

# Health System Factors Serving as Facilitators and Barriers to Rheumatic Heart Disease Care in Sudan

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## Research

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# Abstract

**Background:** Rheumatic heart disease (RHD) remains a leading cause of morbidity and mortality in sub-Saharan Africa despite widely available preventive therapies. In this study, we sought to characterize facilitators and barriers to RHD treatment in Sudan.

**Methods:** We conducted a mixed-methods study, collecting survey data from 398 patients who had enrolled in a national RHD registry between July and November 2017. The surveys included information on demographics, healthcare access, and patient perspectives on treatment barriers and facilitators. Factors associated with increased likelihood of RHD treatment adherence were assessed using multivariate logistic regression. These data were enhanced by focus group discussions with 20 participants, further exploring health system factors impacting RHD care.

**Results:** Our analysis revealed that female gender (Odds ratio (OR) = 1.94; 95% CI 1.14-3.29), increased household income (monthly income above 2000 Sudanese pounds; OR = 2.02; 95% CI 1.26-3.25), and a perceived appropriate level of healthcare staffing by doctors and nurses (OR = 2.07; 95% CI 1.16-3.71) were all factors associated with increased odds of treatment adherence. Further, qualitative data revealed significant barriers to RHD treatment arising from health services factors at the systemic level: The primary barriers to RHD treatment included patient lack of understanding of disease, lack of access due to inadequate healthcare staffing, lack of faith in local healthcare systems, and poor ancillary services. Facilitators of RHD treatment included stronger interpersonal support.

**Conclusions:** Enhancing RHD patient education/engagement, while strengthening local health systems, may lead to improved treatment adherence in this vulnerable population.

## Background

Rheumatic heart disease (RHD) is a chronic cardiovascular disease whose complications are preventable; yet it is responsible for an estimated 10.5 million disability-adjusted-life-years lost and over 300,000 deaths worldwide each year.<sup>1</sup> The majority of these mortalities occur in developing nations, with low and middle income countries (LMICs) accounting for most of the deaths from RHD.<sup>1-3</sup> It is the second leading cause of heart failure in children and young adults, as well as the third leading cause of heart failure for adults in sub-Saharan Africa (SSA).<sup>4-7</sup> The high prevalence of RHD in SSA, which despite having only 10% of the world's population accounts for half of the pediatric cases of RHD worldwide, remains in stark contrast to the low prevalence of the disease in high income countries.<sup>5</sup>

Group A streptococcus (GAS) infection is the root cause of RHD, as it induces an abnormal immune response to the organism.<sup>2</sup> Without adequate treatment, GAS infections can cause acute rheumatic fever (ARF), a serious complication that causes inflammation and fibrosis of cardiac structures including the valves, myocardium, pericardium, and conduction system. The cumulative injury from recurrent episodes of ARF is classified as RHD. To avoid recurrent episodes of ARF from repeated GAS infections, patients

with RHD are advised to take prophylaxis in the form of intramuscular benzathine penicillin G (BPG) monthly for either ten years or until the patient turns 21 years of age (whichever is longer), with some guidelines suggesting lifelong prophylaxis.<sup>8–10</sup>

Secondary prophylaxis has proven to be effective in preventing progression of disease in RHD patients.<sup>9,11,12</sup> Despite the efficacy of BPG, the REMEDY study, a multicenter RHD survey across LMIC settings, revealed that over 20% of enrolled patients did not regularly receive a monthly dose.<sup>3</sup> Previous studies in other countries have suggested potential reasons for low treatment adherence in RHD patients, including urban versus rural setting, education level, pain associated with injections, and availability of transportation funds.<sup>13</sup> Other qualitative analyses eliciting attitudes towards treatment and barriers to secondary prophylaxis found that key impediments to adherence included lack of resources (transportation, medications, clinic availability), injection pain, and poor communication between patients and providers.<sup>14</sup>

In Sudan, low adherence rates to secondary prophylaxis in populations with RHD are believed to be linked to high rates of preventable heart valve injury. However, there is inadequate knowledge of the true adherence rates and subsequent correlation with valvular disease due to a lack of adequate tracking in national public hospitals and registries. There is also a lack of pre-existing literature describing causes of low adherence rates in Sudan.

A more comprehensive understanding of treatment adherence in the RHD patient population in Sudan will enable public health interventions to effectively target the root causes of non-adherence and help providers limit further complications from RHD. Thus, we conducted a mixed methods analysis evaluating barriers and facilitators to RHD treatment adherence, utilizing a comprehensive patient survey, along with a series of in-depth focus group discussions.

## Methods

### Study Population

We completed a mixed methods study (qualitative study with quantitative methodology) at the Alzaeim Alazhari University in Khartoum, Sudan. We collected survey data from 397 patients aged 12 to 90 years who were enrolled in a regional RHD registry between July and November 2017. The population included all patients within the university hospital catchment areas of Al-Shaab Hospital and Ahmed Gasim Hospital. Survey participants were selected via consecutive sampling using admitted patients or individuals attending routine clinic visits. Surveys were administered during the hospital admission or after clinic appointments by Sudanese medical students or physician trainees in English or Sudanese Arabic depending on participant preference.

To enrich our analysis by identifying key themes not captured by our surveys, we conducted four focus group interviews with 20 patients and patient family members aged 20–66. Focus group participants

were selected via convenience sampling that occurred during clinic visits. All participants gave written consent to be included in the analysis. The study was conducted in accordance with the National Research Ethics Review Committee of Alzaeim Alazhari University, No. 4-5-2017, and Institutional Review Board of Stanford University, Protocol #40884.

