PREVALENCE AND FACTORS ASSOCIATED WITH GROUP A STREPTOCOCCAL PHARYNGEAL CARRIAGE AMONG PRIMARY SCHOOL CHILDREN IN BOMET COUNTY

BY

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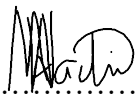
DECLARATION

I certify that this dissertation is my original work and has not been presented for the award of a degree in any other university.

Signed:  …… Date: …8th November 2021....

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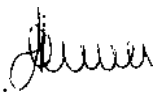
Signed: …  …… Date: …8th November 2021…

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DEDICATION

I dedicate this work to the many primary school children I met in the course of carrying out my research. They are full of life and are our future leaders. They deserve a life free from the debilitating sequelae of *S. pyogenes* infections.

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ABBREVIATIONS

APSGN	Acute post-streptococcal glomerulonephritis
ARF	Acute rheumatic fever
CDR	Clinical decision rule
CLIA	Clinical Laboratory Improvement Amendments
CI	Confidence interval
DNA	Deoxyribonucleic acid
ELISA	Enzyme linked immunosorbent assay
ERC	Ethics Research Committee
FISH	Fluorescence in situ hybridization
GAS	Group A *Streptococcus*
IDSA	Infectious Diseases Society of America
KNH	Kenyatta National Hospital
NACOSTI	National Commission for Science, Technology and Innovation
OIA	Optical immunoassay
PANDAS	Paediatric Autoimmune Neuropsychiatric Disorders Associated with *Streptococcus pyogenes*
PCR	Polymerase chain reaction
RADT	Rapid Antigen Detection Test
RHD	Rheumatic Heart Disease
SPSS	Statistical Package for Social Scientists
UoN	University of Nairobi
WHO	World Health Organization

OPERATIONAL DEFINITIONS

Acute Pharyngitis: inflammation of the throat and/or the tonsils present for less than one week.

GAS pharyngitis: acute pharyngitis caused by Group A *Streptococcus*.

Streptococcal pharyngeal carrier: asymptomatic patient with confirmed pharyngeal presence of GAS as evidenced by a positive throat culture or RADT.(1)

Scarlatiniform rash: finely papular erythematous rash that spares the face, may be accentuated in skin folds, and may desquamate during convalescence.

ABSTRACT

Background: Asymptomatic streptococcal pharyngeal carriers act as reservoirs for invasive Group A *Streptococcus* (GAS) clones, are important drivers for GAS transmission and are predisposed to acute rheumatic fever/rheumatic heart disease on acquisition of new rheumatogenic clones. Bomet County is considered to be within the 'rheumatogenic' belt but local studies around GAS are lacking despite the high burden of streptococcal complications. There is limited utilization of point of care rapid antigen detection tests (RADTs) which facilitate quick diagnosis and treatment of GAS pharyngitis.

Objectives: The aim of this study was to determine the prevalence of and factors associated with GAS pharyngeal carriage among primary school children in Bomet County, Kenya.

Methods: A cross-sectional study targeting children age 5-15 years in primary schools from Bomet County was conducted between December 2020 to March 2021. A semi-structured questionnaire was used to collect data including school characteristics, socio-demographics, and clinical features. For every enrolled child, a throat swab was taken and subjected to the RADT and the results recorded. Those who tested positive were categorized as GAS pharyngeal carriers. Analysis was done using the IBM SPSS v.24 with prevalence of GAS pharyngeal carriage being presented as a percentage with a 95% confidence interval (CI). Associated risk factors were analysed using Chi-square tests and Fischer's exact with statistical significance set at $p < 0.05$.

Results: Out of the 210 children screened, twenty tested positive for GAS pharyngeal carriage giving a prevalence of 9.5% (95% CI= 6.3-14.3), with most carriers attending overcrowded classrooms. However, none of the factors examined were statistically significant.

Conclusion and recommendations: The prevalence of GAS pharyngeal carriage among children aged 5-15 years old attending primary schools in Bomet county was 9.5%. Notably, overcrowded classrooms recorded higher carrier rates. We recommend improving care seeking practices for sore throats in this age group, utilizing a rapid test for point of care diagnosis of GAS and maintaining a maximum occupancy of not more than 0.9pupils/m^2 of classroom area as stipulated in the Safety Standards Manual for schools in Kenya.

1. INTRODUCTION

1.1. BACKGROUND AND EPIDEMIOLOGY OF GROUP A *STREPTOCOCCUS*

Group A *Streptococcus* (GAS) or *Streptococcus pyogenes* (*S. pyogenes*) is a coccoid-shaped, gram-positive bacterium which grows in chains. It is classified as beta-haemolytic because it haemolyses red blood cells of sheep completely leading to an area of complete haemolysis surrounding its colonies when cultured on the media of blood agar. Based on a specific polysaccharide in its bacterial cell envelope, it is further classified as Lancefield group A and sub-classified further into > 230 serotypes premised on the M protein antigen on the cell surface.(2)

The only natural hosts to GAS are humans and it has been termed a 'hazard' in school-going children with a peak incidence among those aged 5-15years.(3) *S. pyogenes* can affect any organ system with varying morbidity and mortality levels, with high levels being seen mainly in children, young adults and less developed countries worldwide.(4) These diseases range in severity and are classified into suppurative and non-suppurative diseases (Figure 1).

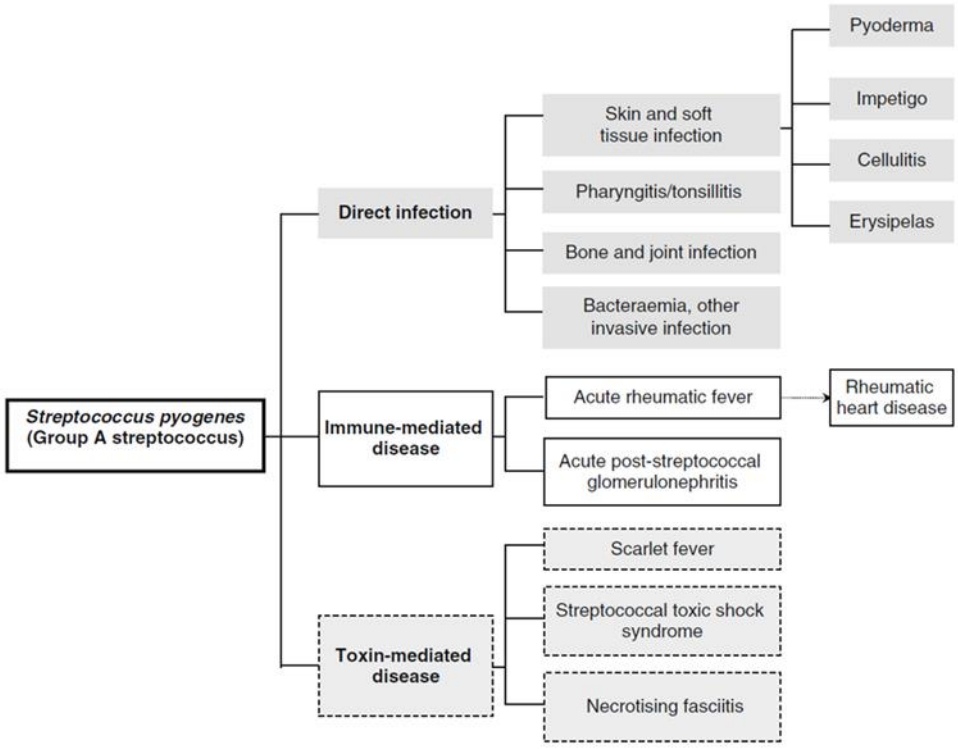


Figure 1: Spectrum of Group A Streptococcal disease with major manifestations shown. *Adapted from Ralph AP, Carapetis JR. Group A Streptococcal Diseases and their global burden. Current Topics in Microbiology and Immunology. 2013; 368: p3*

Suppurative infections consist of acute pharyngitis, impetigo and the invasive diseases with the former two making up the vast majority of diseases caused by GAS globally.(5–7) Invasive disease occurs when GAS is isolated from a normally sterile body site. It includes 3 overlapping syndromes: streptococcal toxic shock syndrome, necrotizing fasciitis and focal and systemic infections that do not fit in the other 2 syndromes e.g. meningitis, bacteraemia and others.(3,6,7)

Invasive disease occurs in more than 18 million people with over 1.7 million incident cases occurring per annum. Within a week of acquiring the infection, about 23% of patients die making it responsible for 517,000 deaths each year.(6,8) According to a population-based study in Kilifi on invasive GAS infection among children in rural Kenya, most of the cases involved skin and soft tissue infections (70%), severe pneumonia (23%) and primary bacteraemia (14%).(9)

Non-suppurative diseases are post-infectious sequelae that occur after GAS pharyngitis or impetigo. These include acute rheumatic fever (ARF), rheumatic heart disease (RHD), acute post-streptococcal glomerulonephritis (APSGN), Paediatric Autoimmune Neuropsychiatric Disorders Associated with *Streptococcus pyogenes* (PANDAS), and post-streptococcal reactive arthritis.

Acute rheumatic fever (ARF) is an immune sequela of acute streptococcal pharyngitis largely affecting children aged 5 to 14 years.(3) Following untreated streptococcal pharyngitis, the risk of developing ARF is 0.3-3% with a greater risk for individuals with a prior history of rheumatic fever.(10–12) Following repeated episodes of streptococcal pharyngitis and ARF, 60% of individuals develop progressive and persistent heart valve damage and scarring known as rheumatic heart disease (RHD).(3)

RHD is the most common acquired paediatric heart disease with the highest prevalence in children ages 5-15 globally at 5.7 per 1000 cases being in Sub-Saharan Africa.(6) It is estimated that Kenya has a high prevalence at 741 cases per 100,000, with one-third of these affecting children 5-14 years of age.(13) Death and disability from RHD exacts a great economic and sociocultural burden on children and young adults in their most productive years, and on their communities. Given the high morbidity and mortality related to ARF/RHD, efforts are being increased to prevent it at a primary, secondary and tertiary level.(14)

Majority of the streptococcal diseases with high illness and death rates i.e. 79% of RHD, 95% of ARF, 97% of APSGN and 97% of invasive GAS cases, are from less developed countries.(8) In particular, ARF/RHD and invasive disease are of major public health concern.

1.2. ACUTE PHARYNGITIS

Pharyngitis, derived from Greek '*pharynx*' meaning throat and *'-itis'* meaning inflammation, refers to swelling accompanied by pain or discomfort in the throat, often resulting in difficulty in swallowing. A consultation at the paediatrician's office is more often than not due to acute pharyngitis with a reported 15 million appointments in the United States annually.(3,15)

Viruses are the most implicated cause, with respiratory viruses such as rhinovirus among others being implicated. *S. pyogenes* is the number one cause of bacterial pharyngitis. Other causative bacterial organisms include Group C and G Streptococci, *Mycoplasma pneumoniae Corynebacterium diphtheriae* and *Neisseria gonorrhoeae* among others.(16)

Streptococcal pharyngitis makes up 5-15% and 20-30% of pharyngitis cases in adults and children respectively with children aged 5-15years being the most affected age group. Seasonally, it peaks in the cold months.(15)

In developing countries, 2.4 million children are affected, half of whom reside in Sub-Saharan Africa.(15) In high-income countries, 15% of school-going children and 4-10% of adults experience a case of symptomatic GAS pharyngitis yearly as compared to less developed countries where the rates are 5-10 times higher.(3) In families having a primary case of GAS pharyngitis, 43% report a secondary case within the family indicating a high transmission rate.(4)

Streptococcal pharyngitis causes a great illness burden with associated high healthcare expenditure and high societal costs, with almost one half being attributed to non-medical costs.(3,17) This also includes indirect costs incurred when the parent misses work.(15)

Streptococcal pharyngeal carriage is important in the epidemiology of *S. pyogenes*. A pharyngeal streptococcal carrier is considered to be one in whom the pharyngeal presence of GAS has been verified without any of the accompanying signs and symptoms.(18) There has been much interest over the years on the rate of carriage among healthy and ill children, especially in lieu of the renewed interest to eradicate rheumatic fever and prevent other streptococcal diseases.(5)

1.3. PATHOGENESIS OF GROUP A STREPTOCOCCAL INFECTIONS

S. pyogenes has two broad types of virulence factors – cell surface and secreted virulence factors as illustrated in figure 2. The cell surface factors e.g., capsule, adhesins etc. are used for adherence, internalization and to help evade the host's first line of defence, opsono-

phagocytosis. The secreted factors such as streptolysins, streptokinase etc. are used to help the organism spread through tissues and for their immune stimulatory and evasion properties.

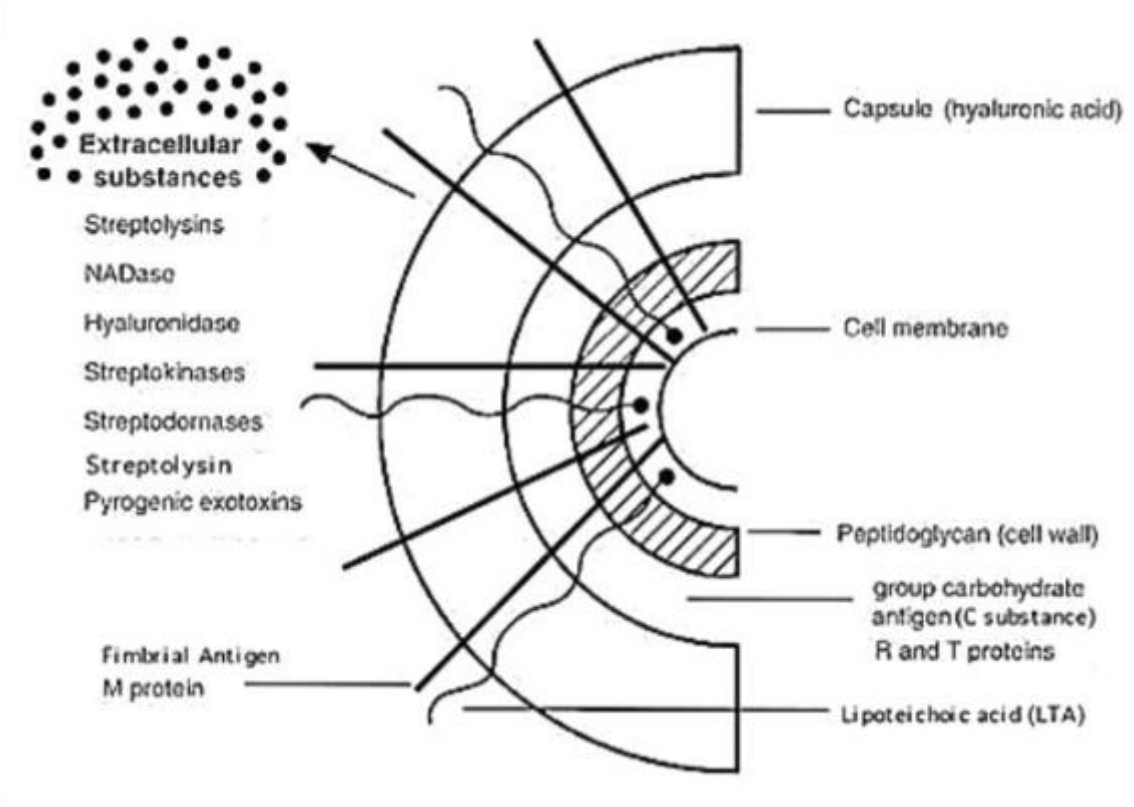


Figure 2: Cell surface structure of *Streptococcus pyogenes* and factors associated with virulence. *Adapted from Todar K: Streptococcus pyogenes and Streptococcal disease*. In Todar's Online Textbook of Bacteriology, *Wisconsin, 2015*

S. pyogenes is transmitted through inhalation of infected respiratory droplets and nasal discharge.(2–4) This is greatly favoured by overcrowding and/or close proximity as is seen in day-care, schools, homes and military barracks. Though uncommon, outbreaks may occur after transmission by consuming food contaminated by food handlers.(2,4) Despite person-to-person transmission, *S. pyogenes* remains predominantly community acquired and has not become recognized as an endemic nosocomial organism.(3)

Normally, the host's defence mechanisms are able to avert colonization by the organism or development of disease. The pharynx and skin are the main sites of asymptomatic GAS colonization and persistence with subsequent facilitation of spread to a new host.

