

# Rheumatic Heart Disease Patients' Adherence to Secondary Prophylaxis and Associated Factors at Hospitals in Jimma Zone, Southwest Ethiopia: A Multicenter Study

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**Background:** Rheumatic heart disease (RHD) is a major cause of preventable premature cardiovascular-related death in developing countries. However, information regarding adherence rates and associated factors is limited and inconsistent in Ethiopia.

**Methods:** A cross-sectional study was conducted from August to November 2019 among selected RHD patients on follow-up at four hospitals in Jimma zone. Data were collected using a structured questionnaire. Adherence of RHD patients to secondary prophylaxis in the previous consecutive 12 months was assessed based on the annual frequency of received prophylaxis (monthly injection of benzathine penicillin). Good adherence was considered the patient receiving >80% of the annual dose. The collected data were entered into Epidata 3.1 and analysed using SPSS 23.

**Results:** A total of 253 RHD patients taking prophylaxis were included in the analysis, and of those 178 (70.4%) were female, giving a male:female ratio of 1:2.4. The mean age was 24 ±11 (6–65) years. About 63% had good adherence to benzathine penicillin prophylaxis. New York Heart Association functional class I and II, rural residence, >30 km from health facility, and duration of prophylaxis >5 years were associated with poor adherence (respectively: AOR 12.6 [95% CI 2.5–63],  $P=0.016$ ; AOR 6.8 [95% CI 1.9–24.4],  $P=0.003$ ; AOR 5.5 [95% CI 1.2–26.7],  $P=0.046$ ; AOR 1.2 [95% CI 1.1–3.2],  $P=0.021$ ). Leading barriers to good adherence were long distance from the treatment setting (56.9%), followed by lack of money (38%).

**Conclusion:** Patients with class I and II heart failure and those living in rural areas, especially >30 km from a hospital, were identified to be poorly adherent to secondary prophylaxis.

**Keywords:** rheumatic heart disease, adherence rate, secondary prophylaxis, associated factors, Jimma zone hospitals, Ethiopia

## Introduction

Acute rheumatic fever (ARF) and its sequela, rheumatic heart disease (RHD), remain important causes of morbidity and mortality in areas of socioeconomic deprivation.<sup>1–3</sup> The Global Burden of Disease study estimated in 2013 that there were 33 million cases of RHD worldwide, causing 275,000 deaths annually.<sup>4,5</sup> Many echocardiographic screening studies even put the prevalence of RHD at eight to 57 in 1,000 children, with true prevalence of 62–78 million individuals

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worldwide<sup>6</sup> and about 1.4 million deaths each year.<sup>7,8</sup> The prevalence of RHD is estimated to be higher in developing countries than developed countries, ranging from 24 in 1,000 to 0.3 in 1,000, respectively.<sup>9</sup> It is estimated that 95% of cases of RHD and deaths related to this disease occur in developing countries.<sup>10–12</sup> Moreover, significant costs are associated with the treatment of RHD, including heart-valve replacement.<sup>13,14</sup> The severity and prognosis of RHD depends on the extent of cardiac involvement and the frequency of recurrent events.<sup>15,16</sup>

Systematic reviews of hospital-based death and cause-of-death studies in Africa have highlighted RHD as the main cause of cardiac morbidity and mortality in children and young adults.<sup>17–19</sup> The clinical course of acute rheumatic carditis in Africa runs a fulminant course and seems more malignant.<sup>20,21</sup> ARF and its complications, eg RHD, remain an enormous health problem in poor countries.<sup>22–24</sup> Ethiopia is one of the African countries that share the burden of ARF and RHD, where it accounts for 50% of cardiac admission, with prevalence of 39.6% and 32.8% among Ethiopian cardiac patients in Addis Ababa and Jimma town, respectively.<sup>25,26</sup> A retrospective study of deaths between 1995 to 2001 at the Tikur Anbassa Teaching Hospital, Addis Ababa, Ethiopia reported that 26.5% of cardiovascular deaths were due to RHD.<sup>27</sup>