## Study Design

The surveys included data on demographics (age, household income, education level), healthcare access (distance from facility, insurance status), and opinions on treatment barriers (Supplementary Material 1). The primary outcome variable was medication adherence, defined as survey responses that indicated monthly BPG prophylaxis based on the prior six months. Since six injections in the preceding six months would indicate monthly BPG prophylaxis (standard treatment), participants were classified as non-adherent if they reported fewer than six BPG injections and adherent if they reported six or more injections. Patients and the public were involved in the study design, by providing the list of most common barriers to care for RHD patients, participating in the pilot survey, and ensuring that the research was culturally appropriate.

Next, focus groups were administered by two Sudanese psychologists, who were trained in qualitative research methods and performed as semi-structured interviews of 3–4 patients and/or family members in Arabic using a prepared focus group discussion guide created by the investigators (Supplementary Material 2). Themes of both documents include specific programmatic and more general barriers and facilitators of receiving RHD treatment, specifically focusing on BPG treatment.

## Data Analysis

Demographic variables and survey responses were described as counts, medians, and proportions (%). To assess which demographic and healthcare system factors were associated with an increased likelihood of adherence, we first constructed univariate binomial logistic regressions with each variable. To control for major demographic confounding factors, we constructed a multivariate logistic regression model using forward stepwise variable selection with a significance cutoff of  $p\text{-value} < 0.05$ . For both the univariate and multivariate logistic regression models, a  $p\text{-value} < 0.05$  was used to determine statistical significance regarding hypothesis testing. Robustness of the multivariate model was assessed using the Hosmer-Lemeshow goodness-of-fit test and area under the receiver operating characteristic curve (ROC). All quantitative statistical analyses were completed using Stata-SE, version 16.1 (College Station, TX).

Focus group interview data were translated from Arabic into English by the research team and coded until thematic saturation was achieved using the Dedoose qualitative analysis package (Los Angeles, CA) and Microsoft Word (Redmond, WA). Two independent readers from the analysis team (JE, AC) reviewed the transcripts and subsequently compared coding for the purposes of internal validity. Differences in coding were resolved with discussion. From this coding process, key themes and concepts were identified and classified.

# Results

## Demographic Factors

The demographic distribution of the survey (Table 1) revealed that the participants were mostly female (74.8%) and their ages ranged from 12 to 90 (median 40). Most of the respondents were homemakers or unemployed (72.5%) and had limited formal education, with the majority reporting their highest level of education as primary school or no formal schooling (66.7%). Nearly all participants (94.7%) reported a household monthly income less than 4000 Sudanese pounds (~ 88 US dollars) with a median household size of 6 people. 28.7% of participants reported that they had a history of carditis, though 51.4% of participants claimed to have had heart valve surgery. Only 32% of participants were found to be optimally adherent to BPG prophylaxis.

Table 1  
Survey Participant Characteristics (N = 397)

<b>Gender</b>	<b>n (%)</b>
Female	297 (74.8%)
Male	100 (25.2%)
<b>Highest Level of Education</b>	
No formal schooling	124 (31.2%)
Primary school	141 (35.5%)
Secondary school	84 (21.2%)
University	48 (12.1%)
<b>Employment Status</b>	
Homemaker	220 (55.4%)
Employed	91 (22.9%)
Unemployed	68 (17.1%)
Student	18 (4.5%)
<b>Monthly Income Level</b>	
Less than 2000 Sudanese Pounds (SDG)	275 (69.3%)
2000–3999 SDG	98 (24.7%)
4000–7999 SDG	19 (4.8%)
Greater than 8000 SDG	2 (0.5%)
Not reported	3 (0.7%)
<b>Household Setting</b>	
Rural	179 (45.2%)
Urban	175 (44.2%)
Suburban	42 (10.6%)
<b>Insurance Status</b>	
Insured	278 (70.0%)
Uninsured	107 (27.0%)
Not reported	12 (3.0%)
<b>History of Carditis</b>	

<b>Gender</b>	<b>n (%)</b>
Yes	114 (28.7%)
No	283 (71.3%)
<b>History of Heart Valve Surgery</b>	
Yes	204 (51.4%)
No	193 (48.6%)
<b>Adherence to Penicillin Prophylaxis</b>	
Yes	127 (33.0%)
No	270 (67.0%)

## **Association of Factors with Penicillin Prophylaxis Adherence**

Our univariate analysis (Table 2) revealed that female gender (Odds Ratio (OR) = 1.94; 95% CI 1.14–3.29;  $p = 0.01$ ), increased monthly household income (income over 2000 Sudanese pounds; OR = 2.02; 95% CI 1.26–3.25;  $p < 0.01$ ), higher educational level (OR = 2.14; 95% CI 1.07–4.30;  $p = 0.03$ ), and an appropriate level of healthcare staffing by doctors and nurses at site of treatment (as reported by patients; OR = 2.07; 95% CI 1.16–3.71;  $p = 0.01$ ) were all factors significantly associated with increased odds of BPG adherence. Further, participants who listed "Lack of Awareness of the Severity of RHD" as their primary barrier to receiving care had a significantly reduced odds of adherence with an OR of 0.217 (95% CI 0.08–0.56,  $p < 0.01$ ).

