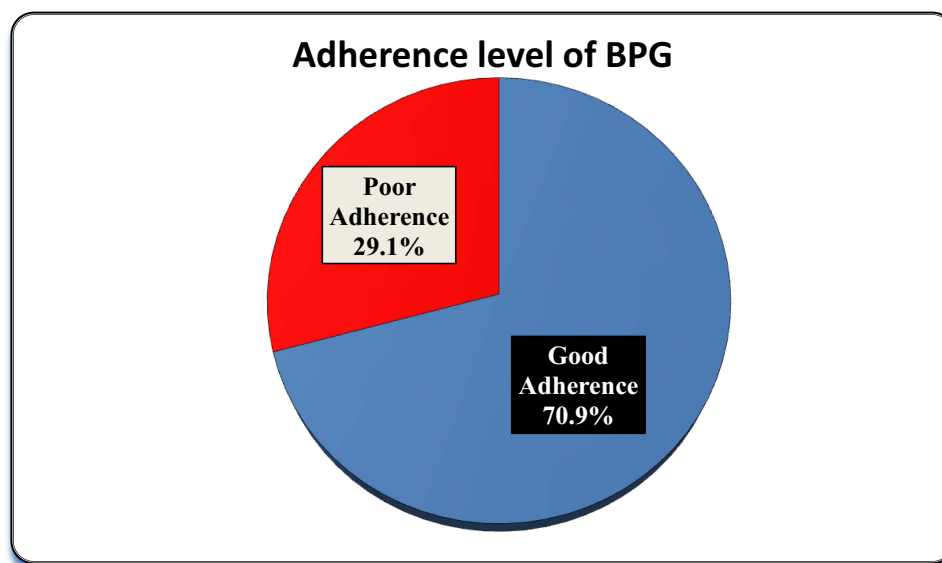
Adherence level of BPG

Poor Adherence 29.1%

Good Adherence 70.9%

Figure 2 Adherence to secondary prophylaxis patients with RHD at selected governmental hospitals in Addis Ababa, Ethiopia, 2022.

Reason for Poor Adherence to Secondary Prophylaxis

Regarding the reason for missing injection of BPG, most of the patients 204 (53.5%) were due to lack of medication supply (ie, stock out [46.5%] and expired of the drug [3.1%]) followed by fear of injection pain 145 (38.1%) and poor awareness about the disease and prophylaxis 127 (33.3%) with respect, as detailed in (Figure 3).
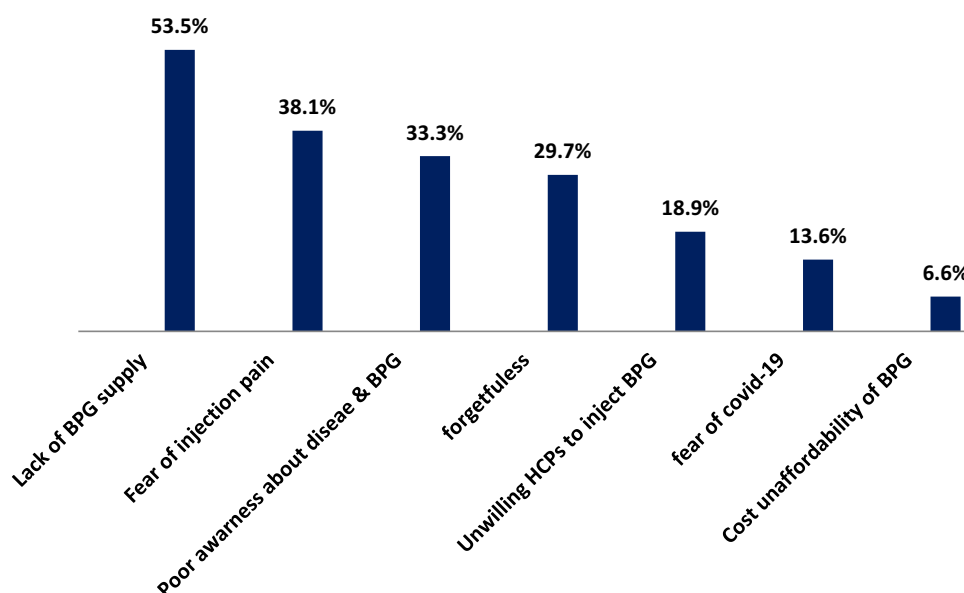

Figure 3 Reasons for poor adherence to secondary prophylaxis among patients with RHD at selected governmental hospitals in Addis Ababa, Ethiopia, 2022.