Rational use of secondary prophylaxis (regular intramuscular injections of benzathine penicillin G) is a critical cost-effective intervention for preventing morbidity and mortality related to RF.<sup>28</sup> A patient with RHD is expected to receive at least 80% of the annual prescribed injections. Otherwise, there is a higher risk of recurrent ARF and its complications.<sup>29,30</sup> However, ensuring adequate adherence to secondary prophylaxis has been a challenge, and the adherence rate is poor among adolescents and chronic patients,<sup>31–36</sup> due to different factors<sup>34,37–42</sup> and barriers.<sup>43–48</sup> There are no reliable and consistent data in Ethiopia, as studies have been conducted only at a single institution. Therefore, the present study aimed to assess adherence of RHD patients to secondary prophylaxis and associated factors at multiple hospitals in Jimma zone, southwest Ethiopia.

## Methods

### Study Setting and Design

The study was conducted at four public hospitals in Jimma zone (Jimma Medical Center, Shenen Gibe Hospital, Agaro Hospital, and Seka Chekorsa Hospital), which are

located in Oromia region, southwest Ethiopia. Jimma Medical Center and Shenen Gibe Hospital are located in Jimma town, 354 km from the capital — Addis Ababa. Jimma Medical Center is one of the country's teaching hospitals, and serves as a referral hospital for southwest Ethiopia. Agaro Hospital is a district hospital located in Agaro town, about 45 km from Jimma to the west direction, where Seka Chekorsa Hospital is a district hospital located in Seka Chekorsa town, 20 km from Jimma to the south.

A cross-sectional study design was employed at cardiac clinics of Jimma medical center, outpatient clinics of Agaro, Seka Chekorsa and Shenen Gibe hospitals from August to November 2019 among RHD patients on follow-up who fulfilled inclusion criteria (all age-groups, on benzathine penicillin prophylaxis for at least 1 year before the date of interview). Sample size was calculated using the single-population formula by taking  $P^2=50\%$  with margin error of 0.05. Finally, a total sample of 278 RHD patients were considered to represent RHD patients after computing the finite population-correction formula and 10% contingency for nonresponse. Patients who met the inclusion criteria were consecutively recruited until the estimated sample was reached.

### Data Collection

Data were collected with a structured questionnaire administered by face-to-face interviews. Necessary medical data were reviewed from patient records. Information on demographic and socioeconomic characteristics, health care team-related factors, system-related factors, condition-related factors, therapy-related factors, and patient-related factors were collected according to WHO recommendations.<sup>32</sup> Adherence of RHD patients was determined based on frequency of annual prophylaxis received, and possible barriers were assessed if they had missed more than three shots by providing multiple-choice questions. Data were collected by trained medical interns and nurses working at cardiac clinics, supervised by internal medicine residents.

### Data Processing and Analysis

Data were entered into EpiData version 3.1 and then exported to SPSS version 23 for further analysis. Cross-tabulation and logistic regression were applied to examine associations between predictors and the outcome variable (adherence status). Descriptive statistics, ie, means  $\pm$  SD, frequency, and percentages were used to express variables.

ORs and 95% CI were used to quantify the strength of associations. All statistical tests were two-tailed, and  $P < 0.05$  was considered statistically significant.

## Operational Definitions

### Adherence

RHD patients were regarded as having good adherence when the rate of adherence to secondary prophylaxis was  $\geq 80\%$  of the expected injections (if injected more than ten times per year) while good adherence was regarded as the patient missing prophylaxis at least three times per year.<sup>29,36,49</sup> In Ethiopia, adherence to secondary prophylaxis is focused to eradicate/prevent the disease by promoting injections for patients every 4 weeks.<sup>50</sup> Benzathin penicillin G injection is given, in accordance with the WHO 2003 guideline recommendation.<sup>51</sup>

## Results

### Sociodemographic Characteristics of Participants

From 278 expected RHD patients, 253 participated in the study, giving a response rate of 91%. These patients, all of whom were on benzathine penicillin, were included in the analysis, of which 178 (70.4%) were female, giving a male:female ratio of 1:2.4. The mean age of patients was  $24 \pm 11$  (6-65) years, and the majority (109, 43.1%) were aged  $>24$  years. The majority of the patients (73.1%) were Oromo in ethnicity and Muslim in religion (75.5%), rural residents (66%), and attending Jimma Medical Center (77.9%). The mean annual income was US\$50, as detailed in Table 1.