Table 2  
Regression Analysis of Factors Associated with BPG Prophylaxis Adherence

Variable	Univariate Analysis		Multivariate Analysis	
	Odds Ratio	P Value	Odds Ratio	P Value
Age <sup>a</sup>	<b>0.983</b> (0.969–0.997)	0.020*	<b>0.973</b> (0.952–0.995) <sup>k</sup>	0.015*
Gender <sup>b</sup>	<b>1.938</b> (1.142–3.293)	0.014*	^^	^
Employment Status <sup>c</sup>	<b>1.373</b> (0.807–2.338)	0.243	^	^
Household Monthly Income <sup>d</sup>	<b>2.022</b> (1.256–3.254)	0.004*	^^	^
Educational Level <sup>e</sup>	<b>2.145</b> (1.070–4.300)	0.032*	^^	^
# of People in Household <sup>a</sup>	<b>1.003</b> (0.938–1.073)	0.931	^	^
# of Rooms in Household <sup>a</sup>	<b>1.142</b> (0.990–1.317)	0.069	^	^
Urban/Rural Residence	<b>0.357</b> (0.142–0.895)	0.028*	^^	^
Insurance <sup>g</sup>	<b>0.898</b> (0.559–1.444)	0.658	^	^
History of Reported Carditis <sup>h</sup>	<b>1.359</b> (0.860–2.147)	0.189	^	^
History of Heart Valve Surgery <sup>h</sup>	<b>1.246</b> (0.816–1.903)	0.308	^	^
Distance to healthcare facility in km <sup>a</sup>	<b>0.997</b> (0.994–1.000)	0.051	^	^
Wait-time at healthcare facility in minutes <sup>a</sup>	<b>0.997</b> (0.994–0.999)	0.004*	<b>0.995</b> (0.992–0.999) <sup>k</sup>	0.006*
Perceived Adequate Staffing at Healthcare Facility <sup>i</sup>	<b>2.072</b> (1.158–3.708)	0.014*	<b>3.472</b> (1.475–8.172) <sup>k</sup>	0.004*
Transportation Costs <sup>a</sup>	<b>0.999</b> (0.997–1.001)	0.469	^	^
Treatment Costs <sup>a</sup>	<b>1.013</b> (1.002–1.025)	0.022*	<b>1.015</b> (1.002–1.028) <sup>k</sup>	0.025*

	Univariate Analysis		Multivariate Analysis	
<b>Primary Barrier to Treatment Listed as Lack of Understanding<sup>j</sup></b>	<b>0.217</b> (0.083–0.563)	0.002*	<b>0.319</b> (0.164–0.619) <sup>k</sup>	0.001*
Key:				
a Continuous variable				
b Reference: Male; Comparison: Female				
c Reference: Employed; Comparison: Homemaker				
d Reference: <2000 SDG; Comparison: 2000–3999 SDG				
e Reference: No formal schooling; Comparison: University				
f Reference: Rural; Comparison: Suburban				
g Reference: No insurance; Comparison: Has insurance				
h Reference: Negative history; Comparison: Positive history				
i Reference: Reports inadequate staffing; Comparison: Reports adequate staffing				
j Reference: Listing barrier other than lack of understanding of disease; Comparison: Listing lack of understanding of disease as primary barrier				
k Adjusted for age, treatment costs, and wait-time at healthcare facility				
* p value < 0.05				
^ Excluded from multivariate stepwise regression as p value > 0.05				
^^ Excluded from multivariate stepwise regression because of estimability				

Participants living in a suburban household setting were associated with a lower odds of adherence (OR = 0.36; 95% CI 0.14–0.89, p = 0.03). Lower wait-time at the healthcare facility (OR = 1.00 per minute; 95% CI 0.99–1.00, p < 0.01) was marginally associated with increased odds of adherence. For every Sudanese pound increase in treatment cost, there was a 1% increase in odds of adherence (OR = 1.01; 95% CI 1.00–1.03, p = 0.02). Similarly, for every year increase in age, there was a 2% decrease in odds of adherence (OR = 0.98; 95% CI 0.969–0.997, p = 0.02).

In multivariate analysis (Table 2), listing “Lack of Awareness of the Severity of RHD” as the primary barrier was associated with reduced likelihood of adherence (OR = 0.32; 95% CI 0.16–0.62, p < 0.01) after accounting for age, treatment costs and reported wait times at health care facilities. The health center having a perceived appropriate level of healthcare staffing (OR = 3.47; 95% CI 1.48–8.17, p < 0.01) was associated with higher likelihood of adherence after accounting for those same factors.

## Qualitative Analysis

Twenty individuals aged 20–66 (median age of 41) were represented in four focus groups, with eleven patients and nine patient family members. 55% were female, 55% reported a monthly income level less than 2000 SDG, and 75% of participants lived in a rural setting (Table 3). Of the eleven patients, four (36.4%) had undergone valve surgery. Analysis of the focus group discussions revealed recurring major and minor themes that were categorized as facilitators or barriers to receiving treatment in one of three domains: individual, interpersonal, or systemic (Fig. 1).

