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## Clinical and geographic patterns of rheumatic heart disease in outpatients attending cardiology clinic in western Kenya



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#### ABSTRACT

*Introduction:* Rheumatic heart disease (RHD) remains a leading cause of cardiovascular mortality in sub-Saharan Africa. Identifying high risk populations and geographic patterns of disease is crucial to developing RHD prevention and screening strategies in endemic areas.

Objectives: To identify clinical and geographical trends in RHD throughout western Kenya

Methods: We conducted a retrospective chart review of all patients < 50 years old attending adult cardiology clinic at a national referral hospital in western Kenya. Demographic information, residential location and cardiac history were collected. We mapped the spatial distribution of cardiac disease rates and analyzed the effect of distance from the hospital on RHD status.

Results: Two-thirds (64%) of cardiology clinic patients <50 years old (n=906) had RHD. RHD patients were younger (26 vs. 33 years, p < 0.001) and more often female (69% vs. 59%, p=0.001) than non-RHD patients. Global clustering of disease rates existed within 200 km of the hospital with significant clustering of the RHD and non-RHD rate difference surrounding the hospital (Moran's I: 0.3, p=0.001). There was an interaction between ethnicity and distance from the hospital such that the odds of RHD decreased with further distance for Nilotes, but the odds of RHD increased with further distance for non-Nilotes

Conclusion: Most adult cardiology patients treated at a national referral hospital in western Kenya have RHD. Young people and females are commonly affected. Ethnicity and distance to the hospital interdependently affect the odds of RHD. Future studies in this area should consider the impact of ethnic predisposition to RHD.

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#### 1. Introduction

Rheumatic heart disease (RHD) is a leading cause of cardiovascular morbidity and mortality worldwide, affecting over 15.6 million people throughout the world and accounting for over 233,000 deaths annually [1]. While there has been a radical decline in the incidence of RHD in high-income countries (HIC) over the past fifty years, RHD prevalence remains high in low and middle-income countries (LMIC) [2,3] with a disproportionate number of cases in sub-Saharan Africa (SSA) [4]. A combination of environmental, bacterial and host factors has been thought to influence geographic patterns of disease and contributes to the increased burden of RHD in SSA [5].

RHD is considered a disease of poverty, and increased rates of RHD are associated with low socioeconomic status, urbanization, overcrowding, poor nutrition and lack of access to medical care [3,6,7].

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Additionally, an unequal geographic distribution of various strains of Group A Streptococcus (GAS), the bacteria traditionally held responsible for RHD, across certain regions of the world may play a role in global variation of RHD frequency [8]. SSA is one of the poorest regions of the world, comprised of the largest number of LMIC worldwide, and is one of the regions most affected by RHD [9]. The burden of cardiovascular disease attributable to RHD in SSA ranges from 14 to 40%, as evidenced by single and multi-national studies across the continent [4,10, 11]. Limited access to specialized cardiovascular care and surgical intervention across SSA leads to high mortality rates among young people with advanced disease [12].

Kenya is a lower-middle-income country in SSA with an ethnically diverse population, where little is known about the current prevalence or distribution of RHD. Prior reports from Kenya are thought to underestimate the actual prevalence due to limitations in sampling methods [13–15]. Our own clinical experience together with epidemiologic evidence of unexpectedly low rates of culture-positive group A streptococcal (GAS) pharyngitis in febrile children presenting to a rural hospital in

an ethnically homogenous area of western Kenya [16] suggest geographic disparities in RHD distribution in the region.

Identifying geographic trends and demographic characteristics correlating with RHD in western Kenya can inform epidemiologic hypotheses about GAS and RHD for targeted prevention and screening efforts in the future. Our study aimed to better characterize the burden of RHD among patients presenting to an outpatient, cardiology clinic at a national referral hospital in western Kenya. We sought to describe the clinical profile of RHD patients, identify demographic factors associated with RHD, and determine if a pattern of geographic distribution of RHD exists throughout the region.

#### 2. Methods

#### 2.1. Study site & design

We conducted a retrospective, cross-sectional chart review of patients attending adult cardiology clinic at a national referral hospital in western Kenya to determine the demographic, clinical and geographic factors associated with RHD in this region. Our study site, Moi Teaching and Referral Hospital (MTRH), is the clinical care arm of one of the eleven National Heart, Lung and Blood Institute (NHLBI) funded Centers of Excellence in cardiovascular care worldwide and provides highly specialized inpatient and outpatient cardiovascular care through collaborations between Kenyan and American cardiologists [17]. MTRH is located 300 km northwest of Nairobi and is the only public cardiac referral facility outside of the capital city.

This study was approved by the Institutional Review and Ethics Committee (IREC) at the Moi University School of Medicine who waived the need for informed consent.

#### 2.2. Data collection

We used convenience sampling to review the paper medical charts of all patients who attended the adult cardiology clinic at MTRH at least once between January 2012 and August 2014. We collected data only on patients <50 years old who carried a cardiac diagnosis in order to maximize the percentage of RHD patients represented in our sample.