Adherence to the pharyngeal mucosa and skin initially occurs by use of the adhesins like M-protein and lipoteichoic acid. This attachment has to be strong enough to evade the host's physical barriers i.e. mucus and salivary flow in the nasopharyngeal mucosa, and on the skin

epithelial exfoliation.(5) Once adherence has successfully occurred, invasion of these cells by the organisms occurs. This intracellular invasion has been hypothesized to be important in streptococcal carriage and persistence, with internalization leading to invasion of deeper tissues.(6)

The organism must evade the immune system by utilizing its secreted factors to cause further local invasion and systemic disease. It then multiplies and disseminates via the hematogenous route to various tissues and organs to cause disease. It secretes a variety of proteins and products e.g. streptolysins and streptokinase, that facilitate its spread and invasion of tissues to cause deep infections and other complications.(5,6)

In some genetically susceptible hosts, there is an interval of 2 weeks (1-5 weeks) between an episode of streptococcal pharyngitis and the onset of rheumatic fever.(12) In this period there is formation of a cross-reactive immune response involving the humoral and cellular arms of the adaptive immune system which attack the host's tissues i.e., molecular mimicry. This cross-reaction is responsible for the clinical features associated with the disease.

2. LITERATURE REVIEW

A search of published literature using PubMed, Cochrane Library, University of Nairobi repository and Google scholar was conducted. The focus of the search was on streptococcal pharyngeal carriage and pharyngitis with an aim of demonstrating the gaps in knowledge and the importance of these gaps. Keywords used in the search were 'Group A *Streptococcus* OR *Streptococcus pyogenes'*, 'pharyngeal carriage', 'streptococcal pharyngitis', 'asymptomatic', 'prevalence', 'child OR pediatric OR paediatric', 'rapid antigen detection tests', 'throat culture' and 'clinical decision rules'. A summary of the review is found in Tables 1 and 3.

2.1. RHEUMATOGENIC AREAS

S. pyogenes plays a central role in the occurrence of rheumatic fever and rheumatic heart disease in that it is the primary initiating event. However, not all 230+ serotypes are implicated. Serotypes associated with development of rheumatic fever are thus deemed rheumatogenic strains. Those strains that colonize the throat to cause pharyngitis are the ones implicated, with certain M serotypes e.g., M types 1, 3, 5, 6, 14, 18, 19 and 24, being associated with both pharyngitis and rheumatic fever. This is in contrast to pyoderma and acute glomerulonephritis-related M serotypes like 2, 49, 57, 59, 60 and 61.(5)

According to the 2015 Global Burden Disease Study, the prevalence of RHD remains highest in Oceania with an estimated 15 persons per 1000 population living with RHD, followed by central Sub-Saharan Africa and South Asia at 10 persons per 1000 population.(19) These three regions also had the highest age-standardized death rates i.e. more than 10 deaths per 100,000 population from RHD globally.

The incidence of ARF is still very high in low- and middle-income countries, and among disadvantaged communities living in industrialized countries despite access to better standards of healthcare. In a longitudinal study carried out in Australia using a RHD registry, those most at risk for ARF are Indigenous children 5-14 years of age with incidence rates of first episodes of ARF being 228 and 162 per 100,000 in girls and boys respectively.(20) The indigenous population consist mainly of the Aboriginal population. In New Zealand, ARF has an unequal distribution being limited almost entirely to Māori and Pacific children and young people between the ages of 4 and 19 living in lower socio-economic regions in the North Islands.(21)

Despite Sub-Saharan Africa being a hotspot, incidence rates and clinical profiles of GAS pharyngitis and in turn ARF are poorly documented.(22) This led to the adoption of the Drakensberg Declaration on the Control of Rheumatic Fever and Rheumatic Heart Disease in

Africa that calls upon all African countries to establish national programs to prevent rheumatic fever and rheumatic heart disease.(23) A systematic review in South Africa found a high prevalence of asymptomatic echocardiographic RHD of 20.2 cases per 1,000 children (95% confidence interval [CI] 15.3-26.2) among school-children in Cape town.(24)

Little is known about the current prevalence and distribution of RHD in Kenya. Humanitarian efforts geared towards prevention and early detection of ARF and RHD assist not only in early management, but also in providing much needed data that may be used to control these conditions. Such efforts include a school-based rheumatic fever and rheumatic heart disease prevention outreach program run by Mater hospital, a hospital-based outreach program located in the highland regions of the Rift Valley and a fixed clinic-based outreach service located in Kisumu.(25) It is from the hospital-based program run from Litein Hospital that a possible rheumatogenic region in the country has been identified. This is based on the referral patterns to the Mater Hospital heart unit and includes the region served by the hospital i.e., Kericho, Bomet, Kisii, Nyamira, Olenguroni and Molo. Rheumatic heart disease was responsible for 40.4% of the cardiovascular cases diagnosed over a six-year period (November 2006 to February 2012).(25)

The challenge of primary prevention of RF/RHD in low and middle income countries is worsened by the lack of data on the incidence of GAS pharyngitis, prevalence of the carrier state and the health seeking behavior for GAS pharyngitis in these countries.(25) Such data is vital to establish sustainable strategies to control and possibly eradicate rheumatic fever and rheumatic heart disease.

2.2. STREPTOCOCCAL PHARYNGEAL CARRIAGE

Much debate has ensued over the importance of streptococcal pharyngeal carriage. It is believed carriers are not susceptible to developing non-suppurative diseases as they do not exhibit signs of disease or elicit an immune reaction which is paramount in the pathogenesis of complications like ARF or APSGN.(18,26) However, this does not preclude them from acquiring different rheumatogenic clones while they are carriers. Acquisition of these new clones makes them vulnerable to acquiring acute rheumatic fever if genetically predisposed. Should a carrier present with pharyngitis symptoms that do not suggest a viral aetiology and test positive for GAS, it is recommended that they be treated as if they have a new streptococcal infection.(26)

The carrier state is a common occurrence among the close contacts of invasive disease patients suggesting that carriers most likely serve as a reservoir of infection for these patients. An investigation after an invasive streptococcal disease outbreak in Minnesota showed that the outbreak clone was highest (78%, $p<0.001$) among asymptomatic pharyngeal carriers who were school-going children in the outbreak area. Four of the 7 patients with the disease had had contact with these children.(27)

Carriers may also serve as important drivers of GAS transmission. When asymptomatic for respiratory symptoms, they are ineffective as transmitters. However, transmission is more likely once they develop community-acquired viral pharyngitis.(26)

Globally, carriage rates differ greatly based on the population and area under study as shown in Table 1. Such variations could be due to seasonal variation at the times the studies were being carried out, geography, socio-demographic variations and sample size.(28)

Shaikh et al in a meta-analysis of 29 hospital-based studies in paediatric patients spanning 37 years from regions around the world determined that the pooled prevalence of GAS carriage was 12% (95% confidence interval[CI]: 9-14%).(1) A recent meta-analysis by Oliver et al that reviewed 285 studies had a lower pooled carriage rate of 8% with a disparity in carriage rates among countries; Prevalence rates were higher among high income countries at 10.5% compared to low/middle income countries at 5.9%.(29)

There is a paucity of data on the carriage rates of GAS in Africa. Studies in Tunisia and Ethiopia report a carriage rate of between 9% and 12.2%.(28,30,31) In Uganda, a low/middle income country that has similar population and climate like Kenya, the carriage rate among school children is higher at 16%.(22,32) School-based studies provide a different perspective on carriage in that they are more community based. This is especially important because *S. pyogenes* is prevalent in that age-group and is predominantly community acquired.

2.2.1. Risk factors for streptococcal carriage

As humans are the sole natural hosts, *S. pyogenes* has become well adapted to enhanced transmission within populations that are overcrowded, with poor hygiene status and that lack adequate medical care. All these attributes are mainly seen in communities with low socioeconomic status.(3)

Other factors thought to increase carriage risk include young age, female gender (OR 1.6, $p=0.04$),(33) low income of parents, poor education status of the parents, residing in rural areas

(COR 3.1 [95% CI 1.7-5.8], p=0.002),(28) group living e.g. orphanages (26.6%, p<0.001), (34) and the winter and/or rainy seasons.(28,32–34)

Table 1: Studies on Streptococcal pharyngeal carriage and risk factors

Author	**Study design, population and setting**	**Results**
Shaikh N et al, 2010 (1)	Systematic Review 29 studies	Pharyngeal carriage prevalence 12%
Oliver J et al, 2018 (29)	Systematic review 285 studies	Pooled carriage rate in children 8.0%, Carriage rate 10.5% in high income versus 5.9% in low-income countries
Ethiopia **Anja A et al, 2019** (28)	Cross-sectional study 287 children in Hawassa town Community-based	Carriage rate 12.2%; risk factors female gender, occupational status of mother, low income, history of hospitalization, rural residence, families with >5 people per household
Ethiopia **Abdissa A et al, 2011** (30)	Cross-sectional study 937 children in Addis Ababa, Gondar and Dire-Dawa Community- based	Carriage rate 9.7%
Tunisia **Mzoughi R et al, 2004** (31)	629 children aged 2-8years Hospital based	Carriage rate 9.0%
Uganda **Nayiga I et al, 2017** (32)	Cross-sectional study 366 children aged 5-15 years Community-based	Carriage rate 16%; significant risk factor peri-urban school location
Uganda **DeWyer A et al, 2020** (22)	Cross-sectional and cohort study 1028 children aged 5-15 years Community-based	Carriage rate 15.9%; no significant difference between gender and age, higher among Northern schools
Yemen **Othman AM et al, 2019** (33)	Cross-sectional study 813 school children Community-based	Carriage rate 12.8%; significant risk factor female gender

Turkey **Durmaz R et al, 2003** (34)	Cross-sectional study 909 children aged 4-13years Community-based	Carriage prevalence 14.3%; carriage higher among those in orphanages 26.6%

2.3. STREPTOCOCCAL PHARYNGITIS

2.3.1. Case definition

Classically, streptococcal pharyngitis starts abruptly with fever, malaise and sore throat with pain on swallowing. There could also be headache, nausea, vomiting and abdominal pain. Accompanying signs are a temperature often higher than 38ºC, tonsillar-pharyngeal erythema and oedema. A patchy exudate that is white or yellowish may be overlying the tonsils/pharynx and the anterior cervical lymph nodes are enlarged, tender and firm. Petechial haemorrhages on the soft palate and a scarlatiniform rash may be present.

Most or all of these clinical characteristics are indicative but not definitive for diagnosis. Lack of fever or development of symptoms such as conjunctivitis, cough, hoarseness, rhinitis, anterior stomatitis, discrete intra-oral ulcerative lesions, viral exanthema and diarrhoea are highly suggestive of a non-streptococcal, usually viral, aetiology.(2,15,16,35)

A systematic review by Shaikh et al to identify signs and symptoms useful in diagnosing streptococcal pharyngitis found that scarlatiniform rash, palatal petechiae, pharyngeal exudates and tender cervical lymphadenopathy were fairly useful.(36) Tonsillar swelling/exudate, temperature >38ºC and lack of cough were independent predictors among children in Ethiopia ($p < 0.05$),(37) whereas in Kenya, an inflamed pharynx (p 0.032) and scarlatiniform rash (p 0.044) were more significant.(38)

Due to considerable similarity between the clinical features of streptococcal and non-streptococcal pharyngitis, combinations of signs and symptoms were developed into clinical decision rules (CDRs) to assist clinicians identify GAS pharyngitis.(39) These would help identify patients with a reduced streptococcal pharyngitis risk in whom further testing and treatment would be unnecessary.(15)

The World Health Organisation (WHO) has two recommendations for presumptive therapy of GAS pharyngitis by use of clinical signs. The WHO Cardiovascular Disease Program lists common signs of GAS but does not specify a rule or case definition to assist in management.(40) The WHO Acute Respiratory Infection (ARI) control programme suggested a CDR to be used by health care workers when a child under 5 years presents with a sore throat: “acute

streptococcal pharyngitis should be suspected and presumptively treated in a patient with sore throat when pharyngeal exudates plus tender, enlarged cervical lymph nodes were present".(41)

In a multiregional study in 3 middle income countries- Brazil, Egypt and Croatia, the WHO CDR was found to have low sensitivity in children under 5 years of age (0.0-4.6%) and in those aged 5 years and above (3.8-10.5%) in all 3 sites.(42) In low-resource settings where rheumatic fever and rheumatic heart disease are prevalent, clinical application of this CDR with its low sensitivity may be unsuitable for either individual patients or for public health policy as many true cases of streptococcal pharyngitis will be missed.

As healthcare workers are more likely to favour increased sensitivity in diagnosing a condition of public health significance, some countries attempted to develop prediction rules with higher sensitivity. In Cairo, Steinhoff et al proposed a 3-variable CDR for GAS pharyngitis in a child presenting with sore throat.(43) The variables were enlarged or tender anterior cervical lymph nodes, absence of rash and absence of rhinitis. When applied to 410 children aged 2-12 years, the CDR had a sensitivity of 92%, specificity of 38% and reduced antibiotic use in GAS negative cases by 40%.