Table 3  
Focus Group Demographics (N = 20)

<b>Gender</b>	<b>n (%)</b>
Female	11 (55.0%)
Male	9 (45.0%)
<b>Highest Level of Education</b>	
No formal schooling	8 (40.0%)
Primary school	7 (35.0%)
Secondary school	4 (20.0%)
University	1 (5.0%)
<b>Employment Status</b>	
Homemaker	9 (45.0%)
Unemployed	5 (25.0%)
Employed	4 (20.0%)
Student	2 (10.0%)
<b>Monthly Household Income</b>	
Less than 2000 SDG	11 (55.0%)
Greater than 2000 SDG	9 (45.0%)
<b>Household Setting</b>	
Rural	15 (75.0%)
Urban	5 (25.0%)
<b>Focus Group Location</b>	
Al-Shaab Hospital	10 (50.0%)
Ahmed Gasim Hospital	10 (50.0%)
<b>Patient Status</b>	
Patient	11 (55.0%)
Family Member	9 (45.0%)
<b>Valvular Involvement (N = 11)</b>	
Mitral valve only	7 (63.6%)
Aortic valve and mitral valve	2 (18.2%)

<b>Gender</b>	<b>n (%)</b>
Not reported	2 (18.2%)
<b>History of Heart Valve Surgery (N = 11)</b>	
Yes	4 (36.4%)
No	7 (63.6%)

**Table 4A – Facilitators of RHD Treatment**

Domain	Major Theme	Minor Theme	Exemplar Quote	
Individual	Patient knowledge of disease process	In-depth knowledge of treatment	"If my anticoagulation levels were high I would eat some watercress [leafy vegetable] for 3 days and lower them to 2-2.5 if find they are 1-1.5 I would eat some ginger for 3 days and it will return to a 3. I find people here who are hospitalized for a month because of anticoagulation not controlled. Once they were shocked and told me my INR is 10, I said ok, just leave me for a few days in which I ate lentils and liver. After 3 days I returned and they checked it... it was 2.5."	
		Knowledge of disease etiology	"Tonsillitis caused my disease. I take medications to prevent that [from happening again]."	
		Knowledge of disease symptoms	"I used to get pricking sensations and tonsillitis but it has now gone after the operation. Before the operation I used to get very tired."	
	Perception of improved symptoms with treatment	Perceived improvement of symptoms with BPG injections		"The tiredness comes before I take it, I take the injection on the 7 <sup>th</sup> of the month, I get the tiredness on the 3 <sup>rd</sup> and 4 <sup>th</sup> . But after the injection I get better."
				"When I was sick I used to skip school for a month and continue the rest of the year...after I did this operation within 15 days I got back and I got to first grade in high school. After another 15 days I took the exams."
		Optimism surrounding treatment options	"It is treated if one treats it, takes good nutrition and [does other things] and then [they have] hope"	
Positive influence of faith on attitude	No subtheme present	"Praise be to Allah, it's all for the best, but we expect to be better after		

towards disease

the operation.”

**Interpersonal**

Positive influence from other's treatment success

No subtheme present

“I see how [another patient] is living since she lives in our neighborhood. She is very active and goes out with us without being annoyed from her disease and –thanks to Allah- she has done the operation trusting Allah that she will be ok and recover. She is the one who is encouraging me to do the operation and get relieved from this stress. Praise to God she was travelling to the operation the next day and we had the wedding of her cousin in our same house and everybody was coming to say farewell to her. She was normal and the wedding proceeded normally and she did not suffer, God protected her.”

Family support

Emotional support during treatment

“All of this was a result of my mother's prayers. She fought real hard for me, she is my whole family to me, she spent almost 20 years at the side of my hospital bed, my other family members didn't do anything for and they fought her.”

“The antibiotics, the penicillin. When he first got the disease, he used always go to doctors and then I said to him for this disease you should do an ultrasound to show you where the disease is and you should you go to a doctor to show you the direction to go to.”

Financial support with treatment costs

“[My family members] are all worried and keep comforting and ask us not to worry about the rent and operation money, meaning they will help us.”

Motivation to undergo treatment to support family

No subtheme present

“I was really sick, and I wanted to do [treatment] to relieve my family.”

<b>Systemic</b>	Perceived superior quality of care at referral hospital	Perceived superiority of healthcare providers at referral hospitals	<p>“But honestly I see Ahmed Gasim hospital [a referral hospital] as one of the best hospitals and this a truth. The doctors are great and collaborative with the patients.”</p> <p>“Al-Shaab [referral hospital] is good as our relatives said...I am getting [the care] exactly as I had it in my mind.”</p>
		Availability of medical treatment at referral hospitals	“[Medical treatment] is available if you can afford it. If you have money you get treatment or else may God help you.”
		Good quality of ancillary service/cleanliness of referral hospital	<p>“The toilets are good and the food is regular [at Al-Shaab].”</p> <p>“The healthcare here [Ahmed Gasim] is great, the doctors and the nurses are helpful and the bathrooms are always clean the whole 24 hours and there is no problem.”</p>
	Financial assistance from institutions/groups	Financial support from the government	“The Alms chamber, the ministry of finance and the insurance gave us 450 SDG [to help pay].”
		Financial support from hospitals/pharmacies	“There are some doctors who will do [the operation] for free.”
			“I go to the Central Supplies [the main government drug store] and the nurses solve the problem.”
		Financial support from the community	“People help each other, there has been no time that anyone is left wanting.”