### Clinical Characteristics of Participants

Almost three quarters (74.3%) of patients had a history of hospitalization for RHD. More than half (56.5%) were in NYHA class II. There were no other cases of RHD in the family among 94.5% of respondents, and only 14 (5.5%) reported family member/s suffering from a similar illness (Table 2).

### Adherence of RHD Patients to Secondary Prophylaxis

Of the 253 RHD patients receiving secondary prophylaxis, 86 (34%) had received all annual injections and 167 (65.2%) had missed their regular injection at least once in the past year. The proportion of patients who had missed injections once/twice and three or more times was 29% and 37%,

**Table 1** Sociodemographic characteristics of patients with rheumatic heart disease on monthly benzathine penicillin at four hospitals in Jimma zone from August to November 2019

		n	%
Hospital	Jimma Medical Center	197	77.9
	Agaro	8	3.2
	Shenen Gibe	37	14.6
	Seka Chekorsa	11	4.3
Age (years)	<15	47	18.6
	15–24	97	38.3
	>24	109	43.1
Sex	Male	75	29.6
	Female	178	70.4
Ethnicity	Oromo	185	73.1
	Amhara	30	11.9
	Kafa/Dawuro	19	7.5
	Gurage	14	5.5
	Silte	4	1.6
	Kimant	1	0.4
Religion	Muslim	191	75.5
	Orthodox	41	16.2
	Protestant	21	8.3
Residence	Rural	167	66.0
	Urban	86	34.0
Distance from health facility (km)	1–5	62	24.5
	6–10	10	4.0
	11–20	49	19.4
	21–30	37	14.6
	>30	95	37.5
Family size	$\leq 5$	72	28.5
	$> 5$	181	71.5
Monthly household income (US\$)	$\leq 33.3$	85	38.1
	33.3–66.67	88	39.5
	$> 66.67$	50	22.4

respectively. In sum, 160 (63%) were identified as having good adherence, while 93 (37%) were considered poorly adherent to monthly benzathine penicillin injections (ie, missing fewer than and three or more injections in the past year, respectively), as detailed in Figure 1.

### Factors Associated with Adherence of RHD Patients to Secondary Prophylaxis

To determine factors associated with adherence of RHD patients to secondary prophylaxis, cross-tabulation and logistic regression were applied. For binary logistic

**Table 2** Clinical characteristics of participants with RHD on monthly benzathine penicillin at four hospitals in Jimma zone from August to November, 2019

	Categories	n	%
Any hospitalization history for RHD	Yes	188	74.3
	No	65	25.7
Duration on medication (years)	≤5	144	56.9
	>5	109	43.1
Condition of patient (NYHA class)	NYHA class I	89	35.2
	NYHA class II	143	56.5
	NYHA class III	13	5.1
	NYHA class IV	8	3.2
Other cases of RHD in the family	Yes	14	5.5
	No	239	94.5

**Abbreviations:** RHD, rheumatic heart disease; NYHA, New York Heart Association.

regression, eleven independent variables (age, sex, urban/rural residence, distance from health facility, family size, monthly household income, duration of prophylaxis, duration of disease, NYHA class, hospitalization history, and family history of RHD) were selected ( $P < 0.25$ ) as potential predictors of adherence status. Finally, four variables (NYHA stage I and II, rural residence, distance from health facility  $> 30$  km, and duration of prophylaxis ( $> 5$  years)) were determined as the factors associated with poor adherence (Table 3).