Smeesters et al developed a more complex prediction rule for identification of non-group A streptococcal pharyngitis in Brazil that focused on three variables- age, viral signs and bacterial signs.(44) When used in 3 public hospitals, the CDR had a sensitivity of 41% and specificity of >84% for detection of non-group A streptococcal pharyngitis and reduced antibiotic prescription by 41-55%. Both CDRs had a higher sensitivity than that of WHO, reduced unnecessary antibiotic prescriptions significantly and were developed with the lower resource setting in mind. However, they are not widely used as they are yet to be validated in different settings using different patients and clinicians.

The McIsaac score/Modified Centor score, a clinical scoring system that combines both clinical and epidemiological features, is the most preferred.(45) It uses 5 criteria: tonsillar exudates/swelling, tender anterior cervical lymph nodes, temperature >38ºC, absence of cough and age. It modifies the Centor score by taking into account the epidemiological differences in children versus adults, adding one point if the patient is younger than 15years and subtracting 1 point if aged 45 years and above.(45) The total score indicates the likelihood of GAS infection and recommends diagnostic and therapeutic options as shown below in Table 2.

Fine et al validated the McIsaac score on 206,870 paediatric and adult patients in the United States but no such validation has occurred in developing countries.(46) In addition, this score

identifies only 53% of patients with confirmed GAS pharyngitis even when ≥4 criteria are present.(15,45,47,48)

Table 2: McIsaac score, risk of streptococcal pharyngitis and suggested management

Criteria	**Points**	**Total score**	**Risk of GAS pharyngitis**	**Management**
Temperature >38ºC	1	-1	1-2.5%	No investigation or antibiotics required
Absence of cough	1	0		
Tender anterior cervical adenopathy	1	1	5-10%	
Tonsillar exudate or swelling	1	2	11-17%	RADT ± throat culture; if positive, antibiotics
Age 3-14 years	1	3	28-35%	
Age 15-44 years	0	≥4	51-53%	RADT ± throat culture; if positive, antibiotics
Age ≥45 years	-1			
Total Score	----			

No individual clinical feature or prediction rule can be used for conclusive diagnosis or exclusion of streptococcal pharyngitis and thus, bacteriologic confirmation is required.(36) A case of GAS pharyngitis in children is defined as a child who complains of sore throat or has the clinical features of pharyngitis and in whom a rapid test or culture confirms the presence of GAS.(15,22)

2.3.2. Prevalence of streptococcal pharyngitis

The prevalence of streptococcal pharyngitis in children varies depends on the setting of the study and what recruitment methods were employed. Most hospital-based studies have a high prevalence as they employ passive recruitment; this being where the participants present themselves to the health practitioner with features of pharyngitis. The pooled prevalence of GAS pharyngitis in both high and lower income countries is 37% and this is similar to Kenya at 38.4%.(1,29,38)

Active recruitments on the other hand tend to have lower rates as patients, who usually have less severe pharyngitis and would not have sought treatment for their symptoms, present to

sore throat management programmes that actively recruit them. This is demonstrated by Oliver et al where the prevalence in active recruitment programs was lower at 11.6% in high income countries and 9.2% in lower income countries.(29)

School-based studies also tend to have lower GAS pharyngitis prevalence rates as most of the participants are generally well with those who are sick missing school. For instance, in a school-based study in Uganda by Nayiga et al, GAS pharyngitis had a very low prevalence of 2.5%.(32)

As transmission is by inhalation of infected respiratory droplets and/or nasal discharge from infected persons or carriers, poor ventilation is a key risk factor to developing streptococcal pharyngitis. Overcrowding as evidenced by evidenced by having more than 5 people in a household, shared bedrooms or a classroom having more than the recommended number of pupils is a major contributor.(32,38,49) Also implicated are households with no separate kitchens, being around tobacco smoke, winter and rainy seasons, and age.(49) A summary of studies on GAS prevalence, risk factors and significant clinical features is found in Table 3.

2.4. LABORATORY DIAGNOSIS OF STREPTOCOCCAL PHARYNGITIS

The definitive test in the diagnosis of streptococcal pharyngitis is the isolation of *S. pyogenes* from throat culture.(15,50) The major hindrance to its use in clinical practice is the relatively long lag time, which can be 18 hours or more from the collection of specimens to final microbiological confirmation. This delay is not practical for patients to return for a second visit to receive confirmation of their diagnosis and the necessary antibiotics, especially in low resource settings.(50,51) The delay is worsened by the recommendation that negative culture plates should be re-examined at 24hours and at 48 hours.(15)

Another limitation to its use is that the laboratory infrastructure required may be lacking.(52) The proportion of positive results can be increased by utilizing anaerobic incubation and selective culture media. However, the increased cost and effort required for this are limiting in such resource-constrained settings.(15)

The early 1980s saw the creation of rapid antigen detection tests (RADTs) to ease the laboratory detection of GAS pharyngitis. Several generations with different methodologies have been developed. The first-generation RADTs were latex agglutination tests that were insensitive. Subsequently, enzyme linked immunosorbent assays (ELISA), lateral flow and

Table 3: Studies on prevalence of GAS pharyngitis, associated risk factors and clinical features

Author	**Study design and population**	**Study setting**	**Results**
Shaikh N et al, 2010 (1)	Systematic Review 29 studies		Pharyngitis prevalence 37%
Oliver J et al, 2018 (29)	Systematic review 285 studies		Pooled pharyngitis rate in children 37% in passive recruitment; Active recruitment- 11.6% in high income countries versus 9.2% in lower income countries
Tunisia **Mzoughi R et al, 2004** (31)	Prospective study 629 children aged 2-8years	Hospital based	Pharyngitis prevalence 17.7%
Uganda **Nayiga I et al, 2017** (32)	Cross-sectional study 366 children aged 5-15 years	Community based	Pharyngitis prevalence was 2.5%
Uganda **DeWyer A et al, 2020** (22)	Cross-sectional and cohort study 1028 children aged 5-15 years	Community based	Pharyngitis prevalence 41.8%; significant clinical features- pain that lasted all day, palatal petechiae, tonsillar exudates and swelling
Kenya **Kunga BM et al, 2018** (38)	Cross-sectional study 198 children aged 2-15 years with pharyngitis	Hospital based	Pharyngitis prevalence 38.4%; significant clinical features - inflamed pharynx and scarlatiniform rash.
India **Nandi S et al, 2001** (49)	Prospective cohort study 536 children aged 5-15 years	Community based	Pharyngitis incidence higher among 11-year-olds, in winter and rainy seasons, among children living with no separate kitchen and those around tobacco smoke.
Ethiopia **Tesfaw G et al, 2015** (37)	Cross-sectional study 355 children with pharyngitis	Hospital based	Pharyngitis prevalence 11.3%; Independent predictors - absence of cough, tonsillar exudate or swelling, temperature >38ºC

immune-chromatographic assays, and optical immunoassays (OIAs) which offered better sensitivity were produced. Molecular-based techniques such as polymerase chain reaction (PCR), deoxyribonucleic acid (DNA) probes and fluorescence in situ hybridization (FISH) methods are the most recent but expensive developments.(15,51)

In assessing the diagnostic accuracy of RADTs compared to throat cultures, RADTs are generally highly specific varying between 90 to 99%.(15,50) There is however considerable variability in sensitivity depending with the type of kit used, with a general sensitivity being between 70% and 95%.(15,50) The different sensitivity values could be due to differing disease severity among study population, culture methods and the individual's ability to collect the throat swab samples and carry out the rapid antigen test.(50,52)

Lean et al demonstrated this by carrying out a systematic review with meta-analysis that included 48 studies, 36 from developed countries and 12 from developing countries, using different generations of RADTs.(51) The combined estimate of sensitivity and specificity for the RADTs was 86% (95% CI 83-88%) and 96% (95% CI 94-97%) respectively. The best performing method was the molecular technique with a sensitivity of 92% and specificity of 99%. Lateral flow/immune-chromatographic assays, which are the most commonly used, had the greatest variability in sensitivity of 59% to 96%.

The Infectious Disease Society of America (IDSA) and European guidelines recommend that RADTs be used in routine clinical practice when the McIsaac/Centor score is greater than 3.(15,50) The high specificity among RADTs prevents unnecessary antibiotic prescription for non-group A streptococcal pharyngitis.(15,51) The variable sensitivity, however, led the American Academy of Paediatrics and IDSA to recommend a confirmatory throat culture for all negative RADT results in the paediatric population.(15,47) This recommendation was also informed by the higher occurrence of streptococcal pharyngitis and rheumatic fever in children. On the contrary, owing to differing opinions between expert groups on this issue, the European guidelines do not recommend this backup culture.(50,51)

There are many pros to the use of RADTs in clinical practice over throat culture in diagnosing GAS pharyngitis. They are a more feasible alternative because they are 'point of care' tests in that they have a quick turnaround time of 15mins compared to throat culture that takes 18 to 48 hours.(15,51,52) They are also simple to perform and can thus be carried out both at initial contact and in the laboratory. This leads to rapid diagnosis and treatment of patients resulting in reduced GAS transmission, early return of the child to school and parents to work, reduced

GAS morbidity and improved antimicrobial stewardship by reducing unnecessary antibiotic prescriptions.(15)

In addition, RADTs have been found to be cheaper when compared to culture. For instance, in Australia where both RADTs and throat cultures are used, RADTs cost between 5 and 10 Australian dollars per test compared with 30 Australian dollars per throat culture.(51) This cost difference brings up the question of whether it is cost-effective to run a backup culture for every negative RADT test, considering the resource constraints developing countries face.

Standardized production and the presence of internal controls ensure diagnostic accuracy in RADTs. In resource-constrained environments where throat culture is impractical owing to either lack of qualified staff, delays associated with culture or both, RADTs without the confirmatory throat culture are a viable alternative to clinical diagnosis alone.(51,52) This is especially true if the RADT to be used has comparable performance to throat culture locally.

A highly sensitive, inexpensive rapid antigen test that can be used at 'point of care' may contribute significantly to the efforts to control acute rheumatic fever and subsequent rheumatic heart disease. This will help achieve one of the aims set out in The Addis Ababa Communiqué on Eradication of Rheumatic Heart Disease in Africa as part of primary prevention against rheumatic heart disease; "In addition to effectively treating streptococcal pharyngitis with penicillin as part of routine child health care, countries should aim at having RADTs for GAS to offer diagnosis at point of care at the primary and district levels of health care".(14)

2.5. PROBLEM STATEMENT

S. pyogenes poses a great public health burden with high mortality and morbidity especially in resource-poor countries. Sub-Saharan Africa, Kenya included, still has a high prevalence of ARF/RHD and invasive GAS diseases, which diverts a lot of much needed resources to its management.(8,9) Effective prevention is key in a bid to eradicate these diseases.

In Kenya, some regions are considered 'rheumatogenic' as acute rheumatic fever/rheumatic heart disease has been diagnosed in many children as per school-based and hospital RF/RHD programs.(25) Much needed surveillance systems and epidemiological data on GAS pharyngeal carriage, pharyngitis and other GAS related disease is needed but lacking to help inform effective translation of primary prevention strategies.(8,9,14)

The development of rapid antigen tests has made diagnosis of GAS pharyngitis easier and initiation of treatment faster. However, their use is quite limited in developing countries, despite their frequent use in high income countries.

3. STUDY JUSTIFICATION AND UTILITY

Acute rheumatic fever is still a very common disease with Sub-Saharan Africa having the highest disease burden. Group A streptococcal pharyngitis should be promptly diagnosed and effectively treated to prevent the development of acute rheumatic fever. A rapid test offers confirmatory diagnosis at point of care to enable early initiation of appropriate treatment yet its use is very limited locally. This study aims to use the RADT to detect the GAS carrier state in Bomet, a rheumatogenic region, in a bid on improving the point of care diagnosis of GAS. This will ultimately help reduce the high disease burden of and eradicate ARF/RHD as GAS pharyngitis will be quickly diagnosed and treated. In addition, it can be used to advocate for surveillance programs around *S. pyogenes* in these rheumatogenic areas which will help in formulating prevention and control strategies for streptococcal complications, more so rheumatic fever and rheumatic heart disease.

3.1. STUDY QUESTION

What is the prevalence and factors associated with Group A Streptococcal pharyngeal carriage in primary school children aged 5-15years in Bomet County?

3.2. STUDY OBJECTIVES

Primary objective:

To determine the prevalence of Group A Streptococcal pharyngeal carriage among primary school children 5 to 15 years of age in Bomet County.

Secondary objective:

To determine the factors associated with GAS pharyngeal carriage.

4. METHODOLOGY

4.1. STUDY DESIGN

This was a descriptive cross-sectional study.

4.2. STUDY AREA AND POPULATION

The study was carried out in five primary schools of Bomet County once the relevant approval was obtained. Bomet County is in the South Rift region of Kenya and is surrounded by four counties: Kericho to the North, Nyamira to the West, Narok to the South and Nakuru to the North-East as shown in figure 3. It has a highland topography with even distribution of rainfall throughout most of the year.(53)

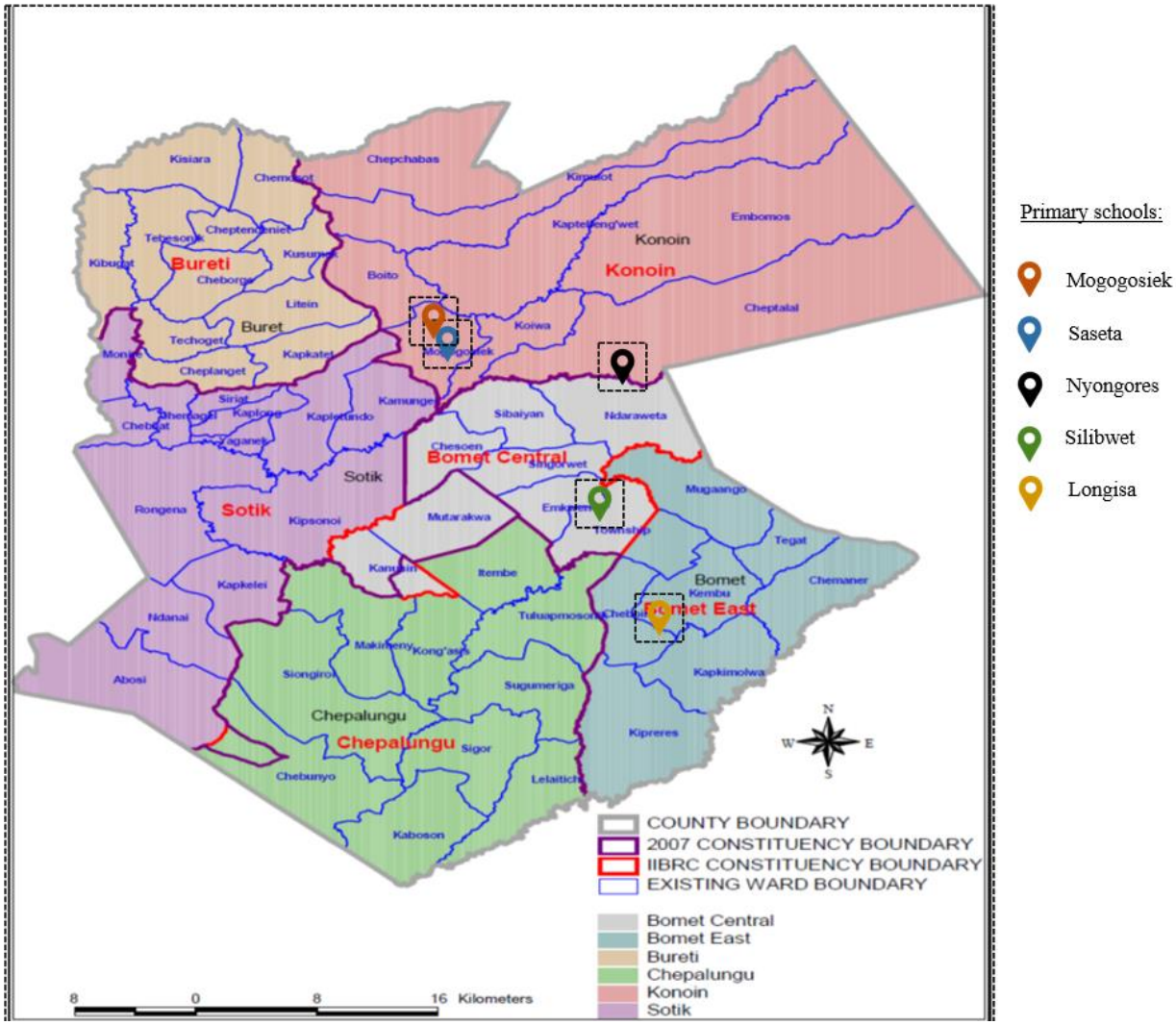


Figure 3: Map of Bomet and its sub-counties indicating the location of the selected schools

