Throat colonization and antibiotic susceptibility of group a β-hemolytic streptococci among rheumatic heart disease patients attending Jakaya Kikwete Cardiac Institute

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THROAT COLONIZATION AND ANTIBIOTIC SUSCEPTIBILITY OF GROUP A β-HEMOLYTIC STREPTOCOCCI AMONG RHEUMATIC HEART DISEASE PATIENTS ATTENDING JAKAYA KIKWETE CARDIAC INSTITUTE

By

Sarah Patrick Wangilisasi

A Dissertation Submitted in (Partial) Fulfillment of the Requirements for the Degree of Master of Pharmacy (Hospital and Clinical Pharmacy) of

Muhimbili University of Health and Allied Sciences
October, 2018

CERTIFICATION

The undersigned certify that they have read and hereby recommend for acceptance by Muhimbili University of Health and Allied Sciences a dissertation entitled: **''Throat colonization and antibiotic susceptibility of group A β-hemolytic streptococci among rheumatic heart disease patients attending Jakaya Kikwete Cardiac Institute'',** in (partial) fulfillment of requirements for the degree of Master of Pharmacy (Hospital and Clinical Pharmacy) of Muhimbili University of Health and Allied Sciences.

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Date

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(Co-Supervisor)

_____

Date

DECLERATION AND COPYRIGHT

I, **Sarah P. Wangilisasi**, declare that this **dissertation** is my own original work and that it has not been presented and will not be presented to any other university for a similar or any other degree award.

Signature: …….. **Date**: …….

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DEDICATION

This dissertation is dedicated to my lovely father, Patrick Wangilisasi who inspired me to believe that as a woman I can achieve anything as long as I work hard. May he continue to rest in peace.

ABSTRACT

Background: Rheumatic Heart Disease (RHD), a complication of Acute Rheumatic Fever (ARF) caused by Group A β-hemolytic Streptococci (GAS) is a major cause of cardiovascular morbidity and mortality in young people in developing countries. If not prevented, recurrence of ARF causes worsening of RHD. Therefore, WHO recommends that all patients with confirmed RHD receive secondary prophylaxis against repeated attacks of ARF. The recommended drug is a long-acting penicillin. For patients allergic to penicillin; sulfadiazine, sulfisoxazole or erythromycin is recommended. Implementation of effective secondary prophylaxis is faced with challenges due to inadequate access to healthcare, prevailing threat of antibiotic resistance as well as physicians' awareness on the importance of secondary prophylaxis to RHD patients. Therefore, there is a need to explore the prevalence and factors causing GAS colonization among RHD patients.

Aim: The aim of this study was to assess throat colonization, antibiotic susceptibility and factors associated with GAS colonization among RHD patients attending Jakaya Kikwete Cardiac Institute (JKCI) in Dar es Salaam.

Methodology: A cross sectional study was conducted at JKCI in which 194 RHD patients aged ≥5 years were enrolled in the study over a period of two months from March to May 2018 to. A structured questionnaire was used to obtain socio-demographic information of the patients as well as factors associated with GAS colonization. In addition, a Morisky drug adherence tool was used to assess the status of penicillin prophylaxis adherence. Throat swabs were taken and cultured to determine the presence of GAS among patients. Isolates of GAS were tested for antibiotic susceptibility by using Kirby-Bauer disk diffusion method according to the Clinical and Laboratory Standards Institute(CLSI) version 2015 standards procedures. Antibiotics of interest were chosen according to the Tanzania Treatment Guidelines and the prescribing patterns of physicians

Results: Out of 194 patients, 12.9% had positive cultures for GAS. Prophylaxis status was independently and significantly associated (p = 0.043) with GAS colonization in multivariate logistic regression analysis. Specifically, patients who stopped prophylaxis were 3.26 times more likely (95% CI = 1.04-10.24) to be colonized by GAS when compared to patients on regular prophylaxis. Majority (96%) of GAS isolates were susceptible to Penicillin, Ceftriaxone and Ciprofloxacin. A small proportion (4%) resistance was observed among Erythromycin, Oxacillin and Co-trimoxazole, with 8% resistance observed for chloramphenicol and 20% for Vancomycin. No GAS resistance was observed against Penicillin, Ceftriaxone, Tetracycline, Ciprofloxacin and Clindamycin.

Conclusion and Recommendations: The throat colonization of GAS among RHD patients suggest inadequate prophylaxis. It is recommended that guidelines should be followed with regard to initiation and duration of prophylaxis. In addition, education on the importance of prophylaxis should be provided to patients and health care providers.

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LIST OF ABREVIATIONS

ARF	Acute Rheumatic Fever
BPG	Benzathine Penicillin G
CPL	Central Pathology Laboratory
CRF	Case Report Form
GAS	Group A β-hemolytic Streptococcus
HIV	Human Immunodeficiency Virus
JKCI	Jakaya Kikwete Cardiac Institute
MNH	Muhimbili National Hospital
MUHAS	Muhimbili University of Health and Allied Sciences
RHD	Rheumatic Heart Disease
SPSS	Statistical Package for Social Sciences
WHO	World Health Organization

DEFINITION OF TERMS

Acute rheumatic fever (ARF): Is a non-suppurative sequela that occurs two to four weeks following group A *Streptococcus* (GAS) pharyngitis and may consist of arthritis, carditis, chorea, erythema marginatum, and subcutaneous nodules.

Adherence: Describes the degree to which a patient correctly follows medical advice.

Prophylaxis: Action taken to prevent disease using a specified means against a specified disease.

Rheumatic heart disease: Is damage to one or more heart valves that remains after an episode of ARF is resolved.

CHAPTER ONE

1.0 INTRODUCTION

Group A β-hemolytic streptococcus (GAS) is an extracellular gram positive cocci that colonizes the throat and skin and can cause a wide range of infections, from uncomplicated pharyngitis to life threatening immunological complications including acute rheumatic fever (ARF), rheumatic heart disease (RHD), post streptococcal glomerulonephritis, toxic shock syndrome and necrotizing fasciitis (1). It is estimated that at least 517,000 deaths each year occur worldwide due to severe GAS disease (2). At least 18.1 million cases of severe GAS disease occur each year, with the incidence of 1.78 million cases each year (2).

The greatest burden of GAS disease is RHD with a prevalence of at least 15.6 million cases, and causing more than 250,000 deaths each year (2). Although RHD has almost disappeared in developed nations it is still a major cause of cardiovascular mortality in young people in developing countries (3). Tanzania which is a developing country also has a burden of RHD disease. A study done among 521 heart failure patients at Muhimbili National Hospital documented that RHD was a cause of heart failure in 12% of the patients (4).

RHD is a serious complication of ARF which involve damage to one or more heart valves and heart muscles. ARF is an abnormal autoimmune response of the body to infection with GAS. The infection usually starts as a sore throat or pharyngitis in children. ARF affects the skin, brain, large joints and causes inflammation of the heart valves and muscles. Recurrent ARF causes further damage to the valves leading to clinically silent valvular disease ultimately resulting in severe valvular damage and heart failure.

GAS are the most common bacterial cause of pharyngitis, with a peak incidence in children 5–15 years of age and causing 15–20% of the pharyngitis episodes (5). Throat colonization has also been observed in asymptomatic children, with surveys reporting carriage rates of 10–50% (5). In addition, GAS colonization has also been observed in RHD patients with one study done in Ethiopia reporting a carriage rate of 6.9% (6). Various factors have been identified as

the risk factors for carriage of GAS including season, age group, socioeconomic conditions such as family size, level of education, level of income, environmental factors and overall the quality of health care (5).

To limit the progression of the disease, World Health Organization (WHO) recommends secondary prevention as the cornerstone of the control of RHD (5). WHO defines secondary prevention of rheumatic fever as the continuous administration of specific antibiotics to patients with a previous attack of rheumatic fever, or a well-documented RHD. The purpose is to prevent colonization or infection of the upper respiratory tract with group A β-hemolytic streptococci and the development of recurrent attacks of rheumatic fever (5). Secondary prophylaxis is mandatory for all patients who have had an attack of rheumatic fever, whether or not they have residual rheumatic valvular heart disease (5). Regarding the duration of secondary prophylaxis, WHO recommends that the duration be adapted to each patient depending on the risk of ARF recurrence. The factors that might influence the risk of ARF recurrence and thus should be considered by clinicians in the decision of duration of secondary prophylaxis includes age of the patient, presence of RHD, number of previous attacks and time from last ARF attack, family size, family history of ARF /RHD, risk of streptococcal infection in the area, place of employment of the patient (whether its crowded or not), socioeconomic and education status of the patient. In addition to this WHO further recommend that for RHD patients with severe valvular disease and those who have undergone valve surgery lifelong ARF prophylaxis should be given.