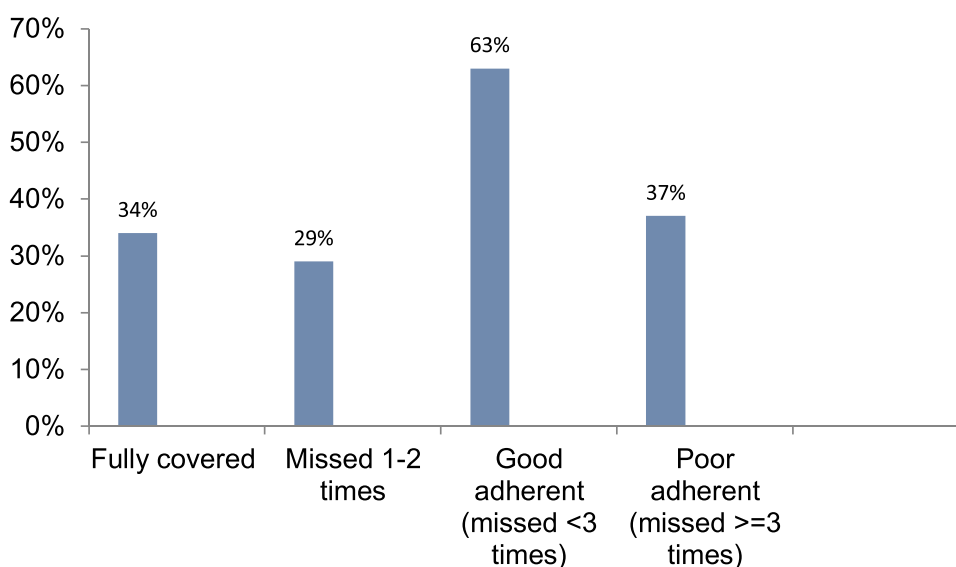
(respectively: AOR 12.6 [95% CI 2.5–63],  $P = 0.016$ ; AOR 6.8 [95% CI 1.9–24.4],  $P = 0.003$ ; AOR 5.5 [95% CI 1.2–26.7],  $P = 0.046$ ; AOR 1.2 [95% CI 1.1–3.2],  $P = 0.021$ )

## Barriers to Good Adherence to Secondary Prophylaxis

The main reasons for missing prophylaxis were long distance from treatment settings (56.9%), lack of money (38%), unaffordability (30.8%), and inconvenient work schedule (22.5%; Figure 2).

## Discussion

A patient with RHD is expected to receive at least 80% of annual prescribed injections. Receiving  $< 80\%$  places them at higher risk of recurrent ARF and its complications.<sup>36,49</sup> The present study revealed an adherence rate of 63%, which is within the range of 29.5%<sup>44</sup> to 93.6%<sup>52</sup> reported so far. This finding was almost comparable with Pelajo et al, who reported an adherence rate of 65% among RHD patients in Brazil.<sup>31</sup> However, our figure was considerably higher than that found by Sayed (29.5%),<sup>44</sup> Thompson et al (48.7%),<sup>48</sup> Prasad et al (50%),<sup>46</sup> Musoke et al (54%),<sup>53</sup> Gasse et al (54%),<sup>38</sup> Mohammed et al (55.2%),<sup>29</sup> Huck et al (58%),<sup>43</sup> and Harrington et al (59%).<sup>34</sup> On the other hand, it was considerably less than of Saxena et al (93.6%),<sup>52</sup> Culliford-Semmens et al (92%),<sup>54</sup> Kumar et al (90%),<sup>45</sup> Mekonnen et al (80.6%),<sup>37</sup> and Sial et al (73.5%).<sup>55</sup>



**Figure 1** Adherence status of RHD patients to secondary prophylaxis.

**Table 3** Factors associated with adherence status of RHD patients to secondary prophylaxis by cross-tabulation and logistic regression