It has 5 sub-counties, from the largest to the smallest, namely Chepalungu, Sotik, Konoin, Bomet East and Bomet Central. As per the latest 2019 Census report, Bomet has a population

of 875,689 with 50.4% being females.(54) A high concentration of the population is made up of children aged 0 to 14 years.(53) Majority of the population (86.1%) reside in the rural setting with the 2 major urban centres in the county being Bomet town in Bomet Central sub-county, and Sotik.

The population of interest was school children attending primary schools in Bomet County aged between 5 and 15 years as this is the population at risk.

The study period was four months i.e., December 2020 to March 2021.

4.3. INCLUSION AND EXCLUSION CRITERIA

These included:

Inclusion criteria:

i. Child in the age of interest whose parents/guardian gives informed consent.
ii. Child > 7 years of age that gives assent

Exclusion criteria:

i. Those who had incomplete data
ii. Those who missed school on the day of data collection

4.4. SAMPLE SIZE CALCULATION

By using the Fischer's formula for sample size determination in prevalence studies:

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

Where:

- Z= normal standard deviation corresponding to 95% confidence interval (1.96)
- P= estimated prevalence of GAS carriage in children (16%).
- d= precision (5%)
- n= desired sample size

$$n = \frac{1.96^2 \, x \, 0.16(1-0.16)}{0.05^2} = 207$$

Calculated sample size (n) was 207.

The study adopted a GAS pharyngeal prevalence of 16% based on the Ugandan study carried out by Nayiga et al. (32); The setting was similar to ours and was also community-based involving primary school children.

4.5. SAMPLING METHOD

A sampling frame with all the public schools divided per sub-county was generated by the County of Bomet Ministry of Education's office. Using the sampling function in Microsoft Excel, 5 schools were randomly selected; Longisa primary school in Bomet East sub-county, Nyongores and Silibwet primary schools in Bomet Central, and Mogogosiek and Saseta primary schools from Konoin sub-county.

The classes within the selected schools were stratified according to classes/grades. Using the class lists as a sampling frame and with the teachers' assistance, an equal number of students was selected from each class randomly using the random number method. This is where every pupil was assigned a number and random numbers were then generated using the random number function in Excel. This was done as a way of getting equal representation across the age group being studied.

The students were invited to participate in the study. They voluntarily took the consent forms and questionnaires after an introductory talk on the study and its objectives. All who returned filled parental consent forms and assent forms, for those aged 7-years-old and above, were enrolled into the study. This was carried out in the 5 schools till the target sample was achieved.

4.6. STUDY VARIABLES

Dependent Variable:

This was recorded as presence of GAS in the participants' pharynx as indicated by a positive rapid antigen detection test.

Independent variables:

i. School characteristics- location, number of pupils per square footage of a classroom

ii. Socio-demographic – Age, sex, parents' occupation, parents' level of education, average household monthly income, household size, place of residence, number of shared bedrooms, presence of separate kitchen

iii. Clinical features:

- Symptoms- pain on swallowing, fever, cough, nausea, vomiting, abdominal pain, headache, number of sore throat episodes in the past 3 months and whether treatment was sought
- Signs –temperature >38ºC, rhinitis, conjunctivitis, tender/large anterior cervical lymph nodes, tonsillar/pharyngeal exudates, scarlatiniform rash, palatal petechiae

The parent's occupation was categorized as formal employment, informal employment and unemployed. In this study, self-employment and casual labor was classified as informal employment. For average household income, the categories were less than Kshs. 5,000 and equal/more than Kshs. 5,000.

The place of residence was categorized as either urban or rural. In Bomet, the main urban centres are Bomet and Sotik. Other centres in the county include Mogogosiek, Silibwet, Longisa, Sigor and Mulot.(53) Participants living in these centres were categorized as urban dwellers while those living outside these areas were categorized as rural dwellers.

Case definitions:

i. Pharyngitis- Inflammation of the back of the throat and/or the tonsils.
ii. Streptococcal pharyngitis- a case of pharyngitis which tests positive for GAS on the rapid antigen test.
iii. Streptococcal carrier- an asymptomatic patient with confirmed pharyngeal presence of GAS as evidenced by a positive RADT result.

4.7. STUDY TOOLS

The study utilized a structured paper-based questionnaire translated into the local languages, both Kiswahili and Kipsigis (Appendix 1). It captured the bio-data, parent(s)'/guardian's socio-demographic details, details of the school environment and signs and symptoms of interest in the child. The results of the throat swab subjected to the RADT was also included.

4.8. STUDY PROCEDURE

4.8.1. Participant recruitment

Approval from the Kenyatta National Hospital-University of Nairobi Ethics and Research Committee (KNH-UoN ERC), the National Commission for Science, Technology and

Innovation (NACOSTI), the Ministry of Education Bomet County and Bomet County Commissioner was sought.

Once the relevant approval was obtained, a research assistant who was a registered clinical officer was identified and trained on the study and its protocols. Sampling was done as outlined in the sampling method and potential study participants identified using the inclusion criteria. They were given the consent forms and questionnaires to take home to their parents. The parent/caregiver filled in the biodata and sociodemographic data. An assent form was also filled by children above 7 years who returned their filled consent forms. Any pertinent questions with regard to the study were addressed by the principal investigator prior to signing the consent forms.

The consent and assent forms contained a brief introduction about the study, described its purpose, the procedure to be followed, and the risks and benefits of participating in the study. They also contained information about safeguarding the participant's privacy and sharing of the study findings (Appendices 2-3). They were also translated into the local language.

Once consent was granted, the eligible participants were enrolled as study participants. The principal investigator/research assistant asked them a few questions on the presence of the symptoms of interest, performed a physical examination and collected the throat swab specimen at the school. The presence/absence of the clinical signs and symptoms of interest together with the RADT result were recorded in the structured questionnaire.

After all the participants in a school were examined, the principal investigator and the research assistant measured the length and width of all the classrooms in the school using a measuring tape to determine the square floor area per classroom.

4.8.2. Physical exam

All study participants were examined for the following signs: temperature >38ºC, rhinitis, conjunctivitis, tender/large anterior cervical lymphadenopathy, tonsillar/pharyngeal exudates, scarlatiniform rash and palatal petechiae.

4.8.3. Throat swab procedure

As the world is currently facing the COVID-19 pandemic, appropriate infection prevention measures were taken in line with the national guidelines prior to obtaining a throat swab sample.(55,56) These measures included:

i. Research staff had daily temperature checks and would only have interaction with the participants if symptom-free with no history of exposure to COVID-19.
ii. All research staff had to put on at least a medical mask, face shield and apron.
iii. Temperature checks for all participants using a non-contact thermometer was done.
iv. Hand-sanitizers for all to use was availed.
v. Physical distancing of minimum 1.5 meters in the designated waiting area and procedure room was maintained.

Following good laboratory practices, the investigator/research assistant collected a throat swab sample while donning an apron, clean disposable gloves, face shield and a mask as follows:

i. With the participant's head tilted backwards and the throat well lit, the tongue was depressed with a clean tongue depressor so that the back of the throat could be inspected. Signs of inflammation and the presence/absence of exudates was noted.
ii. A sterile swab was opened and specimen collected by rubbing the swab on the tonsils and back of throat, while avoiding the teeth, gums, tongue, and cheek surfaces.
iii. The used tongue depressor and gloves were discarded as per recommended infection prevention protocol.
iv. The swab was then subjected to the RADT and results recorded.

The participant flow from recruitment to the RADT test is summarized in figure 4.

4.8.4. Rapid antigen detection test

The test used in this study was the Detector Strep A™ Rapid Test Kit (IDSTREP-25 Immunostics, Inc., USA), a chromatographic immunoassay for the qualitative identification of Group A streptococcal antigen from throat swab specimens. The test is CLIA (Clinical Laboratory Improvement Amendments)-waived, easy to use, stable at room temperature, and results in 5 minutes.

Coated on the test area of the strip is the antibody unique to the Strep A carbohydrate antigen. This reacts with the extracted throat swab specimen and the mixture migrates up the membrane. If Strep A antigen is present, a red line in the test region will appear. Absence of a line in this region signifies a negative result as demonstrated in figure 5.

The manufacturer sets the performance of this RADT at 97% sensitivity and 95% specificity. Kunga demonstrated its performance locally in comparison to throat culture.(38) It had an impressive performance at a sensitivity of 93.4%, specificity of 99.2%, a positive predictive value of 98.6% and a negative predictive value of 96%.

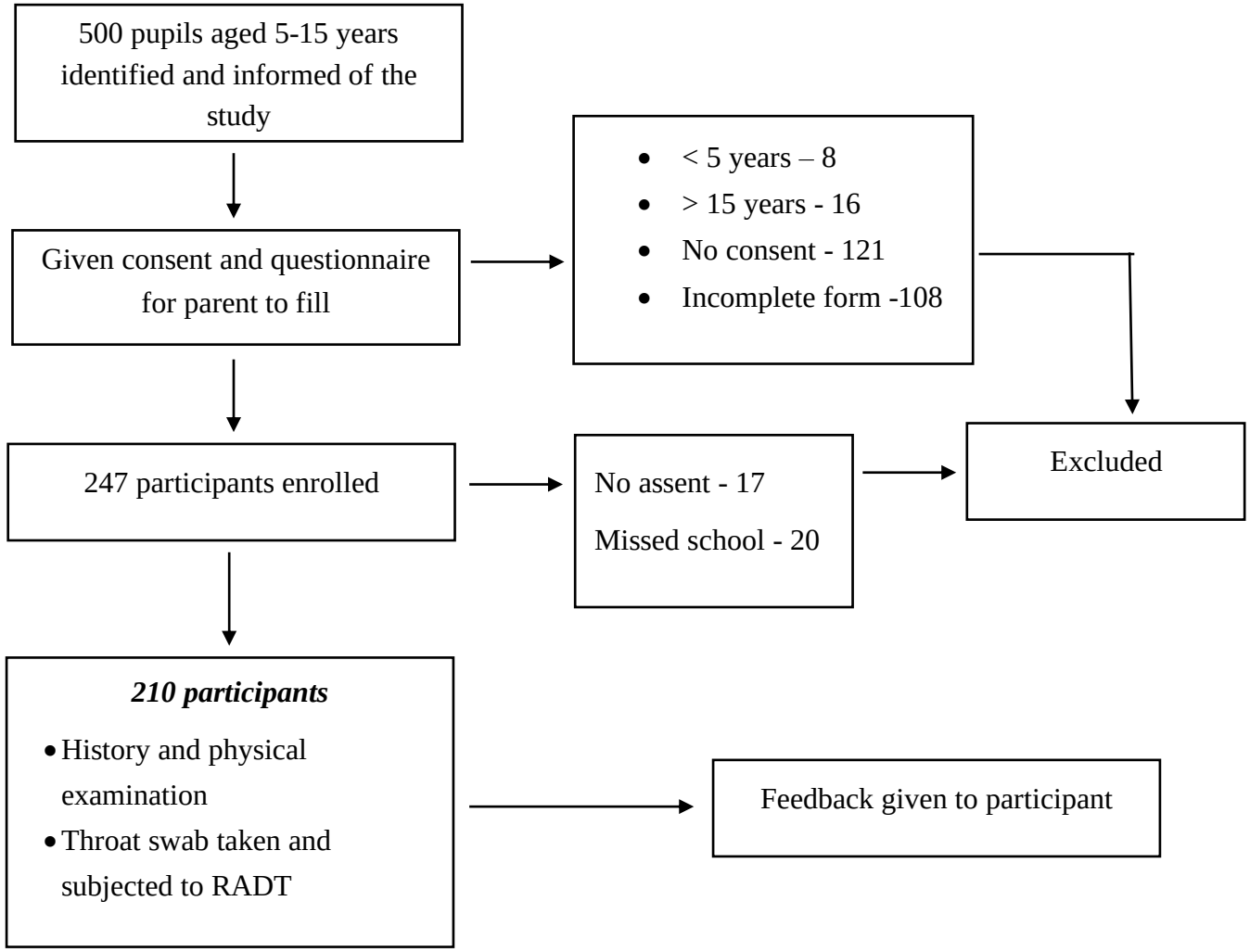


Figure 4: Participant recruitment

Those who tested positive were referred to the closest health facility for treatment. Both the test procedure and result interpretation are depicted in Appendix 4.

Quality Control:

For quality control purposes, there is both an internal and external control. For internal positive procedural control, a red line appears in the control region of the test strip. This indicates sufficient specimen volume was collected and correct procedure was followed.

For external control, a positive and negative control have been provided in the kit. These controls are to be run with every batch of tests, or as often as deemed necessary. To ensure consistent and reliable results, the investigator ran these controls with every batch of tests.