Factors Associated with Poor Adherence to Benzantin Penicillin G for Patients with RHD

Bi-variable logistic regression analysis indicates that age, address, educational status, family size, distance from home to a health facility, insurance, admission, co-morbidity, lack of drug, fear of catching Covid-19, and duration of BPG

prophylaxis were variables which qualify the assumption (p < 0.25) are taken as a candidate for multi-variable analysis. The multivariable logistic regression analysis results indicated that address, family size, distance, lack of penicillin, and fear of catching Covid-19 variables were associated with poor adherence to secondary prophylaxis for rheumatic heart disease. In multivariable logistic regression analysis, participants who had greater than five family members were 2.8 times (AOR = 2.879, 95% CI: 1.282–6.465, p < 0.01) more likely to have poor adherence to secondary prophylaxis compared to those who had ≤ five family members. Study participants who were living a distance from home to an injection facility greater than 30-kilometers were far to be 3.2 times (AOR = 3.247, 95% CI: 1.051–10.033, p < 0.041) more likely to be poor adherence than those who were far less than 30 kilometers distance. Study participants who were living in rural areas were 2.6 times more likely to have poor adherence than those who were in urban residency (AOR = 2.637, 95% CI: 1.068–6.513, p = 0.036). Patients who had a lack of BPG prophylaxis in a followed-up hospital were 6.7 times more likely to be poor adherence than those who did not lack BPG drug (AOR = 6.772, 95% CI: 3.234–14.177, P < 0.01). Similarly, the respondents who were not fear of catching Covid-19 to go to health facilities were 96% less likely to be in poor adherence compared with those who were fearful of catching Covid-19 (AOR = 0.04, 95% CI: 0.014–0.114, P < 0.01) (Table 3).

Table 3 Bi-Variable and Multivariable Regression Analysis of Adherence to Secondary Prophylaxis Among Patients with RHD at Selected Governmental Hospitals, Addis Ababa, Ethiopia, 2022

Categories	Variables	Adherence		COR (95% CI)	AOR (95% CI)	P-value
		Poor (N %)	Good (N %)			
Age category	0–14 years	13 (20.9%)	49 (79.1%)	I	I	I
	15–24 years	26 (23.9%)	83 (76.1%)	1.66 (0.99–2.8)	0.722 (0.209–2.497)	0.607
	≥25 years	72 (34.3%)	138 (65.7%)	1.97 (1.002–3.86)	0.535 (0.158–1.807)	0.314
Place of residency	Rural	46 (60.5%)	30 (39.5%)	5.67 (3.3–9.7)	2.637 (1.068–6.513)	0.036*
	Urban	65 (21.3%)	240 (79.7%)	I	I	I
Educational status	Non formal	19 (65.5%)	10 (34.5%)	5.32 (2.26–12.54)	1.725 (0.456–6.535)	0.422
	Primary	35 (26.3%)	98 (73.7%)	6.9 (2.83–16.76)	0.643 (0.253–1.639)	0.355
	Secondary	33 (30.6%)	75 (69.4%)	4.32 (1.8–10.29)	0.528 (0.224–1.245)	0.145
	Higher	24 (21.6%)	87 (79.4%)	I	I	I
Family size	≤ 5	67 (22.9%)	225 (77.1%)	I	I	I
	> 5		45 (50.6%)	3.3 (1.99–5.4)	2.879 (1.282–6.465)	0.01*
Distance from home to health facility	1–5 km	39 (18.05%)	177 (81.95%)	I	I	I
	6–10 km	10 (38.5%)	16 (41.5%)	3.43 (1.25–9.4)	0.738 (0.188–2.897)	0.663
	11–20 km	24 (33.8%)	47 (66.2%)	4.2 (1.88–9.36)	1.026 (0.32–3.293)	0.965
	21–30 km	8 (33.3%)	16 (66.7%)	4.3 (1.5–12.36)	1.652 (0.387–7.054)	0.498
	>30 km	30 (68.2%)	14 (31.8%)	9.7 (4.7–20.04)	3.247 (1.051–10.033)	0.041*
Health Insurance	Yes	55 (35.3%)	101 (64.7%)	I	I	I
	No	56 (24.9%)	169 (75.1%)	1.64 (1.052–2.57)	0.874 (0.466–1.639)	0.675
Admission	Yes	39 (37.5%)	65 (62.5%)	1.708 (1.057–2.759)	1.104 (0.565–2.156)	0.773
	No	72 (26%)	205 (74%)	I		