The recommended antibiotic used is intramuscular Benzathine Penicillin G (BPG) every three to four weeks with dosage given according to weight (5). BPG is an effective agent in secondary prevention due to its long half-life which provides prolonged bactericidal protection from GAS infection (7). For patients allergic to penicillin, WHO recommends the use of oral sulfadiazine or sulfisoxazole. Erythromycin is recommended for patients allergic to both penicillin and sulfa-containing drugs (5). With effective secondary prophylaxis, recurrence and the progression of rheumatic fever to RHD can be prevented.

In the developing world effective delivery of secondary prophylaxis is hindered by limited access to healthcare, which leads to inadequate prophylaxis and failure to eradicate GAS from the throat among RHD patients. In Tanzania, there is limited information on the effectiveness of secondary prophylaxis and the barriers to its effective implementation. Therefore, it is important to assess prevalence of throat colonization of GAS among RHD and factors which are associated with the colonization.

1.1 Literature Review

1.1.1 Throat ccolonization with Group A β-hemolytic Streptococcus

Throat colonization of GAS has been observed among different areas in low income countries among normal children, patients with pahryngitis as well as RHD patients.

1.1.1.1 Asymptomatic carriage of GAS

β-hemolytic streptococci carrier rates in children living in low-income countries are high ranging from 10 to 50% (5). GAS which is one of the types of β-hemolytic streptococcus and the most common bacteria which causes pharyngitis is estimated to be carried by 5 - 15% of normal individuals without any sign of disease (8). It is more commonly found in children between 5 - 15 years. Various studies have documented the prevalence of asymptomatic carriage of GAS. A study carried out to determine the rate of asymptomatic throat carriage of GAS in 487 school children in Western Nepal revealed a carriage rate of 9.2% (8). In Uganda a GAS carriage rate of 16% was reported by a study done among 366 children from five primary schools (9). The carriage of β-hemolytic streptococci was detected in 18.1% of participants in a study conducted among school aged children in Argentina, with the majority of carriage being GAS (10). A lower rate of GAS isolation was documented by Chauhan et al among 1,849 asymptomatic children in India with a rate being 1.41% (11). In Tanzania, GAS carriage rate of 6.9% was reported among schoolchildren in Mbulu district (12). A similar study done among schoolchildren in Pemba reported prevalence of 8.6% (13).

1.1.1.2 Carriage of GAS among patients with acute pharyngitis

It is estimated that 15 - 20% of episodes of pharyngitis experienced by children are caused by GAS and nearly 80% by viral pathogens (5). A study done in Ethiopia reported the prevalence of GAS in children with pharyngitis being 11.3% (14). In Iran an isolation rate of GAS from children with acute pharyngotonsillitis was 34.1% (15). Many factors have been reported to influence carriage of GAS including age (5 - 15 years), restricted living conditions, family size, over-crowding as well as low availability of penicillin and other antibiotics. All these factors facilitate spread of GAS (15). A lower prevalence of 6.1% was reported by a study done in Mozambique among school children with pharyngitis. It was emphasized that the low

prevalence was due to study being done during the dry season which is not the peak season for pharyngitis (16).

1.2.1.3 Carriage of GAS among RHD patients

Throat carriage of GAS has also been seen in patients with RHD. This was revealed by a study done in Ethiopia among 233 children with RHD who were receiving BPG prophylaxis which revealed the throat carriage rate of β-hemolytic streptococcus was 24% (6). The study also revealed that adherence to prophylaxis predicted the carriage of β-hemolytic streptococcus whereby those who missed at least one dose had higher β-hemolytic streptococcus positivity rate than those who did not miss any (6).

1.1.2 Antibiotic susceptibility pattern of GAS

Antibiotic susceptibility of GAS against various antibiotics has been changing in recent years, mostly due to inappropriate usage of wide spectrum antibiotics (17). There has been increasing frequency of resistance of this organism to antibiotics and the number of drugs to which they are resistant have been increasing worldwide (18). Currently, penicillin is the drug of choice for GAS pharyngitis treatment and secondary prophylaxis of RHD patients, and penicillin resistance to GAS has not yet been reported (18).

In general, GAS has remained to be susceptible to all β-lactam antibiotics. This is supported by a study done in Senegal which documented that GAS was still susceptible to all β-lactam antibiotics including penicillin, amoxicillin, and cephalosporins (19). In Ethiopia a study done among schoolchildren revealed that all GAS isolates were susceptible to penicillin (20). Resistance to other antimicrobial agents such as macrolides has been increasing. A study done in Japan reported resistance of various strains of GAS against erythromycin, clindamycin, telithromycin, and ciprofloxacin. However all strains were susceptible to ampicillin (21). Another study done in India reported resistance to macrolides, tetracycline and co-trimoxazole (17).

1.1.3 Adherence to secondary prophylaxis

Secondary prophylaxis in patients with rheumatic fever is very important in preventing recurrence of ARF and progression of RHD. However, ensuring adherence to secondary prophylaxis for RHD has been very challenging (22). A study done among 536 patients with rheumatic fever on BPG secondary prophylaxis revealed that 35% of patients were non-adherent to medication at any time during follow up (22). Another study done in Caledonia among 70 patients receiving BPG prophylaxis, 46% of the patients were non-adherent to the prophylaxis (23). Non-adherence was also reported in a study done in Mulago Hospital, Uganda whereby 54% of patients receiving BPG prophylaxis had adherence of >80% (24).

1.1.4 Morisky Tool for assessing adherence

Morisky tool has been used to assess adherence in many studies (25). The tool is a questionnaire which is specially designed and validated to capture information from participants on the rate of adherence. It can be modified in ways where it can suit different studies (26). Its first version was used in 1980's and was continued to be used until 2008 when it was revised (27). The scale of adherence is measured depending on the scores resulting after calculation, in which scores greater than 2 is regarded as low adherence, 1 - 2 is medium adherence and 0 is high adherence.

Although this method is likely to result in overestimation of adherence to prophylaxis among RHD patients, questions were designed in such a way that recall biased was minimized. This included asking questions about the recent visits to the health facilities and doses taken since the last visit.

1.1.5 Factors associated with adherence to secondary prophylaxis

Lack of awareness of the patients and parents about the disease is one of the factors causing low adherence. A study done among 70 school children with RHD in Ethiopia found that 15% of parents caring for RHD children had some idea of their children's disease and the importance of prophylaxis (28). A study done in Tanzania by Bergmarket et al (29), discovered that patients' lack of knowledge of GAS and its connection to RHD was a barrier to seeking medical care.

Family income and socio-economic status also affects adherence to prophylaxis. Respicio and colleagues reported in their study that compliance to prophylaxis was related to occupation of the father and family income. They reported that patients from poor families were less adherent to treatment (30). Adherence is also affected by patients having to travel long distances to health facilities as reported by a study done in Jamaica among 39 patients with RHD (31). Waiting long periods to get injections, fear of injections and having to take time off from work or school have also been reported to affect adherence among RHD patients (31,32).

Lack of resources to manage GAS at the provider and systems level is also another factor affecting adherence. In African countries, the lack of resources is due to competing priorities of treating HIV and malaria. Therefore RHD is usually neglected by policy makers hence limited availability of penicillin for the management of RHD (29).

1.1.6 Rheumatic fever recurrence

Morbidity, mortality and disease progression is directly related to recurrences of rheumatic fever (33). Studies have reported the incidence of rheumatic fever recurrence to be about 15 – 34% (34). A study done in Brazil among 148 RHD patients revealed that 14.2% had recurrent episodes of rheumatic fever. Pelajo et al also reported a recurrence rate of 16.5% among 536 patients who were studied (22). In North India recurrence was found in 0.9% of patients. A higher percent was reported by a study done in Alexandria Egypt where rheumatic fever recurrence was 37.3% (32). Risk factors associated with recurrence have been reported to include living in rural and semi-urban areas and lack of adherence to secondary prophylaxis (22,34).