**Table 4B – Barriers to RHD Treatment**

Domain	Major Theme	Minor Theme	Exemplar Quote
<b>Individual</b>	Injection pain	No subtheme present	“Yes, it was painful and that was also a reason of stopping it, but I didn’t realize [stopping it] would deteriorate me to this stage.”
	Misconception of disease/poor understanding of disease	Misunderstanding of cause of disease	<p>“I mean drinking too much coffee and cigarettes. All these things cause complications and affect the heart because the heart is the main building which pushes the body. Also, too much stress affects the heartbeat, which affects the heart arteries.”</p> <p>“Participant: They asked me if I ever got tonsillitis, I told them no. But I had high blood pressure since my twenties and I am on the medication till this July when I got worse.</p> <p>Facilitator: So do you think that high blood pressure is the cause of the disease?</p> <p>Participant: Yes, he diagnosed me with this valve disease and told me that we should look for the cause of this high blood pressure since I got it at a young age.”</p>
			<p>Poor understanding of disease management</p> <p>“I try to live with it by avoiding things that harm me. Avoiding harmful things like cigarettes, coffee. All these things I try to avoid as much as I can.”</p>
<b>Interpersonal</b>	Poor communication between provider and patient	Poor communication regarding diagnosis	“I discovered I had this disease 8 years ago. The doctor didn’t tell me there was something wrong with my valve and I found out by accident when I looked into my file. I then told my mother who said we should go to the doctor and we went to him and she asked him “Does my son have a valve [disease]?” He asked her, “Who told you?” and she just repeated her question adding if he has valve

[disease] we want to refer him to Khartoum.”

Poor communication regarding treatment

“I had two [diseased] valves and at the hospital they would just widen the one valve. They would just widen and widen. I had two [affected] valves and I wanted to know if it's okay to widen one valve and leave the other. Why hide [instead of just] telling me that you can't do both? But they insisted on the [widening) operation. The first time they said they widened a valve, I wondered are they going to widen both valves? I left and came a year later, they said they would do a widening operation but after 9-10 days I got even worse, so I just paid for nothing. After this operation I laid in bed for 4 years and couldn't move. I'm from Al-Duwaim and in the operation there was hemorrhage that they sealed shut and they didn't tell my kin about it. Eventually they made us pay for the operation. There were so many shortages and mistakes in the past that I could have avoided.”

“Also getting a definite date for surgeries is important. Especially for people who live in far areas. Meeting a doctor several times and not getting a definite date is frustrating. It would be very much comforting to be assigned a date at an early time.”

Poor relationship between patients and providers

Patient Perspective

“First the patient should be cool and not speak rudely to the doctors. This is an important point because some patients and their companions are tense and fight with the nurses and doctors. The second thing is you should follow orders and help the nurses and doctors in the treatment and follow their advice if they say take the medicine at 6. By 6, you should take it.”

Provider Perspective

“This is the problem with Sudan. Even if your father is an illiterate farmer and he tells you to do something you would do it. Even if you know it's wrong and you won't ask because it would be considered rude, the same applies to doctors. When an operation can't be done in Sudan but can be done abroad, the doctors assume that

99% of the public can't afford to do it outside the country. They would decide to do something else and they would make the decision alone without telling you."

Negative impact/burden on family members

No subtheme present

"But you know the person who is sick is the problem for the whole house."

"Patient's Mother: Honestly we're patient [regarding interruptions of observing Ramadan]. Last thing before we got her here at Ramadan she used to stay up all night in agony and sometimes vomiting, I ask repeatedly and urged her to go to the Emergency Room but she says there is nothing I'm fine [because of Ramadan]. I keep telling [the patient] 'you must go so you can have painkillers there'. Thank God they helped her and now she is hospitalized here."

**Systemic**

Poor quality of patient education by providers

No subtheme present

"Do you know I worked in this hospital? After three months I asked them 'why didn't you tell me?' They told me that, 'I am semiliterate and won't understand and lack knowledge and can't deal with the warfarin and the anticoagulation and after a year we will do you the mechanical valve for you.' I didn't pay again if I knew I had two valves to be changed [then] I would've told them that I want to work there and after 10 years they would've done the operation for free."

"The treatment is good and the services are good but there is one thing: There is a trainer who comes and shows you, but until now no doctor showed me."

Significant costs associated with treatment

Significant costs of medical treatment/operation

"You tell me you have an operation after 10 years for 50 million. Where can I pay it from? So I told them to give me a job as they knew this and so I worked at the cafeteria and after 3 months I took control of the cafeteria and worked for 7-8 years. Then they said I should pay to have the operation [even after] working in the hospital for 10 years."

“But when you go to the doctor and it is not his specialty he should send you to someone whose specialty it is and not just write prescriptions and make you lose money. He does not know your [financial] situation and you go to the pharmacy and they tell you to pay 300 [SDG], pay 400, pay 200 and he [the doctor] takes 200 or 300 and it isn't even his specialty.”

“Money is fate. God divides it, there are poor and there are wealthy so I don't choose. If I am afraid of something, I don't lose anything if I have nothing.”

Significant costs of non-medical amenities (food, lodging, transportation)

“It's just the harsh questioning from the doormen and not allowing homemade meals in the hospitals and they are not providing meals for the public sector. They gave us breakfast when we were in the private sector.”

“The apartment rent [near the referral hospital] cost 6 thousand SDG [per month].”

Lack of transportation to appropriate healthcare facility

No subtheme present

“Transportation is a major problem between the hospitals and from the house to the hospital. Autumn is 3-4 months and because of the rain you can't leave your house and get medical care, there is also the issue of the bus fee.”

Lack of trust in local health systems

Lack of adequate healthcare (personnel/surgical equipment) at local hospitals/facilities

“It would improve if treatment is available nearby. If not a hospital, a prepared health center. Even if you are diagnosed somewhere else, you can go there for follow-up and to take your medicines.”