		Adherence, n (%)		COR (95% CI)	P-value	AOR (95% CI)	P-value
		Poor	Good				
Residence	Rural	87 (34.4)	80 (31.6)	14.5 (5.9–35)	<0.001 <sup>+</sup>	6.8 (1.9–24.4)	0.003*
	Urban	6 (2.4)	80 (31.6)	1			
Sex	Male	22 (8.7)	53 (20.9)	1	0.113	1	0.071
	Female	71 (28.1)	107 (42.3)	1.6 (0.9–2.8)			
Age (years)	<15	12 (4.7)	35 (13.8)	0.5 (0.2–1.0)	0.079	0.4 (0.1–1.4)	0.164
	15–24	37 (14.6)	60 (23.7)	0.9 (0.5–1.3)	0.740	1.1 (0.5–2.6)	0.836
	>24	44 (17.4)	65 (25.7)	1		1	
Distance from health facility (km)	≤5	3 (1.2)	59 (23.3)	1	<0.001 <sup>+</sup>	10 (1.1–96)	0.056*
	6–10	5 (2.0)	5 (2.0)	19.7 (3.6–107)			
	11–20	22 (8.7)	27 (10.7)	16.0 (4.4–58)			
	21–30	14 (5.5)	23 (9.1)	11.9 (3.1–45)			
	>30	49 (19.4)	46 (18.2)	20.9 (6.1–71)			
Family size	≤5	18 (7.1)	54 (21.3)	1	0.016 <sup>+</sup>	1.5 (0.7–3.4)	0.313
	>5	75 (29.6)	106 (41.9)	2.1 (1.1–3.9)			
Income category (\$US)	≤33.3	38 (17.0)	47 (21.1)	4.9 (2.0–12.2)	<0.001 <sup>+</sup>	1.1 (0.3–3.8)	0.830
	33.3–66.67	37 (16.6)	51 (22.9)	4.4 (1.8–11)	<0.001 <sup>+</sup>	2.1 (0.6–6.6)	0.227
	>66.67	7 (3.1)	43 (19.3)	1		1	
Duration of prophylaxis	≤5 years	42 (16.6)	102 (40.3)	1	0.004 <sup>+</sup>	1.2 (1.1–3.2)	0.021*
	>5 years	51 (20.2)	58 (22.9)	2.1 (1.2–3.6)			
Duration of disease	<5 years	42 (16.6)	101 (39.9)	1	0.006 <sup>+</sup>	1.1 (1.0–3.3)	0.061*
	≥5 years	51 (20.2)	59 (23.3)	2.1 (1.2–3.5)			
Hospitalization history	Yes	73 (28.9)	115 (45.5)	1.4 (0.7–2.6)	0.247	1.4 (0.6–3.3)	0.390
	No	20 (7.9)	45 (17.8)	1			
Family history of RHD	Yes	8 (3.2)	6 (2.4)	1	0.113	0.4 (0.1–1.7)	0.231
	No	85 (33.6)	154 (60.9)	0.4 (0.1–1.2)			
Condition of patient (NYHA)	I and II	91 (36.0)	141 (55.7)	6.1 (1.4–26)	0.002 <sup>+</sup>	12.6 (2.5–63)	0.016*
	III and IV	2 (0.8)	19 (7.5)	1			
Injection pain	Mild	43 (17.0)	69 (27.3)	1	0.775	—	
	Moderate	45 (17.8)	78 (30.8)	0.9 (0.5–1.5)			
	Severe	5 (2.0)	13 (5.1)	0.6 (0.2–1.8)			