1.2 Conceptual Framework

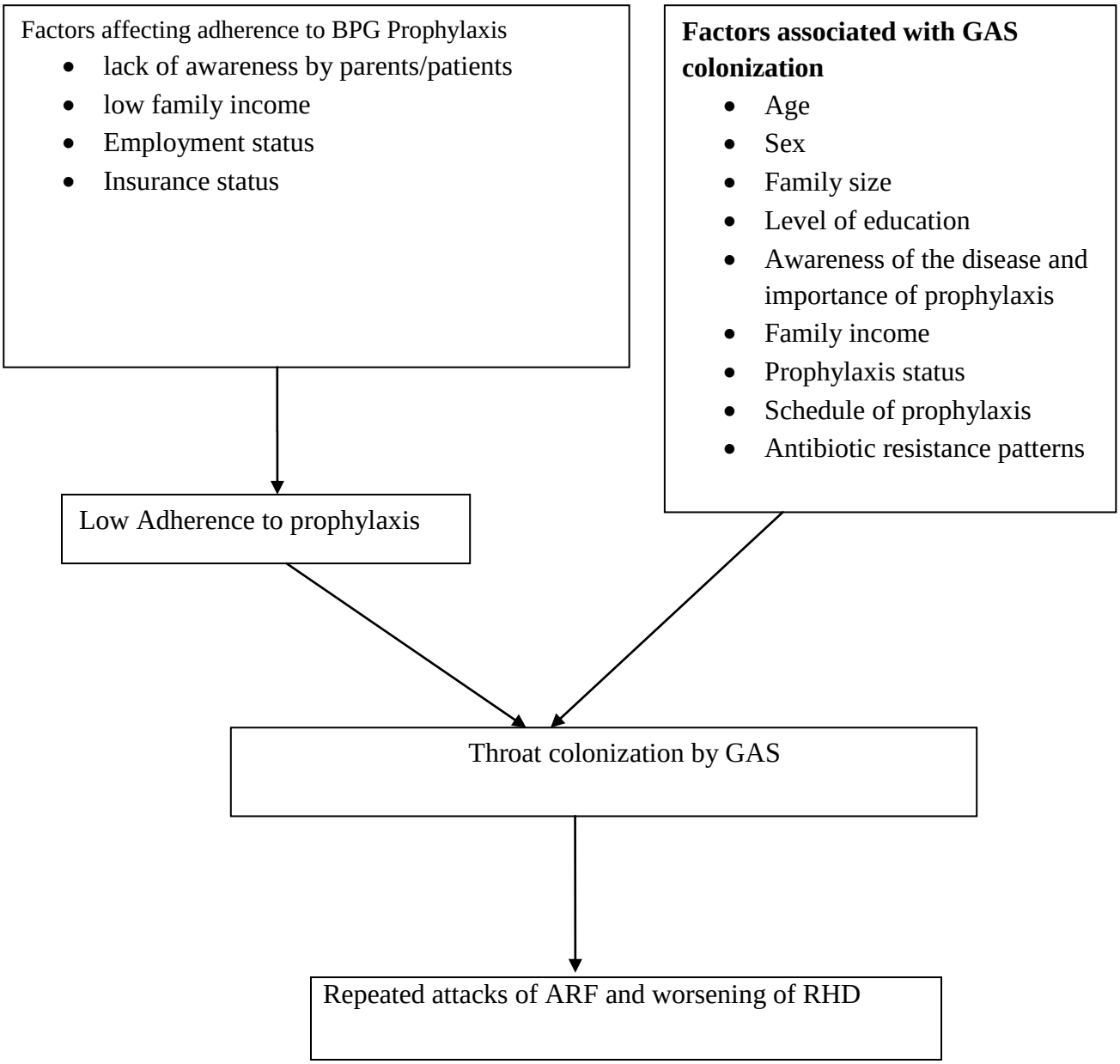

Figure 1: Conceptual Framework

Throat colonization by GAS among RHD patients is influenced by factors which include prophylaxis status of the patient, adherence level to secondary prophylaxis, socio-economic factors such as age, sex, level of education, employment status, insurance status, family size, family income and antibiotic susceptibility patterns.

This study assessed the throat colonization and antibiotic susceptibility of GAS in RHD patients. It also assessed the factors associated with throat colonization of GAS among these patients which may lead to recurrence of ARF. The primary outcome (the dependent variable) was throat colonization with GAS.

1.3 Problem Statement

RHD continues to cause disability and premature deaths among young people in developing world (5). Recurrence of ARF among RHD patients has been shown to be the cause of disease progression and worsening of RHD (5). To prevent ARF recurrence and subsequent worsening of RHD, secondary prophylaxis is needed. BPG injection every 3 or 4 weeks in patients with RHD is the most effective approach (6). However effective delivery of this prophylaxis in the developing world is hindered by limited access to healthcare due to factors including limited awareness, inadequate health literacy, and inadequate health seeking behavior (6). This causes low compliance and adherence resulting in inadequate prophylaxis and failure to eradicate GAS from the throat which eventually leads to recurrence of ARF and hence worsening of RHD.

In Tanzania, there is limited information on the effectiveness of secondary prophylaxis and the barriers to its effective implementation. Furthermore, there is no data on the level of adherence or factors affecting adherence to prophylaxis among RHD patients. Therefore, it is important to assess prevalence of throat carriage of GAS among RHD patients as a way to assess the effectiveness of secondary prophylaxis implementation and its barrier.

1.4 Rationale of the study

With the continued recurrence of ARF and worsening of heart disease among RHD patients on secondary prophylaxis, it is important to know the rate and factors causing GAS colonization among patients with RHD in our setting. Furthermore, understanding the antimicrobial susceptibility pattern of GAS isolated from RHD patients will inform clinicians on the efficacy of the WHO's first line recommended antibiotic (long-acting penicillin G) as well as inform clinicians of the best choice for second line antibiotics prophylaxis against ARF to be used in our local setting. This will help health care givers and policy makers to improve the implementation of BPG secondary prophylaxis programs. Such information will also serve as literature repository for different research communities and ministry responsible for health.

1.5 Study Questions

i. What is the prevalence of GAS throat colonization in RHD patients attending JKCI?
ii. What factors are associated with GAS throat colonization among RHD patients?
iii. What is the antibiotic susceptibility pattern of GAS found in throat cultures of RHD patients?
iv. What is the level of adherence to secondary prophylaxis in RHD patients?

1.6 Study Objectives

1.6.1 Broad objective

To assess throat colonization, antibiotic susceptibility and factors associated with GAS colonization among RHD patients attending JKCI.

1.6.2 Specific objectives

i. To determine the prevalence of GAS throat colonization among RHD patients attending JKCI.
ii. To determine antibiotic susceptibility pattern of GAS found in throat cultures of RHD patients attending JKCI.
iii. To assess the level of adherence to secondary prophylaxis among RHD patients attending JKCI.
iv. To determine the factors associated with throat colonization among RHD patients attending JKCI.

CHAPTER TWO

2.0 METHODOLOGY

3.1 Study area

This study was conducted at JKCI. JKCI is a national hospital specialized in cardiovascular care, training and research. JKCI serves patients across all regions in Tanzania who are referred from regional referral and designated hospitals for cardiovascular medical intervention. Due to its level, JKCI has a number of specialists in cardiovascular medicine and is equipped with advanced diagnostic and treatment facilities. RHD patients from other hospitals all over Tanzania are referred to JKCI for further medical and surgical interventions. Therefore, this was the most appropriate study site to access RHD patients.

Throat swab cultures and antibiotic susceptibility tests were done in the Microbiology section, Central Pathology Laboratory (CPL), Muhimbili National Hospital located 180 meters from JKCI. CPL provides high quality laboratory services to all patients referred to MNH and JKCI and to private patients without referrals. It is the leading diagnostic laboratory service provider in Tanzania and has highly trained laboratory scientists and technicians and sophisticated diagnostic equipments that process high speed automated tests. The laboratory is accredited by the Southern African Development community accreditation services (SADCAS) in accordance to the recognized international standard ISO 15189:2012 (35).

3.2 Study design

This was a hospital-based cross-sectional study.

3.3 Study population

All RHD patients attending cardiac clinics and those admitted at JKCI.

2.5 Inclusion criteria

The study included all RHD patients who were age 5 years and above, on secondary prophylaxis or eligible for secondary prophylaxis and had provided consent to participate in the study.

2.6 Exclusion criteria

Critically ill RHD patients, whom throat swab samples could not be obtained from, were excluded from the study. Furthermore, RHD patients who were on antibiotics (other than those indicated for ARF prophylaxis) at the time of data collection were also excluded.

3.7 Sample size determination

The prevalence of *β*-hemolytic streptococcus from previous study done in Ethiopia by Zegeye et al was 24% (6).

The sample size was calculated using the formula suitable for cross-sectional studies:

$$n = \frac{Z^2 P (1-P)}{d^2}$$

n is the sample size, Z is the statistic corresponding to level of confidence whereby for this study 95% level of confidence was aimed hence z = 1.96, P is expected prevalence which is 24% (6). d represents precision corresponding to effect size and its value should not be more than half of P, therefore precision of 6% will be used in this study (36).

Calculation:

$$N = Z^2 P (1-P)/d^2 = 1.96^2 \text{ X } 0.24 (1-0.24)/0.06^2 = 194$$

Minimum sample size was 194. Adding 10% non-responding or loss to follow patients, the sample size for this study was 214.

3.8 Sampling procedure

Consecutive sampling procedure was employed during recruitment of study participants. Participants were recruited consecutively as they came to the cardiac clinic for their follow up appointment. RHD patients who were on secondary prophylaxis or who were eligible to be on secondary prophylaxis were invited to participate in the study.