“One of the oldest places in Sudan with no laboratories, no specialists, no registrars. There are good doctors and each one stays a year or so in the hospital, so [there is no continuity of care].”

“Now the operation should have been in June but because of the money [it was postponed]. Now the hospital is closed

[for repairs] and she can't do the operation."

Improper use of referrals preventing adequate care

"What I [can't understand] is that one of the consultants I saw was a chest specialist and he should have told me to see a heart doctor to see what is happening to your heart or to do an echocardiography or something like that."

"With all due respect, the doctors should advise people who come to them. They should examine them and know the disease is not theirs [specialty wise]. But nobody advised him and they just write him [a prescription] to go the pharmacy. With all due respect the doctors are like car mechanics: one thing is wrong in your car they tell you it is another."

Misdiagnosis at local facility

"4 months I spent rotating between consultants. With all due respect to you doctors, these are the papers in my file, all the 5 doctors I saw none of them told me to see a heart specialist or told me to do tests. It was only by the grace of God that I was in a pharmacy buying medicines when I met a doctor who told me to do exercise. I was doing the first exercise session when I felt stabbing pain, the exercise was with machines and he [the sports trainer] told me [patient], 'you have to see a heart doctor'. So the specialists told me I had nothing and labeled me as tuberculosis and all these pills caused me complications and increased my plight."

"Her illness became when we went to the doctor and he didn't give her good medicine. The medicine itself causes diseases."

Poor quality of ancillary services (nursing) in local hospitals

"In nursing there are some clever people and they are in the right place but there are those who are in the wrong place and these maltreat people. The responsible people in the ministry of health when they appoint people should send them for

training for two to three years not two or three months and come back to the hospital and they still have lessons and other things [training] left.”

Long wait-times for treatment

Delay in diagnosis

“There is a lot of pressure on the emergency department, they see more than a 100 [patients] and may put patients in beds and the floor. I met a fair colored female doctor when I came from the morning, I was sitting on a chair and we lay down on the stairs till the sunset [before being seen].”

Delay to see specialist

“At the hospital... you have to wait. You get to the ER where they sedate you and after that you meet the specialist on Monday or someday and so you find that you waste time.”

Delay to get surgery

“ The operation takes a lot of time [before occurring]. For one patient, it was one month, but for [me] it was one year.”

Perception of poor quality care by younger/less experienced providers

No subtheme present

“With all due respect, doctors are different, some of them are useless and don’t know anything. They are carrying stethoscopes and examine you and write a prescription which do not make you better and even make you worse. In these hospitals there should be doctors with good certificates, who are well trained and experienced not those who just graduated 2 or 3 months and entered a hospital. These won’t treat you, they will make you more sick.”

Perception of higher quality care in other settings

No subtheme present

“Now I have a [insurance] card and I go for treatment in Asia at a private hospital. They are good and cure me.”

“All these people are sick, 95% of Sudanese are sick but don’t know where to go and get treated. All people now go to Egypt, they take a bus for 600 SDG going, 600 SDG going back and take 10 or 20 thousand SDG and go and get treated well and return back.”

Individual facilitators to receiving RHD treatment included adequate knowledge of RHD by the patient, perception of improved symptoms with treatment, and the positive influence of faith on attitude towards treatment. Interpersonal facilitators of treatment were a motivation to undergo treatment as a means of supporting family members, multifactorial family support with treatment, and a positive influence from other's treatment success. One participant recalled consistent support from their mother, stating "All of this was a result of my mother's prayers. She fought hard for me, she is my whole family to me, she spent almost 20 years at the side of my hospital bed."

Systemic facilitators of treatment adherence were a perceived superior quality of care at referral hospitals and financial assistance from the government or hospital facilities. Participants generally had positive experiences at referral hospitals, with one claiming, "...the healthcare here [Ahmed Gasim] is great, the doctors and the nurses are helpful and the bathrooms are always clean the whole 24 hours and there is no problem." Interestingly, a number of our study participants spontaneously noted that ancillary services such as friendliness of security personnel or cleanliness of lavatories as positive reinforcement of trust in their health center.

Individual barriers to receiving RHD treatment included misconception of the disease process or treatment, as well as pain from BPG injection. The various misconceptions regarding RHD included one participant stating that the cause of RHD was "...drinking too much coffee and cigarettes. All these things cause complications and affect the heart because the heart is the main building which pushes the body. Also, too much stress affects the heartbeat, which affects the heart arteries" (Table 4B). Interpersonal barriers identified were poor communication and poor relationship between patients and providers and the negative impact of the disease upon the patient's family members.

Systemic barriers to treatment adherence were numerous, including poor quality of disease/treatment education by providers, significant costs associated with treatment across several domains, perception of lower quality care by younger/less experienced physicians, a lack of trust in local healthcare systems, a lack of transportation to appropriate healthcare facilities, long wait times associated with treatment, and a perception of higher quality care provision in other settings. Highlighting systemic issues with transportation, one participated noted, "Transportation is a major problem between the hospitals and from the house to the hospital. Autumn is 3–4 months [long] and because of the rain you can't leave your house and get medical care; there is also the issue of the bus fee."