**Notes:** \*Statistically significant; <sup>+</sup>statistically significant on logistic regression analysis.

**Abbreviations:** RHD, rheumatic heart disease; NYHA, New York Heart Association.

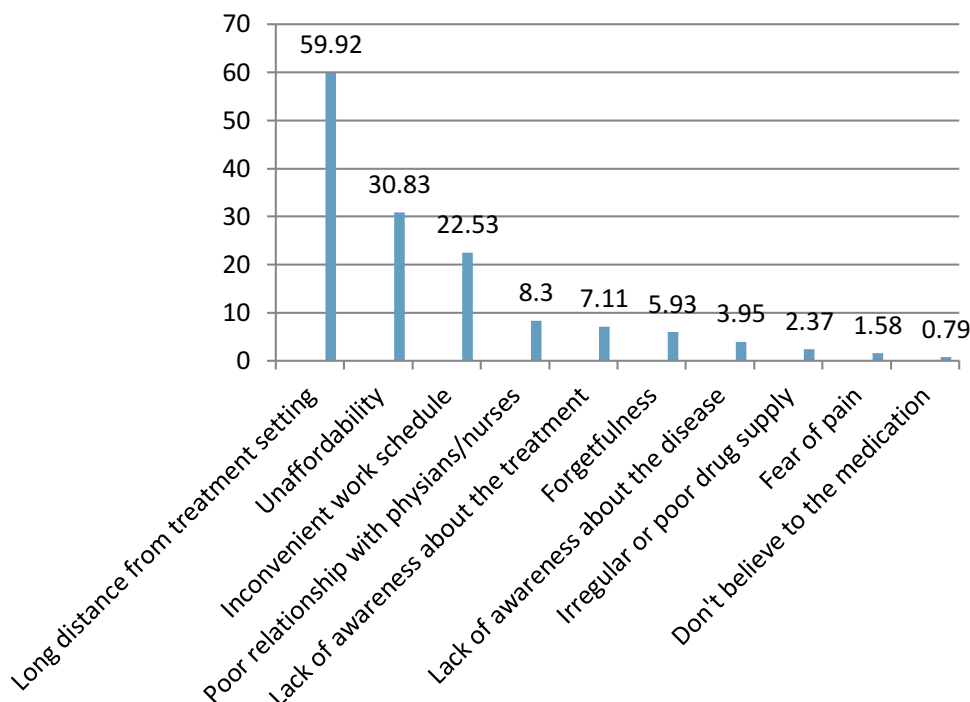
The variability in levels of adherence may reflect the different systems in which these studies were done, duration of followup, different factors that may influence adherence, individual study designs, and population variations.

Factors associated with adherence in the present study were: 1) heart condition of the patients (also supported by Sial et al<sup>55</sup>); 2) residence (also in harmony with Gasse et al,<sup>38</sup> who reported that living rurally where there is no health-

system coverage predisposes RHD patients to poor adherence to secondary prophylaxis); and 3) long distance from the health institution (also supported by a number of studies<sup>34,39,41,48</sup>).

The present finding was also consistent with other studies conducted in Africa: Uganda,<sup>56,57</sup> Malawi,<sup>58</sup> Tanzania,<sup>59</sup> and South Africa.<sup>60</sup>

In this study, the commonest reasons reported for missing monthly benzathine prophylaxis injections was long distance



**Figure 2** Distribution of reasons for missing monthly benzathine penicillin injections among RHD patients on follow-up at the four hospitals in Jimma zone, August to November 2019.

from hospitals (56.9%), lack of money (38%), unaffordability (30.8%), and inconvenient work schedule (22.5%). This finding is also supported by different studies.<sup>40,43–45,47,61</sup>

## Conclusion

After adjusting for confounding effects of other variables, place of residence, duration of prophylaxis, NYHA class, and distance from institution were found to be independently associated with adherence to secondary prophylaxis.

RHD patients dwelling in rural areas, especially >30 km from a hospital, were identified to be poorly adherent to secondary prophylaxis. As such, authors recommend that prophylaxis be delivered at nearby primary health-care units, continuous health education about secondary prophylaxis adherence be strengthened, primary-health facilities be assessed for the delivery of secondary prophylaxis, and further research and solutions directly targeting these barriers to improve patient adherence and decrease overall risk, including recurrence of ARF. Finally, the authors kindly request that all responsible organizations/bodies (Federal Ministry of Health, health institutions, health-care providers) focus on providing health awareness about the disease and prophylaxis to the entire community via different media.

## Data-Sharing Statement

Materials needed can be provided upon request from the corresponding author.

## Ethics Approval and Consent to Participate

Ethics approval for this study was obtained from the Jimma University Ethics Committee. All participants provided informed consent or informed consent was obtained from a parent or legal guardian of any patient aged <18 years, and this study was conducted in accordance with the Declaration of Helsinki.

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## Disclosure

The authors declared that they have no conflicts of interest.

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