3.9 Data collection

3.9.1 Socio-demographic information

Pre-constructed semi-structured questionnaires (Appendix II) was used to collect information from patients and parents/guardians. Information collected include; demographic information, socio-economic information, knowledge on RHD disease and importance of adherence. Socio-demographic information included age, sex, marital status, level of education, employment status, family average income, mode of payment of health services and family size. Knowledge about RHD and importance of adherence to prophylaxis for GAS was assessed by asking questions to patients. These questions included if the patient/parent/guardian knew what they were suffering from, if they knew about getting prophylaxis and if they knew the importance of prophylaxis.

For patients less than 18 years of age, socio-economic information and knowledge of guardians/parents was collected.

3.9.2 Determination of adherence

Modified Morisky Tool was used to scale patients on adherence to medication (Appendix II). This is a special tool with 8 items which complemented the questionnaires and gave the scale of adherence to medication into >2 (low adherence), 1-2 (medium adherence) and 0 (high adherence). This validated tool is widely used for assessing medication adherence and has been used in various published studies (27).

3.9.3 Collection of throat swab

Using a sterile swab, the posterior nasopharynx and the tonsillar arches were swabbed without touching the cheeks, tongue, lips or other areas of the mouth. Each swab was immersed immediately into a test tube containing amies transport medium (Oxford, England) (37). The samples were taken to the Muhimbili National Hospital Laboratory (Central Pathology Laboratory) for culture and antibiotic sensitivity testing.

3.9.4 Clinical data

Clinical data including type and severity of valve lesion and presence of any surgical intervention done was obtained from patients' files.

3.9.5 Patient care and management

The study did not involve any invasive procedure, hence minimum risk to the patient. The results of the culture were informed to the doctors attending the patients. Confirmed patients with GAS colonization were referred to their attending doctors for further management.

3.10 Laboratory Procedures

3.10.1 Throat swab culture

Five percent (5%) sheep's blood agar plates were used in which the throat swabs were inoculated onto the plates and incubated for 24-48 hours at 37^0C in aerobic environment. GAS isolates were identified based on the standard micro-biological techniques which include β-hemolytic activity on sheep's blood agar, small colony characteristics, Gram positive cocci, catalase production negative, and 0.04-U bacitracin disc susceptibility (14,37).

3.10.2 Antimicrobial susceptibility

Antimicrobial susceptibility testing was done by using the Kirby Bauer disc diffusion method according to criteria set by Clinical Laboratory and Standards Institute (CLSI) version 2015(38). Muller Hinton agar supplemented with 5% sheep blood was used (38). Bacterial suspensions at a concentration of 10^5 CFU/mL were inoculated on sheep blood Mueller-Hinton agar plates and incubated in aerobic environment for 24 hours at 37°C.

The antimicrobial discs of interest were chosen according to the prescribing patterns in local settings. The following discs with respective concentration were used: penicillin G (10 units), oxacillin (30µg,), ceftriaxone (30µg), vancomycin (30µg), erythromycin (15µg), tetracycline (30µg), ciprofloxacin (30µg), chloramphenicol (30µg), clindamycin (2µg), and trimethoprim-sulfamethoxazole (25µg). Inhibition zone diameters were interpreted as sensitive, intermediate and resistant according to the principles established by CLSI (38). The respective inhibition zone diameters and their interpretation for the different antibiotics are shown in table 1 below.

Table 1: Criteria for interpretation of antibiotic susceptibility results according to CSLI guidelines version 2015

Name of antibiotic	**Antibiotic concentration**	**Zone of inhibition (mm)**		
		Susceptible	**Intermediate**	**Resistant**
Penicillin	10units	≥24	-	-
Oxacillin	30µg	≥22	-	≤21
Ceftriaxone	30µg	≥24	-	-
Vancomycin	30µg	≥17	-	-
Erythromycin	15µg	≥21	16-20	≤15
Tetracycline	30µg	≥23	19-22	≤18
Ciprofloxacin	30µg	≥16	13-15	≤12
Chloramphenicol	30µg	≥21	18-20	≤17
Clindamycin	2µg	≥19	16-18	≤15
Trimethoprim-Sulfamethoxazole	1.25/23.75 µg	≥19	16-18	≤15

3.11 Data management and analysis

3.11.1 Sources of data

Primary data

Data were obtained from patients and/or guardians using CRF (Appendix II) and laboratory data were obtained after culture. Primary data for this study included age, sex, marital status of guardians/parents, residence, level of education of family, employment status, family size, family income, mode of payment, adherence level, throat culture positivity and antibiotic susceptibility pattern.

Secondary data

Data were obtained from reviewing patients' files at JKCI. The data collected included the types of the valve affected by RHD i.e. single valve or multiple valves and whether surgical intervention was done or not.

3.11.2 Data management

Numbers were used as identity to maintain confidentiality of study participants. Collected data was stored in secured fire-resistant case accessible only to investigator. Raw data in physical storage were transferred into electronic form for cleansing and data analysis. Accessibility to all storage formats was only under custody of investigators while ensuring all ethical issues have been taken into consideration.

3.11.3 Data analysis

Data were entered and analyzed using Statistical Package for Social Sciences (SPSS) computer software version 22 software (USA). For univariate analysis of quantitative variables such as age, measures of central tendency including mean, mode and median and measure of dispersion such as range, variance and standard deviation were used. For categorical data such as sex, level of education and employment status proportions were used. Data summarization was done using pie charts, bar charts, contingency tables accordingly. Chi-square test was employed for testing statistical significance for frequency distribution of categorical data such as level of education versus outcome of interest like throat culture positivity.

Multiple regression analysis was employed to examine the association between potential factors such as family size, family income and the likelihood of the primary outcome which is throat culture positivity. The results were of statistical significance when P-value was <0.05.

3.12 Ethical Considerations

The study commenced after obtaining ethical clearance from Muhimbili University of Health and Allied Sciences (MUHAS) Research and Publication committee. Permission to conduct the study in the hospital was sought from the Head of Research Unit at JKCI. Every study participant signed freely informed consent form (Appendix I) before proceeding with data collection. For confidentiality purposes, each participant was assigned identity number instead of his/her name. Furthermore, a private room was used for conducting interviews. All documents including consent form and data collection tools were kept privately by the investigator. Apart from the research team which included one nurse and one laboratory technician, the data was not accessed by anyone. Patients were also assured that their identity will not appear anywhere in the study documents or publications.

The benefits of RHD patients participating in the study included awareness of the GAS throat colonization status hence ARF recurrence risk. Furthermore, those who were found to be harboring GAS were referred to their attending physicians for further management. In addition, the scientific knowledge obtained will be useful during periodical revision of health policy and practice. Other than minor discomfort experienced during taking throat swab there was no harm or danger which was raised by patients participating in this study**.**

CHAPTER THREE

3.0 RESULTS

During the study period of 10 weeks from March to May 2018, a total of 218 patients with a diagnosis of RHD as per attending Physician's diagnosis were approached for recruitment to participate in the study. Of the 218 patients approached, 14 declined to provide consent, and throat swabs were not obtained from 10 patients hence were excluded from the final data analysis. Therefore, a total of 194 patients provided the information required for the study, and they constituted the present study population. The flow diagram of the study population showing the recruitment process is presented in Figure 2.