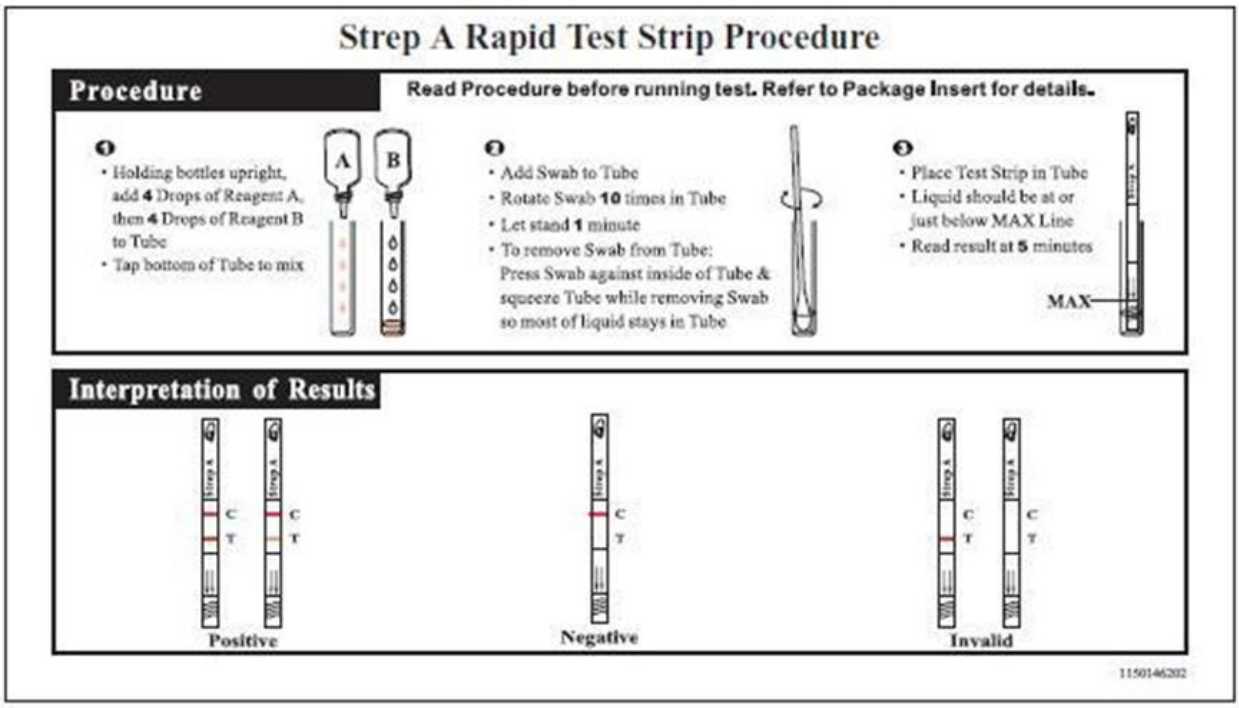


Figure 5: Strep A Rapid Test Strip Procedure

4.9. DATA MANAGEMENT AND ANALYSIS

The collected data was reviewed for completeness prior to entry into a customized password protected Microsoft Excel spreadsheet. This was then exported to IBM™ Statistical Package for Social Scientists (SPSS) version 24 for analysis. All generated output was backed up in a password protected hard drive.

Demographic and clinical characteristics that are categorical were analyzed and presented as frequencies and percentages, while those that are continuous were analyzed and presented as means with standard deviation (SD) or as medians with interquartile range (IQR). Prevalence of GAS carriage with 95% confidence intervals were calculated as a proportion of those that tested positive and presented as percentages.

The factors were tested at univariable stage with the use of Chi-square tests, with the Fischer's exact being used for analysis of occurrences that were less than 5 in a cell. Odds ratio as well as 95% confidence intervals were calculated. Those found to be significant would be subjected to multivariable analysis with the use of logistic regression. All tests would be considered significant where the p-value is <0.05.

4.9.1. Study results dissemination plan

The study results will be submitted to the Department of Paediatrics and Child Health, University of Nairobi as part of the requirements of the Master's Program in both hard and soft copies. Hard copies of the study will be sent to the University of Nairobi repository for storage. Findings will also be made available for publication in peer reviewed scientific journals. The schools and the county administration will also be informed about the study results.

4.10. ETHICAL CONSIDERATIONS

1. Study approval was sort from the KNH-UoN ERC, NACOSTI, the Bomet County Ministry of Education's and County Commissioner's offices. The approval letters and research permit are attached in Appendices 5-8.
2. A written informed consent explaining the details, procedures and protocols of the study was obtained from parents/guardians of the study participants before enrollment. This was translated in both Kiswahili and Kipsigis.
3. For children over the age of 7, a written assent form was obtained. This was also translated into Kiswahili.
4. Only participants of consenting parents were enrolled in the study
5. Participants were informed of the voluntary nature of participation and they could opt out of the study at any time without being disadvantaged in any way.
6. Infection prevention control measures to mitigate against COVID-19 exposure were instituted.
7. To ensure confidentiality, no personal identifiers were used and participants were issued with unique identification codes. The completed questionnaires are under lock and key and the computerized data is password protected. Only the principal investigator has access to the completed questionnaires and the computerized data.
8. Treatment was recommended at the nearest health facility for those found to have a positive RADT result.

5. RESULTS

5.1. PREVALENCE OF GROUP A *STREPTOCOCCUS* PHARYNGEAL CARRIAGE

Out of 210 children examined and their throat swabs subjected to RADT, twenty tested positive for GAS pharyngeal carriage giving a prevalence of 9.5% (95% CI= 6.3%-14.3%) as shown in figure 6.

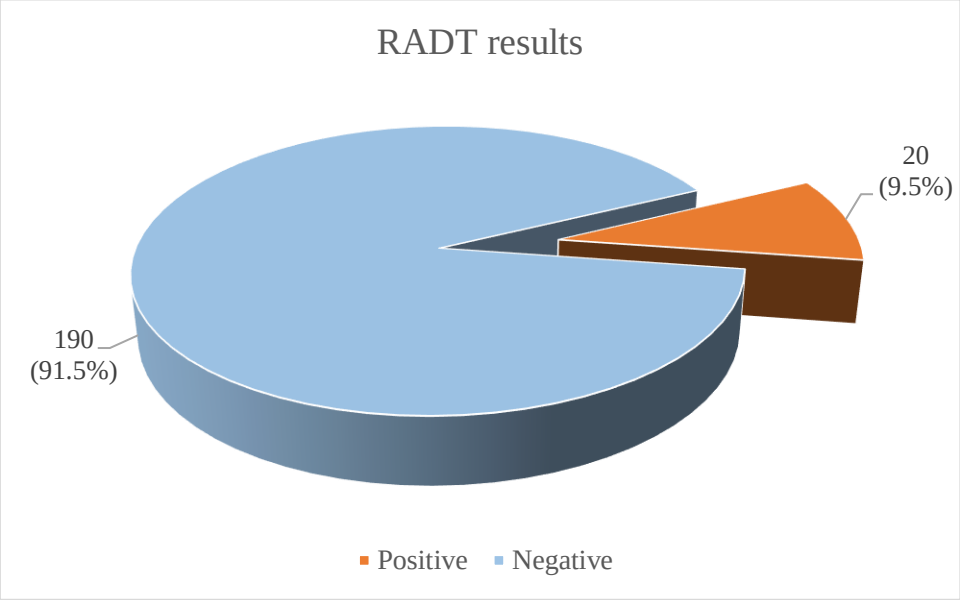


Figure 6: Overall prevalence of GAS pharyngeal carriage

Of the 20 children identified with a positive RADT, Mogogosiek had the highest number (n=7; 35%), followed by Silibwet (n=5; 25%) with Saseta having the lowest (n=2; 10%) as shown in table 4.

5.2. FACTORS ASSOCIATED WITH GROUP A *STREPTOCOCCUS* PHARYNGEAL CARRIAGE

School characteristics

Three out of the 5 schools – Mogogosiek, Silibwet and Longisa – were peri-urban. Children from peri-urban schools were almost two times more likely to have GAS pharyngeal carriage compared to those from rural schools.

The selected schools were overcrowded with an average of 1.1 pupils/m^2, with overcrowding being termed as having classrooms with > 0.9 pupils/m^2. Mogogosiek primary school had the highest carrier positivity rate and the highest population density but the lowest enrolment rates

as shown in table 4. Overall, most carriers were observed to be in overcrowded classrooms as demonstrated in table 5.

Table 4: Distribution of GAS pharyngeal carriage per school

Schools	Total school population	Total number of children enrolled n (%)	Average number of pupils per sqm floor area	GAS positive n (%)	Positivity rate per school (%)
Mogogosiek	726	39 (5.4)	1.7	7 (35)	17.9
Silibwet	192	54 (28.1)	0.5	5 (25)	9.2
Longisa	655	39 (6.0)	1.3	3 (15)	7.7
Nyongores	285	37 (13.0)	0.7	3 (15)	8.1
Saseta	353	41 (11.6)	1.0	2 (10)	4.8
Total	**2211**	**210 (9.5)**	**1.1**	**20 (100)**	**9.5**

Table 5: Univariable analysis to determine school characteristics associated with GAS carriage

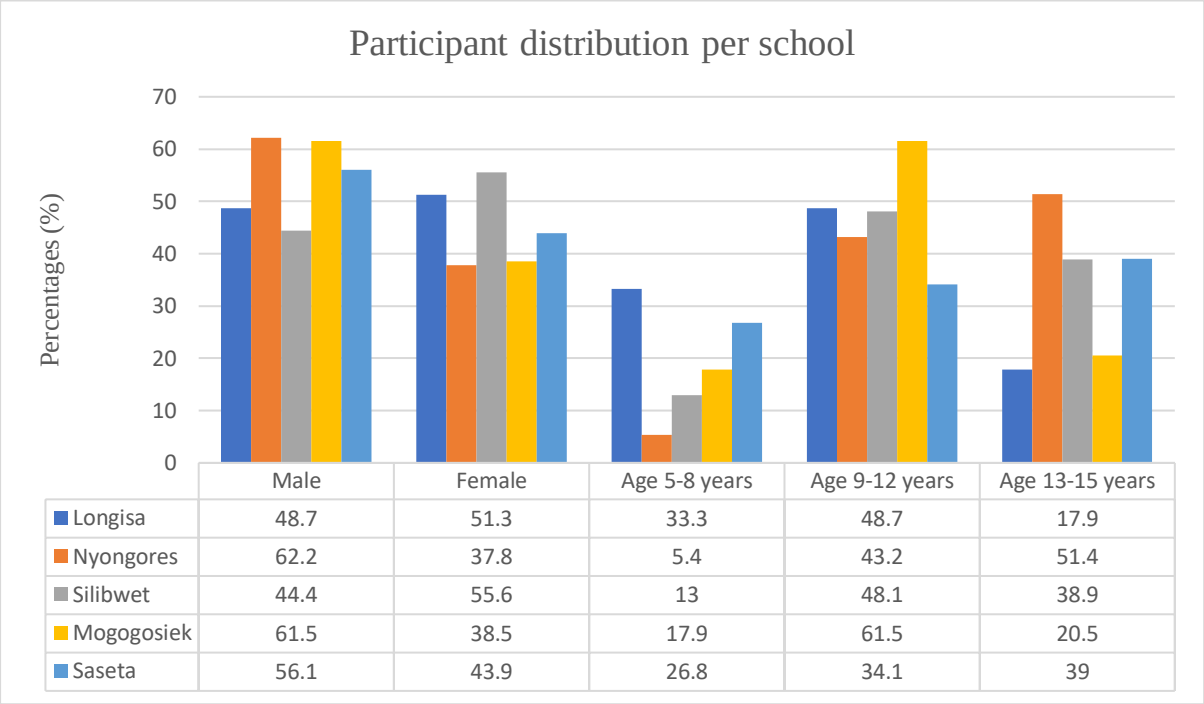
Variable		GAS positive n (%)	GAS negative n (%)	OR (95% CI)	P value
Location of school	Peri-urban	15 (75.0)	117 (61.6)	1.9 (0.7-5.4)	0.243
	Rural	5 (25.0)	73 (38.4)	Reference	
Classroom congestion	≤ 0.9 pupils/m2	9 (45.0)	95 (50.0)	Reference	
	> 0.9 pupils/m2	11 (55.0)	95 (50.0)	1.2 (0.5-3.1)	0.671

However, none of these factors were statistically significant.

Participant characteristics

Majority of the participants were males at 113 (53.8%). This held true when distribution was assessed per school apart from Longisa and Silibwet primary schools, where most of the participants were female at 20 (51.3%) and 30 (55.6%) respectively as shown in figure 7. Being of the male gender was almost 3 times more likely to be associated with carriage OR 2.8, p=0.054 (table 6).

Ninety-nine (47.1%) of the participants were between 9-12 years old with the median age being 11.0 years (IQR 9.0-13.0). When assessed per school, this was reflected in 3 of the schools. Saseta and Nyongores primary schools differed in that most of the participants were 13-15 years of age at 16 (39%) and 19 (51.4%) respectively (figure 7). All carriers, bar one, were in the older age groups with the largest number being in the 9-12 years age group 10 (50%).



	Male	Female	Age 5-8 years	Age 9-12 years	Age 13-15 years
Longisa	48.7	51.3	33.3	48.7	17.9
Nyongores	62.2	37.8	5.4	43.2	51.4
Silibwet	44.4	55.6	13	48.1	38.9
Mogogosiek	61.5	38.5	17.9	61.5	20.5
Saseta	56.1	43.9	26.8	34.1	39

Figure 7: Participant's gender and age distribution per school

In the 3 months prior to the study, majority of the participants, 135 (64.3%), had not experienced any episode of sore throats. For those who had, 51 (68%) of them sought treatment with amoxicillin being the most prescribed at 37.3%. Among the carriers, half of them had experienced ≥ 1 episode of sore throat with 70% of them having sought treatment. This is illustrated in figure 8.

Neither gender, age nor sore throat history was statistically significant at univariable analysis.