## Discussion

Our study offers a detailed survey of the barriers and facilitators to receiving adequate RHD care in the urban setting of Khartoum, Sudan. Although prior analyses have offered estimates of the epidemiologic characteristics of RHD, few have focused on the specific LMIC healthcare system barriers to treatment contributing to the disparate prevalence compared to that of high-income countries. This study's strength lies in its mixed-methods design that bolsters the findings of our quantitative surveys with themes

independently identified in our focus groups. Applying these methods to the relatively poorly studied region of Sudan allows us to identify targeted interventions for context-specific issues.

Reflecting on the patient-level barriers identified in the survey, a lack of understanding of RHD was identified as the primary barrier to receiving adequate care that was most strongly associated with poor BPG adherence. This finding was reinforced by the major themes of poor disease education quality and poor communication between patients and providers in the focus groups. Though this appears to be a robust factor, poor education on RHD can be addressed in a multitude of cost-effective ways. Patient education campaigns, public service announcements (PSAs), and healthcare provider training are all low-cost interventions that can improve patient understanding of disease and serve as both primary and secondary prevention of RHD. In particular, PSAs have been successful at increasing patient knowledge in LMICs in the Caribbean, though sociopolitical differences must be accounted for when adapting that strategy to SSA.<sup>12,15</sup> Female gender and a higher household income were also found to confer a higher likelihood of adherence with RHD treatment in univariate analysis whereas suburban household setting was associated with a decreased likelihood of adherence, which provides insight into possible appropriate targeting of educational interventions. In Zambia, a public-private partnership exemplified the efficacy of targeted educational interventions based on the results of mixed-methods research, which serves as a model for designing interventions in Sudan from this project's findings.<sup>16</sup>

The systemic barriers to treatment adherence identified in our study (high treatment costs and limited access to appropriate healthcare) overlapped with prior studies in Uganda.<sup>14</sup> Our analysis is unique in eliciting patient attitudes toward health system factors, and we identified that perceived inadequate healthcare staffing was a robust barrier to optimal BPG adherence given its significance in univariate and multivariate analysis. In qualitative analysis, this was bolstered by our finding that ancillary health center services such as facility cleanliness, nutritional services, and security also impacted patient trust in the RHD care system. This further outlines the long-term healthcare infrastructure shortfalls existing in Khartoum as it relates to care for chronic illness. Partnership with the Sudanese government can most feasibly be achieved through following the needs assessment tool for developing effective RHD programs, as outlined by Zühlke and colleagues.<sup>17</sup> Based on that approach, this study's results combined with additional stakeholder interviews in Sudan could be used to design community-based interventions. Another approach to achieving policy change could involve guidance from cost-effectiveness models, which may inform policymakers of the prudent investment in primary and secondary prevention costs as compared to the workforce and surgical repair costs associated with severe RHD, as was proposed by researchers in Kenya.<sup>18</sup>

Though transportation costs were not found to be a statistically significant factor associated with lower treatment adherence in our survey, transportation issues were highlighted as major themes throughout our focus group discussions. Given the large distances between many Sudanese towns and its capital, Khartoum, it is understandable that transportation remains a major barrier to receiving care, as identified by 17% of the cohort. Transportation issues could be alleviated through the use of mobile health clinics,

such as those utilized to mobilize maternal health care in Sudan in 2015.<sup>19</sup> Another approach would include the decentralization of RHD care at specialized district level centers, as was done in Uganda.<sup>20–22</sup>

Similarly, though injection pain was only cited by 5% of participants as the primary barrier to treatment adherence, it emerged as a major theme in focus group discussions. Because of the higher efficacy of BPG injections over oral penicillin equivalents for secondary prevention, however, this is unlikely to be addressed outside of providing analgesia to those patients.<sup>23,24</sup> Regarding primary prevention, further development of a previously studied GAS vaccine could provide primary prevention of GAS infections and its complications. Unfortunately, promising vaccine candidates have displayed cross-reactivity with human tissue and the high number of GAS subtypes makes vaccine development challenging at present.<sup>25–27</sup>

In addition to tackling the barriers to receiving adequate RHD care, emphasis should be placed on the identified facilitators of treatment adherence. Family support was revealed as a facilitator of treatment adherence in focus groups, with many participants noting that family members helped with treatment costs, transportation and lodging associated with referral hospital visits, while providing emotional support. This contrasts somewhat with the survey data, which suggested that 89% of respondents self-reported strong family support, even though the adherence rate in that cohort was 32%.

The positive experiences of RHD patients at referral hospitals can also serve as a template for local medical facilities providing care for RHD patients. Though many of the inadequacies of local facilities were not limited to RHD care, these centers can use this information to improve the perception of care quality by those in their communities, for example through the establishment of RHD Centers of Excellence, as has been done elsewhere in sub-Saharan Africa.<sup>28</sup> Moving forward, a comprehensive approach to RHD control, such as the SUR I CAAN program adopted in Sudan, offers a practical model for addressing this multifactorial issue resource-limited settings.<sup>29</sup>

## Limitations

There are several limitations to our current study. As this was a cross-sectional study design, associations observed in our study cannot be considered causal and are susceptible to unmeasured confounding variables. Further, the study represented a convenience sample of patients during the enrollment time period, presenting an opportunity for selection bias. This is partially mitigated by the large number of participants in the study. Lastly, though this study's findings would ideally be extrapolated to develop interventions for other resource-limited settings, the unique geopolitical situation of Sudan may limit the generalizability of this study.