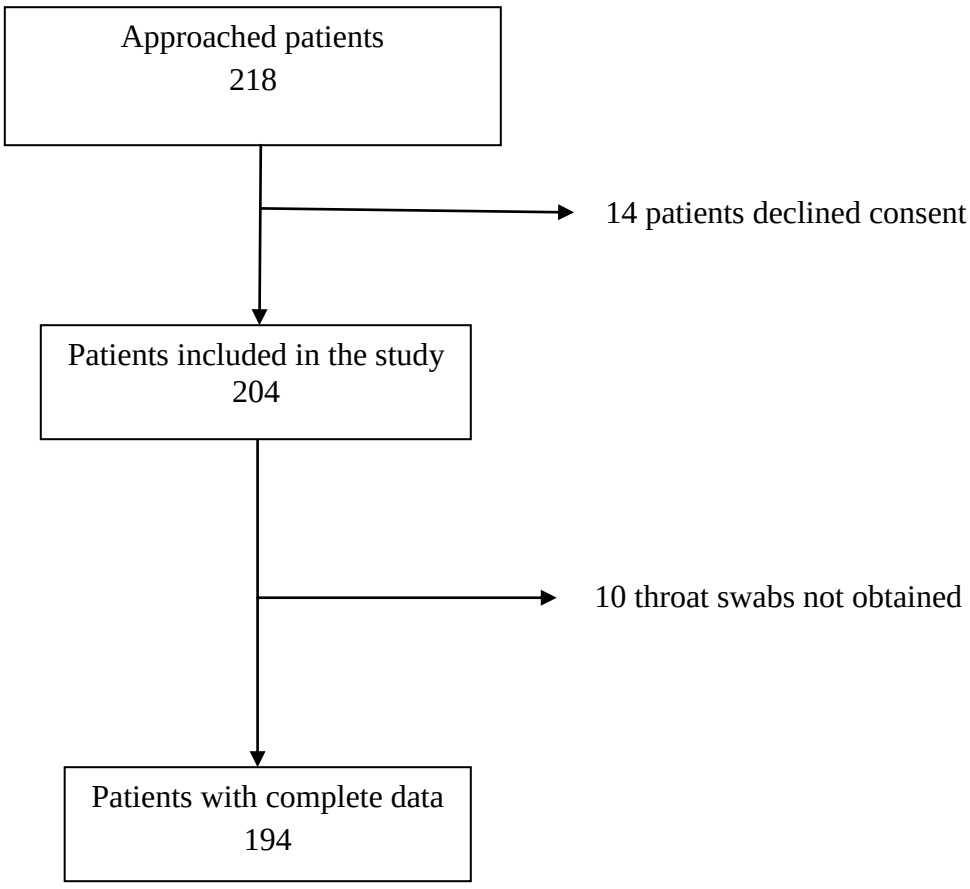

Figure 2: Flow diagram of recruitment of the study participants

3.1 Socio-demographic characteristics of the study participants

The final analysis included 194 patients. The age of the participants ranged from 4 - 75 years with mean age of 28.4 years. More than half (52.6%) of the participants were aged below 25 years. Females made 58.2% of the study population with the remaining 41.8% being males. Most (57.2%) of the patients or parents/guardians taking care of RHD patients were married, and 59.3% had attained primary education as their highest level of education. About a third of the participants were living in a family with ≥7 people and 58.8% had no health insurance cover. Majority of the patients were unemployed (75.7%) and those earning less than TZS 70,000 per month were 58.2%. Table 1 summarizes the socio-demographic characteristics of the study participants.

Table 2: Socio-demographic characteristics of the study participants (N = 194)

Characteristic	Frequency (n)	Percentage (%)
Age groups (years)		
≤ 25	104	53.6
26 – 45	55	28.4
>45	35	18.0
Sex		
Males	81	41.8
Females	113	58.2
Marital status		
Single	65	33.5
Married	111	57.2
Divorced	7	3.6
Widowed	11	5.7
Level of Education		
Primary	115	59.3
Secondary	48	24.7
University	21	10.8
No formal education	10	5.2
Family size (number)		
≤6 people	127	65.5
≥7 people	67	34.5
Mode of Payment		
Insurance	80	41.2
Out of pocket	114	58.8
Average Family Income (TZS)		
<70,000	113	58.2
70,000 – 310,000	52	26.8
>310,000	29	15.0
Employment Status		
Employed	30	15.5
Unemployed	147	75.7
Retired	7	3.6
Student	10	5.2

TZS = Tanzanian Shillings

3.2 Clinical and other characteristics of the study participants

Most of the study participants (84.5%) were aware of their medical condition and they knew what they were suffering from. Furthermore 51% of study participants knew about the need for prophylaxis against repeated attacks of rheumatic fever. In addition, 17.5% of the participants knew the importance of the prophylaxis. Table 2 summarizes the clinical and other characteristics of the study participants.

Table 3: Clinical and other characteristics of study participants (N=194)

Characteristic	**Frequency (n)**	**Percentage (%)**
Know about RHD suffering		
Yes	164	84.5
No	30	15.5
Know about ARF prophylaxis		
Yes	99	51
No	95	49
Know importance of prophylaxis		
Yes	34	17.5
No	160	82.5
Time from diagnosis (months) *		
<12 months	54	42.5
12-36 months	32	25.2
>36 months	41	32.3
Valvular involvement		
Single valve disease	98	50.5
Mixed valves disease	96	49.5
Surgical intervention		
Done	37	19.1
Not done	157	80.9

*RHD = Rheumatic Heart Disease; ARF = Acute Rheumatic Fever *N=127(data for 67 patients were missing)*

3.3 Acute Rheumatic Fever prophylaxis status of study participants

Among 194 patients interviewed, 92 (47.4%) had never been on prophylaxis since diagnosis, 58 (29.9%) were on regular prophylaxis, 39 (20.1%) had stopped prophylaxis and the remaining 5 (2.6%) started prophylaxis on the day of the survey (Figure 2).

Of the 58 patients that were on regular prophylaxis, 10 (17.2%) were found to have good adherence to ARF prophylaxis as determined by the modified Morisky adherence tool (score of 0). The remaining 48 (82.8%) patients had medium level of adherence (score of 1-2). Adherence status of 136 patients could not be assessed because out of these, 131 patients had never been on prophylaxis and 5 patients started prophylaxis on the day of the survey. Among patients on regular prophylaxis, 56.9% were on 4-weekly regime and the remaining 43.1% were on 3-weekly regime.

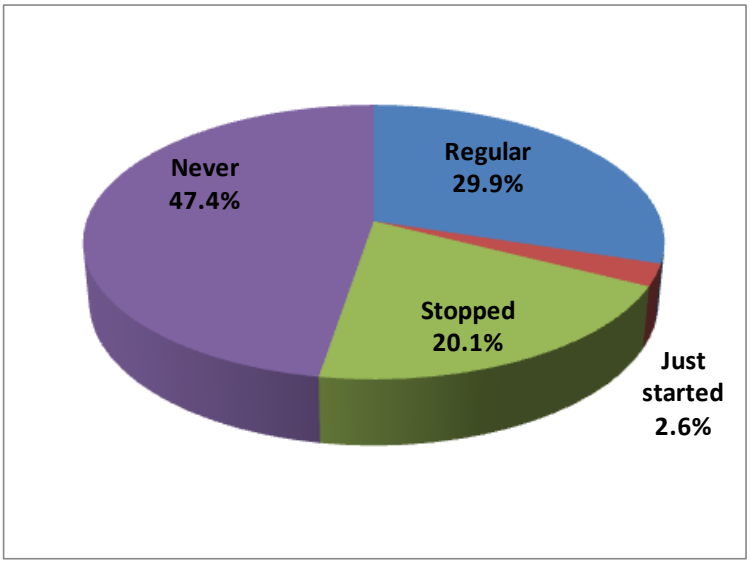

Figure 3: Prophylaxis status of study participants

3.4 Throat colonization and antimicrobial susceptibility of GAS isolated from study participants

In the total study population, throat culture results of 25 patients were positive for GAS, giving the throat culture colonization rate of 12.9%. Throat culture results were negative in the remaining 169 (87.1%) patients.

GAS isolated from the 25 patients were mostly susceptible to Benzathine Penicillin G (24/25, i.e. 96% susceptible), Ceftriaxone (24/25, i.e. 96% susceptible), and Clindamycin (24/25, i.e. 96% susceptible). GAS isolates showed the highest resistance towards Vancomycin (5/25, i.e. 20% resistance) and Chloramphenicol (2/25, i.e. 8% resistance). There were also high intermediate susceptibilities towards most commonly used antimicrobial agents including Oxacillin (20%), Erythromycin (28%) and Co-trimoxazole (32%). Figure 3 shows the susceptibility patterns of GAS towards the 8 antibiotics that were tested. The negative numbers shown in figure 3 represent the number of isolates that were resistant to the respective antibiotics.