(Continued)

Table 3 (Continued).

Categories	Variables	Adherence		COR (95% CI)	AOR (95% CI)	P-value
		Poor (N %)	Good (N %)			
Co-morbidities	Yes	28 (45.2%)	34 (54.8%)	2.3 (1.33–4.09)	0.435 (0.179–1.057)	0.066
	No	83 (26%)	236 (74%)	1	1	1
Lack of drugs	Yes	95 (46.6%)	109 (53.4%)	8.77 (4.897–15.7)	6.772 (3.234–14.177)	0.00*
	No	16 (9%)	161 (91%)	1	1	1
Fear of Covid-19	No	65 (19.8%)	264 (80.2%)	0.032 (0.013–0.078)	0.04 (0.014–0.114)	0.000*
	Yes	46 (88.5%)	6 (11.5%)	1	1	1
BPG prophylaxis started	> 5 years	62 (36.5%)	108 (63.5%)	1.898 (1.2–2.9)	1.1 (0.547–2.209)	0.790
	≤ 5 years	49 (23.2%)	162 (76.8%)	1	1	1

Note: *P-value ≤0.05 is considered statistically significant.
Abbreviations: COR, crude odds ratio; AOR, adjusted odds ratio.

Discussion

This study was a facility-based cross-sectional study designed to determine adherence to secondary prophylaxis among patients with RHD at selected governmental hospitals in Addis Ababa. This study also addressed socioeconomic, health system, condition, patient, and therapy-related factors that affected adherence to secondary prophylaxis for patients with RHD. Then the results addressed objective one and objective two.

In this study, the overall poor adherence level was 29.1% (95% CI: 24.7–33.8%). This finding is comparable with the study conducted in Pakistan's 26.5%[19] and Addis Ababa's 32.1%[16] and slightly low when compared to studies from Egypt, Jimma zones, and Brazil with 34.5%, 37%, and 35%, respectively.[5,20,21] However, this result was considerably less poor[22] adherence than that found by Jamaica 51.3%,[23] India 50%,[24] Uganda 46%,[17] Sudan 68%,[12] and Jimma Medical centre 44.8%.[7]

The variability in the level of adherence may reflect the different systems in which this study was done, different factors may influence adherence, study designs, study times, done in referral hospitals, and more participants were urban residencies in this study. Furthermore, improvement in BPG prophylaxis prescription habits by health-care workers (100%) and having injection cards (98.7%) by RHD patients have vital contributions to enhancing adherence to BPG.

In this study, the reason for poor adherence to secondary prophylaxis was lack of penicillin supply (53.5%), fear of injection pain (38.1%), forgetting of injection date (29.7%), unwilling health-care providers to administer BPG (18.9%), fear of catching Covid-19 to access health facility (13.6%), cost unaffordability (6.6%), distance from a health facility, and poor awareness about RHD disease and importance of BPG (33.3%). Furthermore, different studies reported reasons for poor adherence almost the same except for the new emerging variable (ie, fear of Covid-19) even if a variation in the percentage.[5,7,12,17,23,25]

Regarding Factors associated with poor adherence: The participants who were living in rural residency were positively significantly associated with poor adherence to secondary prophylaxis. This finding is in harmony with the study done in Jimma Zone hospitals, in Uganda, and South India.[5,25,26] The reason that patients who live in rural areas have poor adherence to BPG prophylaxis is due to difficulty in accessing nearby health-care facilities.