Four individuals reviewed charts (RL, SC, AK, VO). Standardized data collection forms were used to extract information from the chart about age, sex, occupation, ethnicity and place of residence. Ethnicity is not routinely collected in the medical chart. Kenyan tribal affiliation was deduced by Kenyan research assistants based on patient name, place of residence, and next of kin, or recorded as unknown if ethnicity was unclear. The presence of RHD was recorded if RHD was directly listed as a diagnosis in any outpatient or inpatient provider notes or hospital discharge summaries and subsequently confirmed by an MTRH-trained cardiologist. For RHD cases, valvular involvement and lesion type (regurgitant and/or stenotic) were explicitly sought from standardized, MTRH echocardiography reports completed by MTRH-trained echocardiography technicians. History of secondary antibiotic prophylaxis was noted if monthly penicillin was prescribed at least once in the chart.

All non-RHD cardiac diagnoses were recorded if listed in any outpatient or inpatient provider notes, hospital discharge summaries, referral notes, or if reported on echocardiogram and/or electrocardiogram reports by an MTRH cardiologist. Systolic heart failure (defined as reduction in left ventricular ejection fraction <45% on echocardiography report), diastolic dysfunction (assessed by echocardiography technician and reported as class I-IV on echocardiography report), pulmonary hypertension (defined by pulmonary artery systolic pressure >35 mm Hg on echocardiogram report), ischemic heart disease (defined by history of myocardial infarction or positive stress test reported by MTRH cardiologist), pericardial disease (including pericarditis of any etiology or pericardial effusion reported by an MTRH cardiologist), and arrhythmias (atrial or ventricular as recorded by MTRH cardiologist or

MTRH electrocardiography technician) were collected. Patients could carry more than one diagnosis. Prescribed medical and surgical therapies and history of diagnostic cardiac imaging were also collected.

Place of residence in Kenya is classified into national administrative units with geographic areas defined from largest to smallest as: County, District, Division, Location, Sublocation, and Village. The residence listed in the paper medical chart was standardized against the most recent Kenyan census survey (2009) including all known administrative units [18]. Both the residences, as listed in the chart and as standardization by the Kenyan census, were recorded. When paper charts had no residence listed, multiple residences listed, unknown Location level information, or a Location of residence that was not listed in the Kenyan census, we searched an electronic hospital record (EHR) to determine residence. If a residence remained unconfirmed through the EHR, we contacted the patient by phone to gather the information directly. After completion of the chart review, we randomly selected charts for quality review for missing or discordant data. We noted a 12% error rate in the 4% of the charts that had been reviewed. These errors appeared to be systematic and related to one data collector. We subsequently reviewed the 220 charts from that one data collector and corrected 100% of errors related to place of residence, demographic information, and cardiac history.

#### 2.3. Statistical analysis

Primary associations of interest included cardiac diagnoses (RHD versus non-RHD) and place of residence (using Division as the geographic unit for analysis). Data analysis was conducted in two stages: cross-sectional analysis to demonstrate the relationship between demographic characteristics and cardiac diagnoses; and geographic analysis to map and quantify the spatial heterogeneity of RHD throughout western Kenya. RHD status was defined as a binary variable (yes/no) for all analyses, with each patient included only once as either having RHD (RHD) or not (non-RHD). We excluded patients without RHD who had a diagnosis of ARF because binary classification of ARF as either non-RHD or RHD could confer bias given ARF patients may be considered pre-RHD on a spectrum of disease and share similar risk factors to patients with RHD. Patients with an existing RHD diagnosis and recurrent ARF were included in the analysis, though, since their disease met our RHD criteria. We grouped the participants from related tribes into larger ethnic sub-group categories for analysis: "Nilote" includes participants from Kalenjin, Luo, and Masaai tribes; "Bantu" includes participants from Kikuyu, Luhya, Kisii, and Kamba tribes; "Cushite" includes participants from the Somali tribe.

For our cross-sectional descriptive analysis, we described the clinical profile of RHD and non-RHD patients and explored associations between demographic variables of age, sex, occupation, and ethnicity and RHD. In our univariate analysis, we used Wilcoxon rank sum test to describe the association between age as a non-normal, continuous variable and chi-square tests or Fisher's exact tests to describe the associations between RHD status sex, occupation and ethnicity as categorical variables. Significance was defined as p-value < 0.05. A fixed effects multivariable logistic regression model was developed to quantify the effects of age, sex, ethnicity and distance from the hospital (in kilometers) on RHD status. Age and distance from the hospital were included as categorical variables after observing a non-linear association between age and distance and RHD status. Ethnicity was transformed into a binary variable of Nilote versus non-Nilote (non-Nilote included Bantu, Cushite and "other" subgroups) since Nilote was the largest ethnic group represented in the dataset. An additional 14 patients with "unknown" or "non-Kenyan" ethnicity were excluded from the multivariable regression analysis. We used logistic regression without any inclusion or exclusion procedure, given the small number of variables included in our model. Random effects for Division were tested in the model but were found to be vanishingly small with no improvement to the output and were ultimately excluded from the model.

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