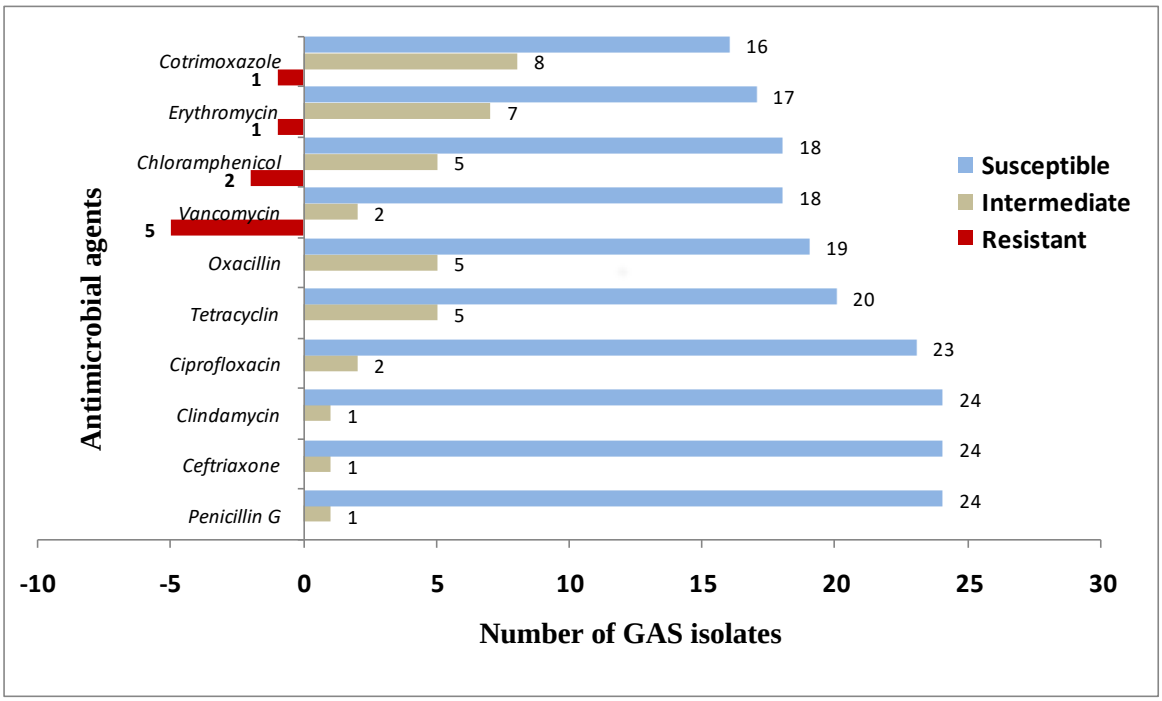

Figure 4: Antimicrobial susceptibility of GAS isolated from RHD.

3.5 Factors associated with GAS throat colonization among study participants

Patients with positive throat culture did not differ from those with negative culture with regards to age distribution, gender, level of education, number of people in the household as well as family income, all $p > 0.05$ (Table 3). They also did not differ in terms of knowledge and understanding of importance of ARF prophylaxis, $p > 0.05$ for both (Table 3). Although not statistically significant, patients with positive culture had higher proportions of un-insured (68% versus 57.4%), unemployed (38% versus 22.5%), those unaware of their medical condition (24% versus 14.2%) as well as patients with multiple valve disease (60% versus 47.9%), (Table 3).

With regards to prophylaxis status, a larger proportion (40%) of patients had stopped prophylaxis among patients who had positive cultures compared to 17.2% in the culture negative group, a significant difference, $p = 0.029$ (Table 3). Of the 58 patients on regular prophylaxis, 6 (10.3%) had positive cultures and the remaining 52 (89.7%) had negative culture results. There was no statistically significant difference between patients with positive culture and those with negative culture with regards to prophylaxis adherence level or schedule of prophylaxis, $p > 0.05$ for both. A trend was however seen towards higher proportion of patients with medium adherence (33.3% versus 15.4%) and four-weekly prophylaxis schedule (83.3% versus 53.8%) to be in the culture positive group (Table 3).

Table3: Socio-demographic, clinical and other characteristics in relation to GAS throat colonization

Characteristic	**Culture Negative (n = 169) n (%)**	**Culture Positive (n = 25) n (%)**	***p*-value**
Age <25 (years)	89 (52.7)	13 (52)	0.559
Female gender	97 (57.4)	16 (64)	0.345
Primary or less level of education	110 (65.1)	15 (60)	0.387
≥7 people in the household	59 (34.9)	8 (32)	0.483
Not insured	97 (57.4)	17 (68)	0.217
Family income TZS <70,000	97 (57.4)	16 (64)	0.345
Unemployed	38 (22.5)	8 (38)	0.211
Didn't know about RHD suffering	24 (14.2)	6 (24)	0.165
Didn't know about ARF prophylaxis	84 (49.7)	11 (44)	0.376
Didn't know the importance of prophylaxis	139 (82.2)	21 (84)	0.545
Had surgical intervention	30 (17.7)	6 (24)	0.331
Had multiple valve disease	81 (47.9)	15 (60)	0.181
Prophylaxis status			
On regular prophylaxis	52 (30.8)	6 (24)	0.029
Stopped prophylaxis	29 (17.1)	10 (40)	
Never been on prophylaxis	88 (52)	9 (36)	
Prophylaxis adherence level*			
High	44 (84.6)	4 (66.7)	0.274
Medium	8 (15.4)	2 (33.3)	
Schedule of prophylaxis*	24 (46.2)	1 (16.7)	
Every three weeks	28 (53.8)	5 (83.3)	0.174
Every four weeks			

*TZS = Tanzanian Shillings; RHD = Rheumatic Heart Disease; ARF = Acute Rheumatic Fever. * N = 58*

Prophylaxis adherence status and other factors that were weakly associated with culture positivity were entered into a logistic regression model to determine the factors that are independently associated with culture positive results. The model comprised of sex, insurance status, number of people in the household, knowledge of RHD, prophylaxis status, number of

valves affected by RHD and history of surgery (Table 4). Having stopped prophylaxis was the only factor that was independently associated with positive culture results in multivariate logistic regression analysis, OR (95% CI) = 3.26 (1.04 – 10.24), p = 0.043 (Table 4). Specifically, compared to patients on regular ARF prophylaxis, patients who stopped prophylaxis were 3.26 times more likely to have positive throat culture results independent of all other factors in the model (Table 4).

Table 4: Multivariate logistic regression analysis of factors associated with GAS colonization among RHD patients

Variable	**Univariate analysis**		**Multivariate analysis**	
	OR (95% CI)	***p*-value**	**OR (95% CI)**	***p*-value**
Female sex	1.32 (0.55 – 3.16)	0.533	1.31 (0.53 – 3.31)	0.547
Un-insured	1.58 (0.65 – 3.86)	0.318	1.62 (0.61 – 4.03)	0.348
Living >7 people in the household	0.88 (0.36 – 2.15)	0.775	0.73 (0.28 – 1.93)	0.524
Unaware of disease condition	1.91 (0.69 – 5.26)	0.212	2.42 (0.77 – 7.59)	0.129
Prophylaxis status				
Regular on prophylaxis	Constant		Constant	
Stopped prophylaxis	**2.99 (0.99 – 9.06)**	**0.053**	**3.26 (1.04 – 10.24)**	**0.043**
Never started	0.89 (0.30 – 2.63)	0.828	0.98 (0.32 – 3.02)	0.975
Multivalve disease	1.63 (0.69 – 3.83)	0.263	1.87 (0.74 – 4.67)	0.189
History of previous surgery	1.41 (0.52 – 3.81)	0.503	1.87 (0.62 – 5.59)	0.265

CHAPTER FOUR

4.0 DISCUSSION

GAS throat colonization is a well-known risk factor for development of sore throat and subsequent ARF in the general population (2), but more importantly among people with previous history of ARF and in those with RHD (5). This is more serious for those who are particularly at a greater risk due to a number of factors including their genetic susceptibility which renders them more sensitive to infection with a rheumatogenic strain of GAS (39). Only few studies from sub-Saharan Africa have reported the prevalence of GAS colonization in the general population (8,18), in patients with pharyngo-tonsillitis (11,(16), and among RHD patients (6). The present study therefore adds to the current knowledge on RHD in the region by demonstrating that among RHD patients attending care at a tertiary health facility in Tanzania, throat GAS colonization is present in 12.9% and is independently associated with stopping ARF prophylaxis among these patients.

The 12.9% prevalence of throat GAS colonization found in this study is much higher than that found among 233 children with chronic RHD attending care at a cardiac clinic in Addis Ababa, Ethiopia (6). Of note, the prevalence of GAS positivity in that study was 6.9% and the difference between the two studies can mainly be attributed to the fact that all patients in the Ethiopian study were on ARF prophylaxis as compared to the present study where prophylaxis was taken regularly by 29.9% of the total studied population. The deleterious effects of GAS colonization among patients with RHD have been well documented (40). The finding of our study is therefore clinically very relevant, meaning that around 13% of RHD patients in our setting are at increased risk of worsening of their disease and therefore progression towards heart failure and other complications brought about by RHD (41).

The finding that stopping ARF prophylaxis is independently associated with positive GAS throat culture results is in agreement with previous reports in literature (6,7,9,14). In the study by Zegeye, et al from Ethiopia (6), children who missed at least one prophylaxis within the last 6 months had a higher culture positivity rate than those who did not miss any scheduled prophylaxis. In the present study, having stopped prophylaxis increased the likelihood of GAS

colonization up to 3 times. The explanation for increased GAS colonization among patients who stop prophylaxis is to a larger extent clear, since interrupting the dose or stopping the prophylaxis means the patient will not have the required level of the antibiotic in blood that is necessary to prevent GAS throat colonization (42).