In this study, participants who live greater than thirty kilometres away from health centers were positively significantly associated with poor adherence. This finding is supported by a study done in Jimma medical center and zonal hospitals.[5,7] This might be due to not being easily accessible and cost affordable transportation.

The participants who had greater than five family members were 2.8 times poorly adhered to BPG prophylaxis. This is similar to a study done on the new Caledonia.[25] This might be attributed to socioeconomic variables such as a family history of RHD as a result of overcrowding living conditions, which is likely secondary to a higher risk of streptococcal transmission in big families,[27] cost unaffordability, and the increased cost of the imported drug.

The participants who had a lack of BPG drug in the follow-up hospitals were 6.7 times more a significant relation with poor adherence. This might be due to the scarcity of drugs secondary to not function of the pharmaceutical industry and country instability.

The respondents who were not fear of the catching Covid-19 pandemic to go health facility were 96% less likely associated with poor adherence to secondary prophylaxis of BPG. This is due to the restriction of patients from health-care facilities due to the declaration of lockdown policy by the countries.

In general, adherence to secondary prophylaxis has been shown to reduce the risk of ARF recurrences, worsening of RHD, and leading to chronic rheumatic valvular heart disease. Promoting adherence of patients to secondary prophylaxis should be addressed and assessed timely as the management modality.

Conclusion

Overall, adherence to secondary prophylaxis among patients with RHD in this finding did not address the expected WHO recommendation of the annual prescribed injection. After adjusting for other confounding variables, the main factors for poor adherence were lack of drugs, rural residency especially far from greater than thirty kilometers, fear of new emerging pandemics (Covid-19) to go health facility, patients had >5 family members were factors associated with poor adherence to secondary prophylaxis among patients with RHD.

Strength and Limitation

Strength

The strength of this study is as it was being done in multiple centers. This study now includes a variable that was not previously included (Covid-19).

Limitation

The study was conducted in Addis Ababa, which is assumed to have better health service coverage and drugs; however, it was better if it was conducted in semi-urban and rural areas. In another way, the period in which it was employed was when there is instability in the pharmaceutical production area and transportation problems, which it will be very difficult to conclude to patient perspectives only. The study was conducted only on patients, but it was better to include the health-care providers because the refusal to give the injection of BPG prophylaxis was 18.9%. Furthermore, the investigator gathered data on adherence based on verbal self-report, which could be sustainable to recall bias among participants.

Abbreviations

AA, Addis Ababa; AOR, Adjusted Odds Ratio; ARF, Acute Rheumatic Fever; BPG, Benzantin Penicillin G; CI, Confidence Interval; COVID-19, Corona Virus Infectious Disease at 2019; COR, Crude Odds Ratio; GAS, Group A Streptococcus; SPSS, Statistical Package For Social Science; RHD, Rheumatic Heart Disease; SPH, Saint Peter Hospital; STPHMMC, Saint Paul's Hospital Millennium Medical College; TBGH, Tirunesh Beijing General Hospital; WHO, World Health Organization; YHMC, Yekatit 12 Hospital Medical College; ZMH, Zewditu Memorial Hospital.

Data Sharing Statement

The data sets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

Ethical clearance was obtained from the institutional review board (IRB) of St. Paul's Hospital Millennium Medical College (SPHMMC). Informed consent was impractical for this study. This is in line with the Helsinki Declaration which is stated as "medical research using identifiable human material or data, physicians must normally seek consent for the collection, analysis, storage and/or reuse. There may be situations where consent would be impossible or impractical to

obtain for such research or would pose a threat to the validity of the research. In such situations, the research may be done only after consideration and approval of a research ethics committee".[28] Information was obtained from the patients and confidentiality was maintained.

Consent for Publication

All authors agreed that this manuscript is eligible for publication.

Acknowledgment

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

Disclosure

The authors declared that have no competing interests in this work.

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