Table 6: Univariable analysis of participants' characteristics associated with GAS carriage

Variable	Total n (%)	GAS positive n (%)	GAS negative n (%)	OR (95% CI)	P value
Sex					
Male	113 (53.8)	15 (75.0)	98 (51.6)	2.8 (1.0-8.1)	0.054
Female	97 (46.2)	5 (25.0)	92 (48.4)	Reference	
Age					
5-8	40 (19.0)	1 (5.0)	39 (20.5)	0.2 (0.02-1.4)	0.106
9-12	99 (47.1)	10 (50.0)	89 (46.8)	0.8 (0.3-2.0)	0.600
13-15	71 (33.9)	9 (45.0)	62 (32.6)	Reference	
Median age – 11.0 years (IQR 9.0-13.0)					
Episodes of sore throat over the past 3 months					
None	135 (64.3)	10 (50.0)	125 (65.8)	0.4 (0.1-1.4)	0.171
1	42 (20.0)	5 (25.0)	37 (19.5)	0.8 (0.2-2.9)	0.682
> 1	33 (15.7)	5 (25.0)	28 (14.7)	Ref	
Treatment sought for those episodes, n=75					
Yes	51 (68.0)	7 (70.0)	44 (67.7)	1.1 (0.3-4.7)	0.884
No	24 (32.0)	3 (30.0)	21 (32.3)	Ref	

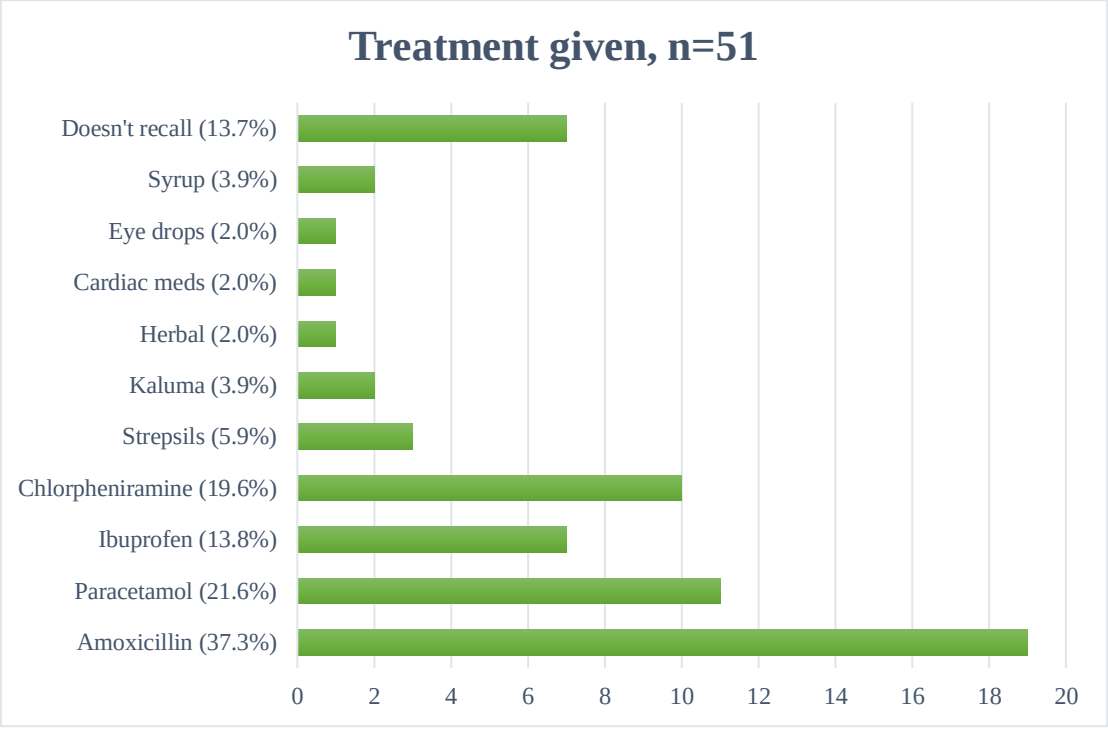


Figure 8: Prior treatment administered to participants to treat sore throat in past 3 months

Clinical characteristics

The most common symptom reported by the participants 1 week prior to the study was cough at 94 (44.8), though its presence was less likely to be associated with carriage. Participants with carriage were almost 2 times more likely to have pain on swallowing. They were also likely to present with a runny nose and abdominal pain. and a temperature [OR 1.1 (95% CI: 0.1-8.8, p=0.958)]. None of the carriers reported nausea/vomiting.

On physical examination, a temperature of >38°C at 10 (4.8%) was the most common sign. However, all the carriers except for one had a temperature of <38°C. None of the participants had features of palatal petechiae, conjunctivitis or a scarlatiniform rash. Among the carriers, none had either tender cervical lymphadenopathy, inflamed tonsils, inflamed pharynx or tonsillar/pharyngeal exudates. The clinical features exhibited by the participants is as shown in table 7.

None of these clinical features, however, were statistically significant.

Household characteristics

In 116 (55.2%) households, the father was the head of the household. Informal employment 138 (65.7%) was the major occupation and most heads of households had attained primary level education and below, 115 (54.8%). Children from households where the head of the household had an education level of primary and below, as well as households where the head of the household was in informal employment, were more likely to be carriers i.e., OR 2.1 (95% CI: 0.8-5.6, p=0.157) and OR 2.1 (95% CI: 0.3-16.9, p=0.486), respectively.

Majority of the households were located in a rural setting at 175 (83.3%) and had a monthly income of less than Kshs. 5000 at 154 (73.3%). Those from urban areas were almost 2 times more likely to have GAS carriage, OR 1.9 (95% CI: 0.7-5.4). The average household size was 6 persons (SD 1.8). Overcrowding, as evidenced by having more than 5 household members, was present at 124 (59%) and was also associated with higher carrier rates.

However, none of these associations were statistically significant as shown in table 8.

Multivariable analysis was not done as no significant associations were realized at the univariable stage.

Table 7: Univariable analysis to determine participants' clinical characteristics associated with GAS pharyngeal carriage

Variable	Frequency n (%)	GAS positive n (%)	GAS negative n (%)	OR (95% CI)	P value
Fever					
Yes	43 (20.5)	4 (20.0)	39 (20.5)	1.0 (0.3-3.1)	0.956
No	167 (79.5)	16 (80.0)	151 (79.5)	Ref	
Cough					
Yes	94 (44.8)	6 (30.0)	88 (46.3)	0.5 (0.2-1.3)	0.163
No	116 (55.2)	14 (70.0)	102 (53.7)	Ref	
Pain on swallowing					
Yes	34 (16.2)	5 (25.0)	29 (15.3)	1.9 (0.6-5.5)	0.261
No	176 (83.8)	15 (75.0)	161 (84.7)	Ref	
Headache					
Yes	62 (29.5)	6 (30.0)	56 (29.5)	1.0 (0.4-2.8)	0.961
No	148 (70.5)	14 (70.0)	134 (70.5)	Ref	
Runny nose					
Yes	74 (35.2)	8 (40.0)	66 (34.7)	1.3 (0.5-3.2)	0.639
No	136 (64.8)	12 (60.0)	124 (65.3)	Ref	
Abdominal pain					
Yes	37 (17.6)	4 (20.0)	33 (17.4)	1.2 (0.4-3.8)	0.769
No	173 (82.4)	16 (80.0)	157 (82.6)	Ref	
Temperature					
> 38°C	10 (4.8)	1 (5.0)	9 (4.7)	1.1 (0.1-8.8)	0.958
< 38°C	190 (95.2)	19 (95.0)	181 (95.3)	Ref	

*****Symptoms were assessed by recall in the preceding one week

Table 8: Univariable analysis of household characteristics associated with GAS carriage

Variable	Frequency n (%)	GAS positive n (%)	GAS negative n (%)	OR (95% CI)	P value
Head of household characteristics					
Relation					
Father	116 (55.2)	11 (55.0)	105 (55.3)	0.6 (0.2-2.1)	0.458
Mother	66 (31.4)	5 (25.0)	61 (32.1)	0.5 (0.1-2.0)	0.319
Other relative	28 (13.4)	4 (20.0)	24 (12.6)	Reference	
Education level					
Primary and below	115 (54.8)	14 (70.0)	101 (53.2)	2.1 (0.8-5.6)	0.157
Secondary and above	95 (45.2)	6 (30.0)	89 (46.8)	Reference	
Employment					
Formal	17 (8.1)	1 (5.0)	16 (8.4)	Reference	
Informal	138 (65.7)	16 (80.0)	122 (64.2)	2.1 (0.3-16.9)	0.486
Unemployed	55 (26.2)	3 (15.0)	52 (27.4)	0.9 (0.1-9.5)	0.946
Monthly Income					
< 5000	154 (73.3)	15 (75.0)	139 (73.2)	1.1 (0.4-3.2)	0.859
≥ 5000	56 (26.7)	5 (25.0)	51 (26.8)	Reference	
Household characteristics					
Residence					
Urban	35 (16.7)	4 (20.0)	31 (16.3)	1.2 (0.4-4.1)	0.675
Rural	175 (83.3)	16 (80.0)	159 (83.7)	Reference	
Household size					
≤ 5	86 (41.0)	7 (35.0)	79 (41.6)	Reference	
> 5	124 (59.0)	13 (65.0)	111 (58.4)	1.3 (0.5-3.5)	0.570
Average household size = 6 persons (SD 1.8)					
Bedrooms					
< 3	136 (64.8)	13 (65.0)	123 (64.7)	1.0 (0.4-2.7)	0.981
≥ 3	74 (35.2)	7 (35.0)	67 (35.3)	Reference	
Separate kitchen					
Yes	165 (78.6)	16 (80.0)	149 (78.4)	1.1 (0.3-3.5)	0.870
No	45 (21.4)	4 (20.0)	41 (21.6)	Reference	

6. DISCUSSION

This study describes the prevalence and factors associated with GAS pharyngeal carriage among children aged 5 to 15 years old attending primary schools in Bomet County, one of the counties present in the possible rheumatogenic region of the country.(25)

The prevalence of GAS pharyngeal carriage was 9.5%. This is similar to that of a study done in the Ethiopian cities of Addis Ababa, Gondar and Dire-Dawa at 9.7% (30) and in outpatient clinics in Sousse, Tunisia at 9.0%.(31) It is however slightly higher than the 8% pooled prevalence in a meta-analysis by Oliver J et al.(29) In Uganda, the prevalence is higher at 16% as reported in two different studies by Nayiga et al., and DeWyer et al.(22,32) The differences in prevalence could be due to study setting, study design, sample size, seasonality and diagnostic tests used in the latter studies.

Direct human-to-human transmission of GAS occurs mainly via inhalation of infected droplets from people with pharyngeal colonization or carriage, and contaminated fomites.(3,4) Poor personal and hand hygiene have been shown to be risk factors for GAS acquisition and infections across all age groups as evidenced by Francis et al.(58) Primary preventive measures against GAS include but are not limited to good hand hygiene with regular handwashing with soap and water, or using alcohol hand rub. *S. pyogenes* is susceptible to 1% sodium hypochlorite and 70% ethanol making the use of hand sanitizer with 70% ethanol, and cleaning of surfaces with sodium hypochlorite effective against GAS transmission.(11) The improved personal and hand hygiene practices brought about by the promotion of the preventive measures against the COVID-19 pandemic the world is currently facing could also have reduced the transmission of GAS. This would lead to the lower GAS pharyngeal carrier rates observed in Bomet compared to Uganda.

Overcrowding is a well-documented risk factor for GAS transmission and subsequent infections.(3,11) This is attributed to poor ventilation and the ease of transmission of the organism from a colonized or infected individual who coughs or sneezes to the other members of the household, classroom etc. According to the Safety Standards Manual for schools in Kenya,(10) a classroom should have a maximum of 0.9 pupils per square meter of classroom floor area i.e., not less than 43.9m^2 of floor area for pupils not more than 40 per class in two-seater desks. In Bomet, the average class size is 1.1 pupils per classroom floor area with congested classrooms, as evidenced by a size of > 0.9 pupils/m^2 of classroom area, having more carriers, 11 (55%). This was similar to a Ugandan study where the crowding index of the

selected schools was 1.3, which was way above their Ministry's recommendation of 0.8 pupils per square meter.(32) Furthermore, Mogogosiek primary had the highest number of carriers as well as the highest population density among the selected schools.

Exposure to air pollutants is a risk factor for GAS infections as it compromises the immune system, thus increasing the risk of infection.(11) This could possibly explain why a larger proportion of carriers were from peri-urban schools 15 (75%). In Uganda,(32) peri-urban schools were a significant risk factor (adjusted OR 2.477, $p < 0.05$). In addition, three of the selected schools were located in the peri-urban area, and that would have contributed to the higher proportion of carriers.

It is observed that a higher proportion of the carriers were males and school-going children, especially boys, are more susceptible to GAS colonization and infection.(11) This increased risk to GAS acquisition may be attributed to more physical interactions and poorer personal hygiene among boys as suggested by Lee at al.(59). Studies in Uganda,(32) Ethiopia (28) and Yemen (33), in contrast, observed the carrier rate to be more among females. Anja et al suggests high female carrier rates may be due to increased contact as they support their mothers in daily tasks.(28)

Majority of the enrolled children were between the age of 9-12 years, with Mogogosiek contributing the highest proportion in this age group at 61.5%. This could explain why most of the carriers were 9-12 years old (n=10; 50%). In this study, age was not statistically significant similar to what was observed in DeWyer et al (22) and Nayiga et al (32).

Despite the study being carried out among relatively well primary school children, some of them had symptoms suggestive of an upper respiratory tract infection. The clinical features would most likely be suggestive of a viral etiology as they are the most common cause of acute pharyngitis.(15,16) Those with GAS pharyngitis tend to be more ill and would more likely have been at home.

The most common symptom was cough (n=94; 44.8%) followed by a runny nose (n=74; 35.2%). Among carriers, 14 (70%) did not have a cough (OR 0.5, p=0.163). This is in keeping with the clinical manifestations of GAS pharyngitis where the absence of cough in presence of a sore throat would more likely suggest the causative organism to be GAS.(16,39) Those who tested positive but had a cough could be GAS carriers with inter-current viral infections.

According to the recent census of 2019, Bomet has an average household size of 5 persons.(54) The average number of persons in a household in this study was 6 persons, SD 2.8. Most of the carriers were observed to be from households with more than five people (n=13; 65%). However, the floor area of the participant's homes was not assessed. Thus, we cannot determine if this influenced the higher carrier numbers seen in households with > 5 persons.

Pharyngeal carriage of GAS and the incidence of GAS infections and related complications is inversely proportional to the level of poverty and socioeconomic status.(11,60) This held true in our study where a higher proportion of carriers were observed to be from households whose monthly income was less than Kshs. 5,000 (n=15; 75%) and where the head of household was in informal employment (n=16; 80%). Proposed reasons why a high burden of GAS carriage and disease is seen in low socioeconomic states is the presence of poor housing conditions which promotes overcrowding, inability to afford or access medical care for prompt treatment of GAS infections and limited resources to promote good hygiene practices.(11,60,61)

6.1. STRENGTHS OF THE STUDY

The study utilized a highly sensitive RADT for the point of care diagnosis of GAS in a rheumatogenic area. This enabled quick detection of the organism with referral for the initiation of appropriate treatment.

To the investigator's knowledge, this is the only study in Bomet to determine GAS pharyngeal carriage. It provides a snapshot of what the prevalence is as it was carried out in a possible rheumatogenic area and during the rainy season. Winter and rainy seasons have been shown to have higher peaks of GAS colonization.(49)

Furthermore, GAS is a community acquired organism (3) and this was a community-based study. Hence, it gives a representation of what the true picture would be in terms of GAS pharyngeal carriage in this population as opposed to if the study were carried out in a hospital setting.