The finding that less than a third (29.9%) of patients with RHD in our setting was on regular prophylaxis is alarming. Furthermore, the fact that almost half of the study participants (47.4%) had never been on any ARF prophylaxis raises even more concerns. Although reasons for not being on regular prophylaxis were not systematically studied in the present study, it is unlikely that the 47.4% patients that were never on prophylaxis had clinically relevant reasons not to be on prophylaxis against ARF. Ideally, any patient with confirmed RHD needs to be on prophylaxis at least for some period of time as per guidelines (43). This is also true for those who stopped taking their prophylaxis. The reasons for stopping prophylaxis is most likely multifactorial and further research focusing on Physicians-related factors, patients-related factors as well as factors related to our health care delivery system need to be studied. All these factors have been found to influence prescribing practice of prophylaxis and adherence among RHD patients elsewhere (3,20,21,22).

Using in vitro susceptibility assay, GAS isolated from RHD patients in this study were almost 100% susceptible to penicillin G. This finding is similar to many previous studies in documented literature, and it is at least encouraging to know that despite being in the market for more than 8 decades, penicillin is still performing well in terms of GAS susceptibility (6,14,41). This may be due to penicillin being limited to use only in few number of diseases including pharyngitis, syphilis, ARF prophylaxis etc. There has been however reports of GAS resistance to penicillin (43,44), and more care should be taken to avoid risk factors that may lead to increased chances to develop resistance to penicillin in our setting. Factors like unreliable and interrupted doses as well as poor quality of penicillin have been reported to increase GAS resistance to the drug in vitro as well as in vivo studies (45). The pattern of reduced GAS susceptibility (intermediate results) and resistance towards Vancomycin, Chloramphenicol, Erythromycin and Co-trimoxazole observed in the current study is similar

to other studies, most likely caused by factors such as increased frequency and irrational use of these antibiotics (46).

We found in this study that knowledge on the need, as well as the importance of being on prophylaxis to be low among patients with RHD. This has negative implications as far as the management of RHD is concerned, considering the chronic nature of the disease and the need for patients to take regular medications and to follow regular visits to the health facilities. The low knowledge could have been one of the contributing factor to stopping the prophylaxis (although this was not actively assessed in this population), as well as could have affected the adherence status in this population. In a brief communication by Bergmark, et al reporting the burden of disease and barriers to the diagnosis and treatment of GAS pharyngitis in Dar es Salaam, clinicians studied stated that identifying and treating Streptococcal pharyngitis was not their priority (47), further explaining the multifactorial nature of the factors related to overall poor management of RHD patients in our local setting. This calls for more efforts to increase awareness of RHD management and the importance of clinicians to follow guidelines.

The baseline socio-demographic characteristics seen in this study population is similar to that found in many other previous studies mostly consisting of young, predominantly female patients with high unemployment rates (45,46). Of note, the mean age of the present study population was 28.4 years, and women comprised 58.2% of the study population. Furthermore, the proportion of patients with primary or less education was 64.5%, and over three quarters of the patients were unemployed. This picture represents the well-known population at risk for GAS pharyngitis, ARF and RHD (48–50). Contrary to previous findings (45,46), none of the socio-economic factors studied in this population was associated with throat GAS colonization. The differences in the findings between the present and previous studies could be due to differences in methods used to assess risks but also it is possible that the present study was not adequately powered to detect these associations and only trends were seen towards more patients with poor socio-economic indices to be aggregated in the group of patients with positive throat culture results (Table 4).

CHAPTER FIVE

5.1 Conclusion

In this study the prevalence of GAS among the RHD patients was relatively high. This means patients who were found to be culture positive are at risk of ARF and subsequent worsening of RHD. In addition, stopping prophylaxis was found to be an independent predictor of culture positivity. Although secondary prophylaxis is the most cost-effective way to prevent GAS colonization, ARF recurrence and subsequent worsening of RHD, a large group of patients in this study was not on prophylaxis.

As reported from various studies most GAS isolates were susceptible to penicillin which is the recommended drug for prophylaxis. This shows that penicillin is still very effective against GAS and should continue to be the recommended drug for prophylaxis.

5.2 Recommendations

In order to protect RHD patients against ARF recurrence and subsequent worsening of RHD, it is recommended that guidelines be followed by health care providers. Although the decision for the duration of prophylaxis varies among different guidelines, it is recommended that health care providers follow the recommended current treatment guideline either from WHO or the adapted country guidelines to ensure there is standard of care among RHD patients including prophylaxis for GAS. To further ensure adherence to guidelines, continual education on the overall management of RHD patients should be provided to health care providers. In addition mentorship programs should also be conducted to make sure the knowledge of the provider is translated to real practice.

To minimize incidences of patients stopping prophylaxis for GAS, health care providers should provide RHD patients with required information about the importance of this prophylaxis. The information should also include factors such as improvement of living conditions and attendance to health facilities for health care.

5.3 Study limitations and mitigation measures

Measurement of white blood cell counts and antistreptolysin antibody titer to investigate the presence of an active infection was not done. It was therefore not easy to know proportion of patients with active infection among the patients with positive cultures. In addition, the rate of acute rheumatic fever recurrence was not determined in this study in order to correlate with GAS colonization among the patients with positive cultures. However, presence of GAS and its strong association with patients who were not using prophylaxis is an indication that these patients are at risk of worsening RHD.

An indirect method which relies on self-report (morisky green questionnaires) was used to assess medication adherence. Although this method is likely to result in overestimation of adherence to prophylaxis among RHD patients, questions were designed in such a way that recall bias was minimized. This included asking questions about the recent visits to the health facilities and doses taken since the last visit.

The sample size used for the study was relatively small. Therefore, associations between the main outcome of the study and other variables may not have been established. In addition, due to limited number of patients, consecutive sampling was used for recruitment of study participants. Although this may result in bias for some of the observed study findings, combination of questions and laboratory testing of swab samples for GAS colonization and antibiotic susceptibility ensured reliability of the findings reported in this study. In addition, the use of different methods of data analysis including multiple regression minimized chances of confounding patient- and clinical-related factors with the main outcome of the study.

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APPENDICES

Appendix I: Consent Forms

Consent form (English version)

INFORMED CONSENT FORM

ID NO | | | |

Consent to participate in the study entitled:

THROAT CULTURE COLONIZATION AND ANTIBIOTIC SUSCEPTIBILITY OF GROUP A BETA-HEMOLYTIC STREPTOCOCCI AMONG RHEUMATIC HEART DISEASE PATIENTS ATTENDING JAKAYA KIKWETE CARDIAC INSTITUTE.

Background: Rheumatic heart disease (RHD), a complication of acute rheumatic fever (ARF) caused by Group a β-hemolytic Streptococci (GAS) is still a major cause of cardiovascular morbidity and mortality in young people living in the developing countries. If not prevented, recurrence of ARF causes worsening of RHD, therefore the World Health Organization (WHO) recommends that all patients with confirmed RHD receive secondary prophylaxis against other attacks of ARF. The recommended drug is long acting penicillin. For patients allergic to penicillin sulfadiazine, sulfisoxazole or erythromycin is recommended. Implementation of effective secondary prophylaxis is faced with challenges due to inadequate access to healthcare, prevailing threat of antibiotic resistance as well as physicians' awareness on the importance of secondary prophylaxis to RHD patients. Therefore, there is a need to explore the prevalence and factors causing GAS colonization among RHD patients.

What participation involves:

1. We will take a throat swab
2. We will not give any additional drug
3. Your file will be reviewed

Confidentiality

Only number will be used for participant identification purpose. All information obtained from you will be handled in confidential manner and access will only be to the study investigators.

Risk expected

Other than minor pain expected during taking throat swab no anticipated harm or danger which will arise by participating in this study. In case of harm directly associated with participation in the study, contact: +255719399729, Ms. Sarah Wangilisasi, Mpharm Clinical and Hospital pharmacy at Muhimbili University of Health and Allied Sciences, PO Box 65013 School of Pharmacy. You can also contact the supervisors of this research Dr. Pilly Chillo (Mobile Telephone number: +255 713 779781) and Professor Appolinary Kamuhabwa from Muhimbili University of Health and Allied Sciences.

Your rights

You are free to agree or refuse to participate in this study.

Benefits

By participating in this study, you will be able to know if you are harboring the bacteria which can cause streptococcal pharyngitis and worsening of rheumatic heart disease. You will also be given treatment promptly if the bacteria are found in your throat. Another benefit is you will be fostering scientific knowledge which may be useful during periodical revision of health policy and practice.

Whom to contact

If you have questions about this study, you should contact the Director of Research and Publications, Dr. Joyce Masalu, Muhimbili University of Health and Allied Sciences, PO Box 65001, Dar es Salaam. Phone number: 2150302-6

I……. confirm that, I have read and understood the contents of this form. My questions have been answered. I agree to participate in this study.

Signature of the participant……Date…….