## Abbreviations

Rheumatic heart disease (RHD); low and middle income countries (LMICs); sub-Saharan Africa (SSA); group A streptococcus (GAS); acute rheumatic fever (ARF); benzathine penicillin G (BPG)

# Declarations

## Ethics approval:

As noted in the manuscript, "...all participants gave written consent to be included in the analysis. The study was conducted in accordance with the National Research Ethics Review Committee of Alzaeim Alazhari University, No. 4-5-2017, and Institutional Review Board of Stanford University, Protocol #40884."

## Consent for publication:

Data only presented in aggregate format with no identifying information. Individual consents obtained for all individuals participating in the study.

## Availability of data and materials:

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

## Competing interests:

The authors declare that they have no competing interests.

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## Authors' contributions:

JGE designed data collection tools, monitored data collection for the study, wrote the statistical analysis plan, cleaned and analyzed the data, and drafted and revised the paper. MB designed data collection tools facilitated relationships between the two institutions, and revised the paper. DE, ME, and MA designed data collection tools, monitored data collection for the study, and revised the paper. BMAE and ZHAM facilitated the focus group discussions, transcribed and translated the discussions, and revised the paper. AEInogomi and ASEE monitored data collection for the study. AElsayed designed data collection tools, monitored data collection for the study, facilitated relationships between the two institutions, cleaned the data, trained the research team and drafted and revised the paper. AYC designed the data collection tools, assisted with writing the statistical analysis plan, analyzed the quantitative and qualitative data, and drafted and revised the paper.

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## Figures

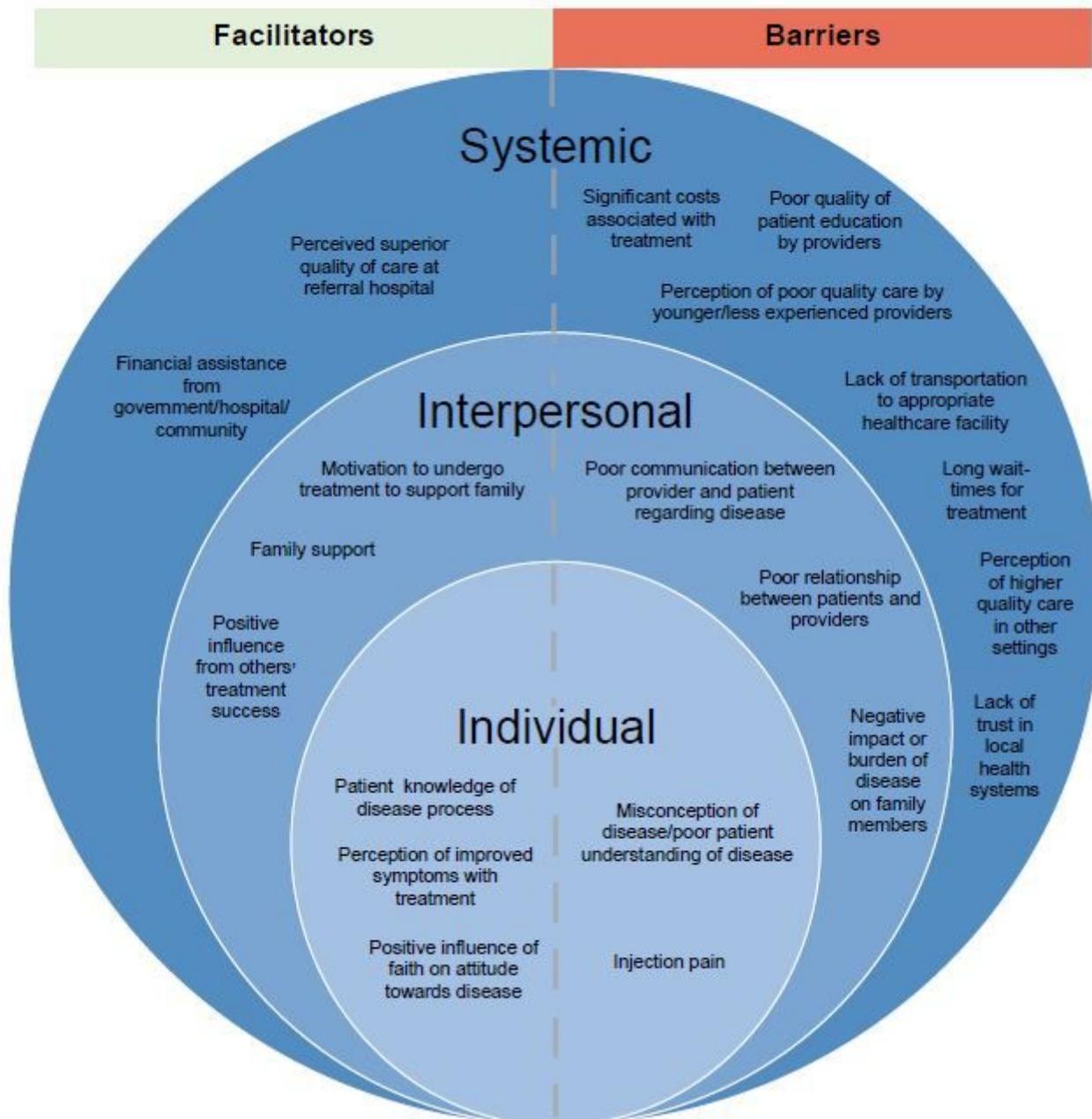


Figure 1

Major Themes of Focus Group Discussions Legend: The major themes that emerged from the focus group discussions with patients and their family members, grouped together by domain (individual, interpersonal, or systemic) and classified as a facilitator or barrier.