The study also brought to light the issue of overcrowding in schools, more so in the peri-urban areas.

6.2. LIMITATIONS OF THE STUDY

The stringent public health measures currently being enforced could have reduced the prevalence of GAS pharyngeal carriage in an area that is thought to be rheumatogenic.

Due to the stigma surrounding the COVID-19 disease, there was fear surrounding testing as the procedure of taking a throat swab was similar. This was cited as a major reason for parents/guardians declining consent.

The study sample size was small and thus was not powered to determine associated factors.

7. CONCLUSIONS AND RECOMMENDATIONS

7.1. CONCLUSION

1. In this study, the prevalence of GAS pharyngeal carriage among primary school children aged 5-15 years old in Bomet County was 9.5%.
2. A high carrier rate was observed in classrooms with a high population density.

7.2. RECOMMENDATIONS

We recommend:

1. Improved care seeking practices for sore throats in children aged 5-15 years old.
2. Uptake of rapid tests for point of care diagnosis of GAS to enable quick detection of the organism with rapid institution of appropriate treatment.
3. Maintaining the occupancy per class as set out in the Safety Standards Manual for Kenyan schools to reduce the population density in schools. Strategies to achieve this may include carrying out inspections to ensure these standards are being maintained, and improving school infrastructure especially in the rural schools to avoid overcrowding in peri-urban schools.
4. Similar studies powered to determine the factors associated with GAS carriage should be conducted in other parts of the country.

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9. APPENDICES

Appendix 1: Questionnaire

PREVALENCE AND FACTORS ASSOCIATED WITH GROUP A STREPTOCOCCAL PHARYNGEAL CARRIAGE AMONG PRIMARY SCHOOL CHILDREN IN BOMET COUNTY

Investigator: Dr. Maryanne Wachu Murugami

Participant No.: _____ Date: _____

Part 1: Socio-demographic data (to be filled by parent(s)/guardian)

Participant's details *(Maelezo yake mshiriki/ Kibeberta netai)*		
1.1	Age of child in completed years *(Umri wa mtoto- miaka/ Kenyisiek chekokotar lakwet)*	___ years
1.2	Gender *(Jinsia/ Ngetet ama chepto)*	1. Male *(Kiume/ Ngetet)* 2. Female *(Kike/ Chepto)*
1.3	How many episodes of sore throat has your child experienced in the past 3 months? *(Je mtoto wako ameshikwa na mafua ya koo mara ngapi katika miezi mitatu iliyopita? / Kiam mokwe lakwet konyil ata en arowek somek chekokobata?)*	
1.3.1	Was treatment sought for these episodes? *(Alipata matibabu yoyote alipougua? / Kikinya kingwam mokwek hii?)*	1. Yes 2. No
1.3.2	If yes, what treatment? *(Kama ndio, ni matibabu gani? / Kikigoi kerich achon?)*	
Head of household details *(Maelezo ya mkuu wa nyumba/ Akobo chito netelelchin gaa)*		
1.4	What is the occupation of the head of the household? *(Mkuu wa familia ako na kazi gani? / Yoe kasit oinon chito netelelchin kai?)*	1. Formal employment *(Ajira rasmi/ Sirat)* 2. Self-employment *(Kujiajiri/ Kisirkei)* 3. Casual *(Kibarua/ Yoe kibarwa)* 4. Unemployed *(Ukosefu wa kazi/ Masirat)*

1.5	What is the highest level of education of the head of the household? *(Kiwango kikuu cha elimu ya mkuu wa familia? / Kisoman koit ono chito netelelchin kai?)*	1. Tertiary *(Elimu ya juu/ Kisir sokondari)* 2. Secondary *(Sekondari/ Sokondari)* 3. Primary *(Msingi/ Kiit primary)* 4. None *(Hakuna/ Mowa sukul)*
1.6	What is the relationship of the head of the household to the patient? *(Kuna uhusiano gani kwa mkuu wa familia na mtoto? / Kurenkee nei chito netelelchin kai ak chito nimioni?)*	*1.* Father *(Baba/ Kwanda)* 2. Mother *(Mama/ Kamet)* 3. Sibling *(Ndugu/ Tupcho kobo moet akenge)* *4.* Other relative *(Jamaa Mwengine/ Tupcho en oret ake)*
Household details *(Data ya familia/ Kiit ne u kaa)*		
1.7	Average monthly income (Kshs.) *(Mapato ya mwezi/ Rabisiek che chutu kila arawa)*	1. <5,000 2. 5,001 – 10,000 3. 10,001 – 20,000 4. 20,001 – 30,000 5. 30,001 – 40,000 6. 40,001 – 50,000 7. >50,000
1.8	Number of people living in the house *(Idadi ya watu wanoishi kwa nyumba/ Biik chemengisye en koi)*	
1.9	Number of shared bedrooms in the house *(Idadi ya vyumba vya kulala kwa nyumba/ Nambait ab korik chekimenye)*	
1.10	Is there a separate kitchen from the family's living room? *(Jiko lako liko kando na sebule? / Mi taban jiket e kot neo?)*	*1.* Yes *(Ndio/ Ei)* 2. No *(La/ Achicha)*
1.11	Place of residence *(Unaishi wapi? / E menye tao ana resop?)*	*1.* Urban *(Jijini/ Tao)* 2. Rural *(Kijijini/ Resop)*

Part 2: Symptoms

Have you had any of the following symptoms over the past 1 week?		
Pain on swallowing	1. Yes	2. No
Fever	1. Yes	2. No
Cough	1. Yes	2. No
Headache	1. Yes	2. No
Nausea/Vomiting	1. Yes	2. No
Abdominal pain	1. Yes	2. No
Runny nose	1. Yes	2. No

Part 3: Physical exam

Temperature	1. >38.0°C	2. <38.0°C
Tender cervical lymphadenopathy	1. Yes	2. No
Inflamed tonsils	1. Yes	2. No
Inflamed pharynx	1. Yes	2. No
Tonsillar/pharyngeal exudates	1. Yes	2. No
Palatal petechiae	1. Yes	2. No
Conjunctivitis	1. Yes	2. No
Scarlatiniform rash	1. Yes	2. No

Part 4: RADT results

Positive 1

Negative 2

Invalid 3

Part 5: School environment

Location of the school	1. Urban 2. Peri-urban 3. Rural
Average number of pupils per class:	
Number of windows in a classroom	
Square footage of a classroom:	

Appendix 2: Consent form for participation in the study

Study title: **PREVALENCE AND FACTORS ASSOCIATED WITH GROUP A STREPTOCOCCAL PHARYNGEAL CARRIAGE AMONG PRIMARY SCHOOL CHILDREN IN BOMET COUNTY**.

Investigator: **Dr. Maryanne W. Murugami**

Supervisors: **Professor Christine Yuko-Jowi**

Associate professor, Department of Paediatrics and Child Health

University of Nairobi

Dr. Jalemba Aluvaala

Consultant and Lecturer, Department of Paediatrics and Child Health

University of Nairobi

I am a postgraduate student at the **University of Nairobi** pursuing a **Master of Medicine degree in Pediatrics and Child Health**.

I am conducting a study on the prevalence and factors associated with Group A streptococcal pharyngeal carriage. The purpose of this consent form is to give you the information you will need to help you decide whether or not your child should participate in the study.

(Mimi ni mwanafunzi wa Uzamili katika Chuo Kikuu cha Nairobi ninaposomea shahada ya afya ya magonjwa ya watoto. Ninafanya utafiti wangu juu ya kuenea na mambo yanayohusishwa na bakteria wa aina ya kundi la streptokokki A. Kusudi kuu ya kukupa fomu hii ya idhini ni kukuwezesha kuamua iwapo utamruhusu mtoto wako kushiriki kwenye utafiti huu.)

(Ane ko kipsomaniat en Sukulit ab barak nebo Nairobi ak o somonjini Kerichek mising ko chebo lakok. Formit ni ko kokonin naet akobo tukuk cheoche inai si kobit I amuan ngot I chomjini lakwengung ketebsen)

The prevalence of rheumatic heart disease is still very high in our population, especially among children. It is a complication that follows sore throat caused by a bacterium called Group A *Streptococcus*. Some children have the bacteria in their throats but do not have sore throat. Such children can spread the bacteria to healthy children and adults leading to the development of other serious complications.

(Kuenea kwa ugonjwa wa moyo (RHD) ni kwa idadi kubwa miongoni mwetu hasa kwa watoto. Hili ni tatizo linalofuata ugonjwa wa koo kutokana na bakteria wa kundi la streptokokki A. Watoto wengine wako na bakteria kwa koo zao lakini hawana ugonjwa wa kuumwa na koo. Watoto hao wanaweza kueneza bakteria hao kwa watoto na watu wazima wasio na ugonjwa na kusababisha matatizo mengine.)

The study aims to learn how many children that attend primary schools in Bomet County have the bacterium in their throats but do not have sore throat. It also aims to learn what factors increase the likelihood of having this bacterium in their throats.

(Utafiti huu utawezesha kujua watoto wangapi wa shule za msingi za kaunti ya Bomet wako na bakteria hawa kwa koo zao. Lengo lengine ni kujua mambo gani yanachangia kuweko kwa bakteria hawa kwa koo zao.)

(Kiit nekimoche missing kenai en tebsoni ko nambait ab lakok chemiten primari en koonti nebo Bomet chetinye bacteria en mokwek ak koame mokwek ak ata en ichek che moame mokwek. Kit ake nekimoche kenai ko tukuk cheimuchi kutese bitunet ab bacteria en mokwek.)

The study will be conducted among primary school children in Bomet County aged 5 to 15 years. Your participation in this study will help us learn how prevalence of this bacterium and which factors are mostly associated with its presence so that we can help reduce the disease burden and complications associated with it.

(Utafiti huu utafanywa miongoni mwa watoto wa shule za msingi za Bomet wa miaka mitano hadi kumi na mitano. Ushirikiano wako kwa utafiti huu utasaidia kupunguza uenezaji wa ugonjwa huu na kasoro zinazotokana na ugonjwa huu.)

(Lakok che kitepsen ko chebo kenyisiek mut akoi kenyisiek taman ak mut.)

The study will be conducted through the use of a questionnaire. The first part will contain some questions regarding your child and household and the remaining part will be completed by us as we examine your child. A throat swab will be taken from your child and a rapid test done. This test will give us results in 5 minutes.

(Utafiti huu utatumia dodoso. Sehemu ya kwanza inayo maswali machache kuhusu mwanawe na familia yako na sehemu itakayobakia itajazwa na sisi tunapomchunguza mtoto wako. Tutatumia kifaa cha kuchukua sampuli kwa koo ya mtoto na majibu yatapatikana baada ya dakika tano.)

(Kiteben chito tebutik che kakisir. Kebeberta netai kunyite sikindet alan ko chito netononchin lakwet ko komosta ake kinyite yon kichikili lakwet. Kicheru tukun en mokwek ab lakwengung ak kebiman sait noton ak kenyor wolutik en minitisiek mut.)

Kindly understand the following *(Tafadhali elewa yafuatayo/ Tukuk che yoche inai)*: -

Participation is voluntary and no remuneration or compensation will be offered to the participants of the study.

(Ushiriki wako ni kwa hiari na hamutapatiwa fidia yoyote ya kifedha kwa washiriki wa utafiti huu.)

(Iyan ketebsenen kochamengung inyeken ako makiliponi ana kekonin zawadi amun keyan ketepsenin.)

Confidentiality shall be maintained at all times. Your name will be removed from all records in our study and a number assigned to your questionnaire will be used instead. Only staff involved in the study will have access to the data. When we report results of the study, we shall not use your name or the child's name.

(Matokeo ya utafiti huu yatakuwa ni ya siri. Jina lako litatolewa kwa rekodi zetu na utapatiwa nambari ya kipekee kwa dodoso. Watafiti peke yake wataweza kupata matokeo hayo. Matokeo hayatakuwa na jina lako wala la mtoto wako.)

(Kiunye kit ake tukul ne kakinai en tebsoni. Koinutik kuk komakiboru en tukuk chekisire kobaten kiboisien nambait nekokinte tebutik kuk ineken. Biik Chekere tukuk chekesir ko bik chetintoi chomchinet kotebisyen biik icheken. Ikimongu wolutik ab tebisyoni ko mokiboisyen kainengung anan ko nebo lakwengung)

Refusal of any participation in the study will not attract any penalties or place your child at any disadvantage.

(Kukataa kujihusisha na utafiti huu hakutaleta matatizo yoyote kwa mtoto wako.)

(Ngot iyesye ketebsenen ko moki birin anan kekerot lakwengung.)

Risks: The throat swabs may cause some discomfort to your child.

*(**Hatari:** Vifaa vya mapimo ya koo vinaweza kuleta usumbufu kidogo kwa mtoto.)*

(Tukuk chekicheru en mokwek komuch komoboiboienchi lakwengung.)

Benefits: If the bacterium is detected, your child shall be referred to the nearest health facility for treatment. Your community will also benefit because the results of the study will help us develop strategies to reduce the disease burden and complications associated with this bacterium.

*(**Faida:** Iwapo bakteria watapatikana, mtoto wako ataelekezwa kwa hospitali iliyoko karibu apate matibabu. Jamii yako pia itafaidika kwa sababu majibu ya utafiti huu yatasaidia kuendeleza mikakati ya kupunguza kiwango cha ugonjwa na kasoro zinazotokana na huu ugonjwa.)*

(Borotet ko ingotkenyor bacteria kiyoktoi lakwengung kwa olekikoitoen kerichek ole nekit en inye si kobit konyor konyoiset.)

If you have further questions or concerns about your child participating in this study, please contact either:

(Kama uko na maswala ama wasiwasi kuhusu mtoto wako kujiunga na utafiti huu, tafadhali wasiliana na:)

(Ngot itinye tebut ake tukul ibirchi simoit anan isirchi ngolyot nenwach chito ne o en tebsoni noton ko:)

- The principal investigator, Dr. Maryanne Murugami

  Phone number: **0720763815**

  Email: maryannewachu@gmail.com

- The lead supervisor, Prof. Christine Jowi

  Phone number: **0722293454**

  Email: yukojowi@gmail.com

For more information about your child's rights as a research participant, you may contact the Secretary/Chairperson, Kenyatta National Hospital-University of Nairobi Ethics and Research Committee Telephone No. **2726300 (Ext. 44102),** email uonknh_erc@uonbi.ac.ke.

(Kwa maelezo zaidi kuhusiana na haki ya mtoto wako kuwa katika utafiti huu, mpigie katibu wa Kenyatta National Hospital-University of Nairobi Ethics and Research Committee Telephone No. 2726300 (Ext. 44102), email uonknh_erc@uonbi.ac.ke.)