Name of the participant……

Appendix II: Consent form-Swahili version

Fomu ya ridhaa

FOMU YA MAELEZO KUHUSU UTAFITI:

NAMBA YA UTAMBULISHO: ☐☐☐

Fomu ya utafiti wenye kichwa cha habari:

KIWANGO CHA UWEPO WA BAKTERIA AINA YA STREPTOCOCCUS KUNDI A KWENYE KOO NA USUGU WA BAKTERIA HAO KWA VIJIUA SUMU AINA YA ANTIBIOTIKI KWA WANGOJWA WA UGONJWA WA MOYO AINA YA RHEUMATIC KATIKA HOSPITALI YA MOYO YA JAKAYA KIKWETE.

Utangulizi

Ugonjwa wa moyo wa rheumatic unatokana na matatizo yanayotokea baada ya homa ya rheumatic inayosababishwa na bakteria aina ya streptococci kundi A. Ugonjwa huu bado ni sababu kubwa ya vifo vitokanavyo na magonjwa ya moyo katika nchi zinazoendelea. Kama isipozuiliwa, kujirudia kwa homa ya rheumatic kunasababisha madhara zaidi kwa wagonjwa wa ugonjwa wa moyo wa rheumatic. Hivyo basi shirika la afya duniani (WHO) linaelekeza wagonjwa wote waliothibitika kuwa na ugonjwa huu wakingwe na dawa aina ya penicillin inayodumu muda mrefu. Kwa wagonjwa wenye mzio(aleji/allergy) na dawa ya penicillin, basi dawa aina ya sulfadiazine, sulfisoxazole au erythromycin zitumike. Lakini utekelezaji wa kutolewa kwa kinga hii unakumbwa na changamoto nyingi kutokana na huduma duni za afya, tatizo la usugu wa bakteria ambao limezidi kukua kwa kasi na pia madaktari kutolipa uzito suala hili la kinga. Hivyo basi kuna haja ya kuchunguza kiwango cha uwepo wa bakteria aina ya streptococci kundi A kwa wagonjwa wa ugonjwa huu wa moyo ili kujua kufanikiwa kwa kinga hii.

Ushiriki una mambo yapi:

1. Hautaongezewa dawa yoyote.
2. Faili lakolitachunguzwa kupata baadhi ya taarifa.
3. Utachukuliwa swabu ya koo.

Usiri

Utambulisho wako utakuwa kwa namba ili kuongeza usiri. Pia maelezo yeyote yatakayochukuliwa yatawekwa siri na kutunzwa na mtafiti.

Matarajio ya hatari

Zaidi ya maumivu kiasi kidogo utakayoyapata wakati wa kuchukuliwa swabu ya koo hakuna madhara yanayotarajiwa kutokana na ushiriki katika utafiti huu.

Ikiwa utapata madhara ya moja kwa moja kuhusishwa na utafiti huu usisite kuwasiliana na bi. Sarah Wangilisasi mwanafunzi wa shahada ya uzamili, S.L.P 65013 Shule ya Famasia, Chuo Kikuu cha Afya na Sayansi Shirikishi Muhimbili. Simu ya kiganjani: +255719399729. Pia waweza wasiliana na wasimamizi wa utafiti huu Dr. Pilly Chillo (Simu ya kiganjani: +255 713 779781) na Profesa Appolinary Kamuhabwa kutoka Chuo Kikuu cha Afya na Sayansi Shirikishi Muhimbili.

Haki yako

Una haki na uhuru wa kuamua kushiriki au kutokushiriki katika utafiti huu.

Faida

Kwa kushiriki katika utafiti huu utaweza kujua kama umepata maambukizi aina ya streptococcus anaesababisha vidonda vya koo na ugonjwa wa moyo wa rheumatic. Pia utaweza kupata matibabu pindi utakapogundulika kuwa una maambukizi hayo. Faida nyingine ni kwamba utasaidia kuongeza uelewa wa kisayansi juu ya mambo ya afya. Uelewa huo waweza saidia katika kuongeza ufanisi nyakati za marekebisho ya sera na utendaji wa mambo yahusuyo afya.

Nani wa kuwasiliana naye

Ikiwa una swali lolote juu ya utafiti huu, wasiliana na mkurugenzi wa tafiti Joyce Masalu, Chuo cha Afya na Sayansi shirikishi Muhimbili, PO Box 65001 Dar es Salaam. Simu ya mezani: 2150302-6

Mimi……. Nathibitisha kuwa nimesoma maelezo yote katika fomu hii na kuyaelewa. Maswali yangu yote yamejibiwa. Ninaafiki kushiriki katika utafiti huu.

Sahihi ya mshiriki: ……..Tarehe: …….

Jina kamili la mshiriki: ……

Appendix III: Case Report Form (CRF)

THROAT CULTURE COLONIZATION AND ANTIBIOTIC SUSCEPTIBILITY OF GROUP A β-HEMOLYTIC STREPTOCOCCIIN RHEUMATIC HEART DISEASE PATIENTS AT JAKAYA KIKWETE CARDIAC INSTITUTE.

Questionnaire for patients/parents/guardians

Patient Code……..Date: .....

Part A: **Socio-demographic information**

1. Patient age (years).....

2. Patient gender:

Male [ ]

Female [ ]

***For patients <18 years the following questions were answered by guardians/parents**

3. **Marital status:**

Single [ ] Married [ ]

Divorced [ ] Widowed [ ]

4. Residence:

Within Dar es Salaam [ ] specify street …….

Outside Dar es Salaam [ ] Specify region……

5. Level of education:

Primary education [ ] Secondary education [ ]

University education [ ] Tertiary [ ]

No formal education [ ]

6. Employment status:

Employed [ ] unemployed [ ]

Self-employed [ ] retired [ ]

Student others [ ] (specify). .....

7. Family average monthly income:

< TZS 70 thousand [ ] TZS 70-310 thousands [ ]

>TZS 310 thousands [ ] Declined to answer [ ]

8. Mode of payment:

Insurance [ ] Out of pocket [ ]

Exemption [ ]

9. Number of people living in the household:

<6 [ ]

>7 [ ]

10. Family history of RHD

Yes [ ]

No [ ]

Part B: Awareness of prophylaxis against GAS

11. Do you know what you/your child are suffering from? Yes [ ] No [ ]

If yes briefly state what it is…….

13. Do you know that you/your child are supposed to be getting monthly injections?

Yes [ ] No [ ]

13. Are you receiving monthly or three weekly injections for secondary prophylaxis of RHD?

Yes [ ] No [ ]*

14. Do you know the name of the injection which you/your child is getting

Yes [ ] No [ ]

If Yes mention the drug……..

15. Do you know the importance of these monthly injections?

Yes [ ] No [ ]

If Yes briefly explain ……

**If no check on the Patient records to see if they are on oral prophylaxis*

Part C: Adherence (Modified Morisky question tool) (Answer yes= 1 or No = 0) (Adapted from Morisky et al (26)**.**

15. Do you sometimes forget to get monthly injections? Yes [ ] No [ ]

16. People sometimes miss taking their medications for reasons other than forgetting.Thinking Over the past six months, were there any months when you/your child did not get monthly injections? Yes [ ] No [ ]

If Yes How many doses did you/your child miss.....

Mention the reason(s) for missing monthly injection

a. …….

b. …….

c. …….

d. …….

17. Have you/your child ever cut back or stopped getting monthly injections without telling your doctor because you/your child felt worse when you got the injections? Yes [ ] No [ ]

18. Did you/your child get injection last month? Yes [ ] No [ ]

19. When you travel do you sometimes forget to get the monthly injection? Yes [ ] No [ ]

20. When you feel like you/your child's symptoms are under control do you sometimes stop getting monthly injections? Yes [ ] No [ ]

21. Getting injections every month is a real inconvenience for some people. Do you/your child ever feel hassled about sticking to your treatment plan? Yes [ ] No [ ]

22. How often do you have difficulty remembering get you/your child monthly injection? (A=1, BCDE=0)

___A. Never/rarely

___B. Once in a while

___C. Sometimes

___D. Usually

___E. All the time

Part D: Information from patient files

23. Diagnosis.....

24. Type of Lesion.....

25. Surgical intervention done Yes [ ] No [ ]

26. If Yes, type of Surgical intervention…….

Part E: Laboratory Results

27. Culture positivity i) Positive [ ] ii) Negative [ ]

Name of Antibiotic	Zone of Inhibition Diameter (mm)	Interpretation of Results. (Interpreted as Resistant, Intermediate or Susceptible)
Penicillin G (10 units)		
Oxacillin (30µg)		
Ceftriaxone(30µg)		
Vancomycin (30µg)		
Erythromycin (15µg)		
Tetracycline (30µg)		
Ofloxacin (5µg)		
Chloramphenicol (30µg)		
Clindamycin (2µg)		
Trimethoprim-sulfamethoxazole (1.25/23.75µg)		

Template for filling in GAS susceptibility results to the tested antibiotics