Certificate of Consent *(Shahada ya idhini/ Koyonchinet)*:

I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions about it and any questions that I have asked have been answered to my satisfaction. I as an informant/parent to _____ consent voluntarily to participate in this research.

(Nimesoma maelezo niliopewa. Nimepata fursa ya kuuliza maswali na maswali yangu yamejibiwa na nimeridhika na maelezo yote. Mimi kama mzazi/mlezi wa _____ ninapeana idhini yangu kwa hiari ya kujiunga na utafiti huu.)

(Karasoman anan kokesomanwon ngalek che mi yu. Kamuch ateb tebutik che tinyeke ak ngalechu ako kakewalwon. Ane sikindet anan tononchinet ab _____ ko kayan atoret en somanani.)

Name of Participant *(Jina la mshiriki/ Kainet ab nekitebsen)*: _____

Signature of participant *(Sahihi ya mshiriki/ Sein)*: _____

Date *(Tarehe/ Torikit):* _____

Researcher's name *(Jina la mtafiti/ Kainet ab kipsomaniat)*: Dr. Maryanne Murugami

Researcher's signature *(Sahihi ya mtafiti/ Sein)*: _____

Date *(Tarehe/ Torikit)*: _____

Appendix 3: Assent form for children older than 7 years of age

PREVALENCE AND FACTORS ASSOCIATED WITH GROUP A STREPTOCOCCAL PHARYNGEAL CARRIAGE AMONG PRIMARY SCHOOL CHILDREN IN BOMET COUNTY

Name of researcher: Dr. Maryanne Wachu Murugami

Supervisors: Prof Christine Yuko-Jowi and Dr. Jalemba Aluvaala

My name is Maryanne Wachu and I am a doctor at Kenyatta National Hospital. I am interested in doing research on germs we might find in your throat that cause sore throat. In some children, it may cause heart disease.

(Mimi in daktari kwa jina la Maryanne Wachu na ninafanya kazi katika hospitali kuu ya Kenyatta. Ninafanya utafiti kuhusu vidudu vinavyoleta ugonjwa wa koo. Vidudu hivi vinaweza pia kuleta ugonjwa wa moyo.)

I shall give you information and invite you to be part of a research study. I have discussed this study with your parent(s)/guardian and they know we are also asking you for your agreement. You can choose whether or not you want to participate. If you want to participate in the study, your parent(s)/caregiver have to agree. If you do not wish to participate, you do not have to, even if your parents have agreed.

(Nitakupa maelezo na kukualika ujiunge na utafiti huu. Nimeongea na mzazi/mlezi wako na wanajua kuwa ninataka ukabaliano wako pia. Uko na hiari ya kujiunga na wazazi wako pia lazima watoe idhini ya kukubali kwao. Kama hutaki kujihusisha, sio lazima hata kama wazazi wamekubali.)

If you agree to participate, we shall ask you some questions asking you how well you have been and then we shall swipe the back of your throat with some cotton wool on a stick. No harm will come to you when you take part in the study but the throat swab may be uncomfortable.

(Ukikubali kujihusisha, tutakuuliza maswali kuhusu afya yako na tutachukua kipimo kwa koo kutumia pamba kwenye kijiti. Hakuna madhara yoyote ukijihusisha na utafiti huu lakini mapimo yanaweza kuleta usumbufu kidogo.)

No gifts will be given to you if you participate in the study. However, the information you give us might help us know more about those germs that give you sore throat and later, heart disease.

(Hakuna zawadi yoyote itapeanwa kwako ukijiunga na utafiti huu, lakini maelezo tutakayopata kutoka kwako yatasaidia kujua kuhusu vidudu vitakavyokupatia kuumwa na koo na baadaye ugonjwa wa moyo.)

We won't tell anyone you took part in this study and we won't share information about you to anyone who does not work in the study. Information about you will have a number and not your name.

You can discuss anything in this form with your parent(s)/guardian. You can decide whether to participate after you have talked it over. If there are words or things you want me to explain more about, please feel free to ask me at any time.

(Hatutaambia mtu yoyote kama umejihusisha na utafiti huu na hatutapeana majibu yako kwa mtu yoyote ambaye hafanyi kazi na sisi. Maelezo yako hayatumii jina lako na tutatumia nambari badala ya jina. Unaweza kujadiliana na mzazi/mlezi wako. Utaamua baada ya kuongea na wao. Kama kuna maelezo unataka nirudie ama nieleze tena tafadhali niulize wakati wowote.)

Certificate of assent/ Shahada ya idhini:

This research study has been explained to me. I have had a chance to ask questions and I know that should I have more questions; I can ask the doctor. I agree to take part in this study.

(Nimeelezwa kuhusu utafiti huu. Nimepata fursa ya kuuliza maswali na ninafahamu ikiwa niko na maswali mengine nitajibiwa na daktari. Ninakubali kujihusisha na utafiti huu.)

Name of participant: _____ Researcher's name: Dr. Maryanne Murugami

Signature of participant: _____ Researcher's signature: _____

Date: _____ Date: _____

Appendix 4: Rapid Antigen Test Procedure

Materials provided

Detector Strep A™ dipstick, 1 vial extraction Reagent A (2M Sodium Nitrite), 1 vial extraction Reagent B (0.15M Acetic Acid), disposable extraction tubes and sterile swabs, 1 positive control, 1 negative control and an insert with instructions for use.

Test procedure

1. With the extraction tube being held upright, add 4 drops of Reagent A, then 4 drops of Reagent B to the tube. Tap the bottom of the tube to mix.
2. Insert the fresh throat swab specimen into the tube, rotate it 10 times in the tube then let it stand for 1 minute.
3. Once 1 minute is over, press the swab against the tube and squeeze the tube firmly while removing the swab to retain most of the liquid in the tube.
4. Discard the used swab.
5. Place the test strip in the tube and read results in 5 minutes.
6. Once the results recorded, discard the test strip and the tube with its contents.

Results interpretation:

i. **Positive result:** Two distinct red lines, one in the test region and one in the control region.

ii. **Negative result:** One red or pink line in the control region with no apparent red or pink line in the test region.

iii. **Invalid result:** Either no red or pink lines in both the control and test regions, or one red or pink line in the test region.

Appendix 5: KNH-UoN Ethics Research Committee approval letter

UNIVERSITY OF NAIROBI
COLLEGE OF HEALTH SCIENCES
P O BOX 19676 Code 00202
Telegrams: varsity
Tel:(254-020) 2726300 Ext 44355

KNH-UON ERC
Email: uonknh_erc@uonbi.ac.ke
Website: http://www.erc.uonbi.ac.ke
Facebook: https://www.facebook.com/uonknh.erc
Twitter: @UONKNH_ERC https://twitter.com/UONKNH_ERC

KENYATTA NATIONAL HOSPITAL
P O BOX 20723 Code 00202
Tel: 726300-9
Fax: 725272
Telegrams: MEDSUP, Nairobi

Ref: KNH-ERC/A/401

12th November 2020

Dr. Maryanne Wachu Murugami
Reg. No.H58/11209/2018
Dept.of Paediatrics and Child Health
School of Medicine
College of Health Sciences
University of Nairobi

Dear Dr.Murugami

RESEARCH PROPOSAL – PREVALENCE AND FACTORS ASSOCIATED WITH GROUP A STREPTOCOCCAL PHARYNGEAL CARRIAGE AMONG PRIMARY SCHOOL CHILDREN IN BOMET COUNTY (P145/03/2020)

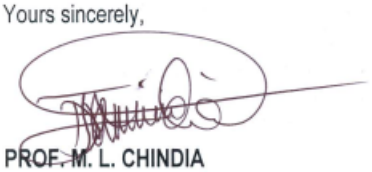
This is to inform you that the KNH- UoN Ethics & Research Committee (KNH- UoN ERC) has reviewed and **approved** your above research proposal. The approval period is 12th November 2020 – 11th November 2021.

This approval is subject to compliance with the following requirements:

a. Only approved documents (informed consents, study instruments, advertising materials etc) will be used.
b. All changes (amendments, deviations, violations etc.) are submitted for review and approval by KNH-UoN ERC before implementation.
c. Death and life threatening problems and serious adverse events (SAEs) or unexpected adverse events whether related or unrelated to the study must be reported to the KNH-UoN ERC within 72 hours of notification.
d. Any changes, anticipated or otherwise that may increase the risks or affect safety or welfare of study participants and others or affect the integrity of the research must be reported to KNH- UoN ERC within 72 hours.
e. Clearance for export of biological specimens must be obtained from KNH- UoN ERC for each batch of shipment.
f. Submission of a request for renewal of approval at least 60 days prior to expiry of the approval period. (*Attach a comprehensive progress report to support the renewal*).
g. Submission of an *executive summary* report within 90 days upon completion of the study. This information will form part of the data base that will be consulted in future when processing related research studies so as to minimize chances of study duplication and/ or plagiarism.

For more details consult the KNH- UoN ERC website**http://www.erc.uonbi.ac.ke**

Yours sincerely,



PROF. M. L. CHINDIA
SECRETARY, KNH-UoN ERC

c.c. The Principal, College of Health Sciences, UoN
The Senior Director, CS, KNH
The Chairperson, KNH- UoN ERC
The Assistant Director, Health Information Dept, KNH
The Dean, School of Medicine, UoN
The Chair, Dept. of Paediatrics and Child Health, UoN
Supervisors: Prof. Christine Yuko Jowi, Dept.of Paediatrics and Child Health, UoN
Dr. Jalemba Aluvaala, Dept. of Paediatrics and Child Health, UoN

Appendix 8: NACOSTI Research Permit

REPUBLIC OF KENYA

NATIONAL COMMISSION FOR SCIENCE,TECHNOLOGY & INNOVATION

Ref No: **190712**

Date of Issue: **06/January/2021**

RESEARCH LICENSE

This is to Certify that Dr.. Maryanne Wachu Murugami of University of Nairobi, has been licensed to conduct research in Bomet on the topic: PREVALENCE AND FACTORS ASSOCIATED WITH GROUP A STREPTOCOCCAL PHARYNGEAL CARRIAGE AMONG PRIMARY SCHOOL CHILDREN IN BOMET COUNTY for the period ending : 06/January/2022.

License No: **NACOSTI/P/21/8341**

190712

Applicant Identification Number

Director General
NATIONAL COMMISSION FOR SCIENCE,TECHNOLOGY & INNOVATION

Verification QR Code

NOTE: This is a computer generated License. To verify the authenticity of this document, Scan the QR Code using QR scanner application.

Appendix 7: Bomet County Ministry of Education approval letter

REPUBLIC OF KENYA
MINISTRY OF EDUCATION
STATE DEPARTMENT OF EARLY LEARNING AND BASIC EDUCATION

Telegrams: "ELIMU",
Telephone: 052-22265
When replying please quote
email:cdebometcounty@gmail.com
Ref/CDE/BMT/ED/AUTH/74/VOL.II/26

COUNTY EDUCATION OFFICE,
BOMET COUNTY,
P.O. BOX 3-20400,
BOMET.

13TH January, 2021

Dr. Maryanne Wachu Murugami
University of Nairobi
P.O Box 19676- 00202
NAIROBI

TO WHOM IT MAY CONCERN

RE: AUTHORITY TO CONDUCT RESEARCH

Reference is made to letter Ref: No NACOSTI/P/21/8341 dated 6th January, 2021 from NACOSTI, requiring the above mentioned person to conduct a research on "***Prevalence and Factors Associated with group A Streptococcal Pharyngeal Carriage among primary school children in Bomet County)***" which is scheduled to be conducted for the period ending 6th January 2022.

The purpose of this letter is to inform you that authority has been granted for him to carry out the study in Bomet County, including learning Institutions among others.

Kindly accord him the assistance he requires.

COUNTY DIRECTOR OF EDUCATION
BOMET
P. O. Box 3-20400, BOMET
Date 13-1-2021

INDIATSI MABALE
COUNTY DIRECTOR OF EDUCATION
BOMET COUNTY.

CC

Director General
NACOSTI
P.O BOX 30623-00100

Appendix 8: Approval letter from Bomet County Commissioner's office

Proceed to conduct the Research, you may share your findings in summary once you conclude
15th July

OFFICE OF THE PRESIDENT
MINISTRY OF INTERIOR AND COORDINATION OF NATIONAL GOVERNMENT

Telegrams: "DISTRICTER", Bomet
Telephone: (052) 22004/22077 Fax 052-22490
When replying please quote

COUNTY COMMISSIONER
P.O BOX 71- 20400
BOMET

REF: EDU.12.1VOL.IV/(35)

13th January, 2021

DCC Bomet East 22/2/2021

The Deputy County Commissioners
BOMET

RE: RESEARCH AUTHORIZATION – DR. MARYANNE WACHU MURUGAMI

The above named person has been authorized to carry out research on **"Prevalence and Factors Associated with Group A Streptococcal Pharyngeal Carriage among Primary School Children ,"** in Bomet County for the period ending 6th January, 2022 by the National Commission for Science, Technology and Innovation vide their letter Ref.No. NACOSTI/P/19/25088/32031dated **31st October, 2020.**

Any assistance accorded would be appreciated.

COUNTY COMMISSIONER
BOMET COUNTY
13 JAN 2021
P. O. Box 71-20400, BOMET

Abdalla S. Mwamzungu
For: County Commissioner
BOMET

Appendix 9: Budget

Category	Remark	Unit	Unit cost	Total (Ksh)
Proposal development	Printing drafts	5	1000	5000
	Proposal copies	9	1000	9000
	ERC fee	1	2000	2000
	NACOSTI fee	1	1000	1000
Data collection	Envelopes	210	10	2100
	Photocopy	1500	3	4500
	Transport	7 days	3000/day	21000
	Research assistant	10 days	1500/ 5 days	3000
Equipment	RADT	11 boxes each with 20 kits	6800	74800
	Gloves	5 boxes	1200	6000
	Masks	2 packs	800/pack of 50s	1600
	Tongue depressors	3 packs	500/pack of 50s	1500
	Apron	10	200	2000
	Face shield	5	200	1000
	Thermometer	1	2000	2000
	Measuring tape for contractors	1	150	150
Data analysis	Statistician	1	30000	30000
Thesis write up	Printing drafts	1	1000	1000
	Printing thesis	4	1000	4000
Contingency fund				10000
Total				181650

Appendix 10: Time frame

Activity	**Estimated time**
Development of Proposal and presentation	January to April 2020
Proposal Submission for ethical review and approval	July 2020
Proposal Submission for NACOSTI review and approval	November 2020
Data Collection	February to March 2021
Data Analysis	March to April 2021
Results Presentation	April 2021
Writing the dissertation	April to May 2021
Submission of the dissertation for internal marking	May 2021
Submission of the dissertation for external marking	July 2021