

**"BACTERAEMIA AND URINARY TRACT
INFECTION COMPLICATING MALARIAL
INFECTION IN CHILDREN ADMITTED AT
KENYATTA NATIONAL HOSPITAL"**

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**A DISSERTATION SUBMITTED IN PART FULFILMENT FOR THE DEGREE
OF MASTER OF MEDICINE IN PEADIATRICS AT THE UNIVERSITY OF
NAIROBI**

BY

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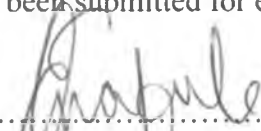
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DEDICATION

This book is dedicated to my beloved father Mr. Isaac Okwara and my mother Mrs. Willbroda Okwara who have inspired and encouraged me in all my endeavors.

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TABLE OF CONTENTS

	Page
ABSTRACT.....	1
1.0 INTRODUCTION AND LITERATURE REVIEW.....	3
2.0 STUDY JUSTIFICATION.....	9
3.0 OBJECTIVES.....	11
3.1 MAIN OBJECTIVE.....	11
3.2 SPECIFIC OBJECTIVES.....	11
4.0 MATERIALS AND METHODS.....	12
4.1 STUDY DESIGN.....	12
4.2 STUDY SITE.....	12
4.3 STUDY POPULATION.....	12
4.4 INCLUSION CRITERIA.....	12
4.4.1 MALARIA CASES.....	12
4.4.2 NON-MALARIA CASES.....	13
4.5 EXCLUSION CRITERIA.....	13
4.6 SAMPLE SIZE.....	14
4.7 PROCEDURES.....	15
4.7.1 PATIENT RECRUITMENT.....	15
4.7.2 SPECIMEN COLLECTION.....	15
4.7.2.1 BLOOD SPECIMEN COLLECTION.....	15
4.7.2.2 URINE SPECIMEN COLLECTION.....	16
5.0 LABORATORY PROTOCOLS.....	17
5.1 PERIPHERAL BLOOD FILMS.....	17
5.2 BLOOD CULTURE METHOD.....	17
5.3 URINE CULTURE METHOD.....	18
6.0 DATA MANAGEMENT.....	19
7.0 ETHICAL CONSIDERATIONS.....	19
8.0 RESULTS.....	20
8.1 GENERAL DESCRIPTION OF THE STUDY POPULATION.....	20

8.2 PREVALENCE OF BACTERAEEMIA.....	24
8.3 PREVALENCE OF U.T.I.....	25
8.4 THE OVERALL ISOLATION RATES FROM BLOOD AND URINE OF THE STUDY POPULATION.....	26
8.5 AETIOLOGICAL ORGANISMS ISOLATED.....	27
8.6 THE EFFECT OF DENSITY OF MALARIA PARASITAEMIA ON ISOLATION RATES IN BLOOD AND URINE.....	30
8.7 THE ASSOCIATION BETWEEN CO-VARIATES AND ISOLATION RATES IN BLOOD AND URINE.....	31
9.0 DISCUSSION.....	33
10.0 CONCLUSIONS.....	42
11.0 RECOMMENDATIONS.....	43
REFERENCES.....	44
APPENDIX I.....	50
APPENDIX II.....	53
APPENDIX III.....	54

LIST OF TABLES.

TABLE 1: Baseline and socio- demographic characteristics of the study population.....	22
TABLE 2: Blood culture isolation rates in children with and without malaria.....	24
TABLE 3: Urine culture isolation rates in children with and without malaria.	25
TABLE 4: A comparison of the specific organisms isolated from blood and urine in children with and without malaria.....	27
TABLE 5: A comparison of isolation rates of gram-positive and gram-negative organisms in children with and without malaria.....	29
TABLE 6: Variation of isolation rates in blood and urine with density of malaria parasitaemia.....	30

LIST OF FIGURES

FIGURE 1: Age distribution of the study population.....	21
FIGURE 2: The overall isolation rates in children with and without malaria.....	26

LIST OF ABBREVIATIONS

K.N.H	- Kenyatta National Hospital
U.T.I	- Urinary tract infection
ml	- Milliliter
SPSS	- Statistical Package for Social Sciences
⁰ C	- Degrees centigrade
Spp	- Species
Staph	- Staphylococcus
Strep	- Streptococcus
E.coli	- <i>Escherichia coli</i>
MSSU	- Mid-stream specimen of urine
WHO	- World Health Organisation
H.I.V	- Human Immune-deficiency Virus
Ig A	- Immunoglobulin A
CI	- Confidence interval
AIDS	- Acquired immune deficiency syndrome
ARC	- AIDS related Complex
CD 4	- Cluster designation

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DEFINITIONS

Bacteraemia – presence of bacteria in blood.

Bacteriuria - presence of bacteria in urine.

Malaria - presence of asexual forms of malaria parasites in blood.

Malnutrition – A weight below the 80th percentile of the Harvard standard

ABSTRACT

Background: Morbidity and mortality from malaria remains high, even with appropriate treatment. Complicating pathologies may contribute to this state. There is laboratory evidence of altered immune function at different stages of the malarial illness. Various studies have reported the occurrence of bacterial infections in various sites in children with severe malaria. Given that peripheral parasitaemia is not a reliable measure of total parasite load, and therefore does not correspond to severity of the illness, the risk for invasive bacterial disease may be present even in non-severe forms of malaria. Studies to demonstrate the magnitude of bacterial co-morbidity in non-severe forms of malaria, especially in non-endemic areas, are sparse and non-conclusive. This study aims at defining the association between bacteraemia, U.T.I and malarial infection in a non-endemic area.

Objective: To determine if malaria parasitaemia is associated with an increased risk of occurrence of bacteraemia and urinary tract infections.

Study site: Kenyatta National Hospital, a teaching and referral hospital in Nairobi, Kenya.

Design: A cross-sectional survey comparing two groups.

Methodology: Study subjects were children aged between 3 months and 12 years admitted with an acute febrile illness, but no obvious focus of infection. One group of children had fever and a positive malaria slide whereas the comparison group had fever with a negative slide for malaria. Children with diagnosed septic conditions, known chronic illnesses or severe malnutrition were excluded. The parent or guardian

was interviewed using standard questionnaire that collected information on their age, sex, and socio-demographic characteristics. The Child's nutrition status was assessed and classified according to the Wellcome classification. A sample of blood was drawn, and a specimen of urine obtained from each child. These were cultured on appropriate culture media and the positive isolates identified.

Results: A total of 264 children were recruited in the months of January to March 2001. Of these, 158 had a positive slide, and 106 a negative slide for malaria. The male: female ratio in both groups was 3:2. The two groups were of comparable age profile, nutrition status, and socio-demographic characteristics except room density, a measure of crowding. The prevalence of bacteraemia in those with malaria was 11.4%, which was not significantly different from 13.2% found in those with a negative slide (P value = 0.66, OR = 0.85, 95% CI = 0.40 – 1.78). Of those with malaria, 13.3% had 'significant bacteriuria' compared to 16.0% in those without malaria. This difference was not significant (P value = 0.53, OR = 0.80, 95% CI = 0.40 – 1.60).

Conclusions and recommendations: Children admitted with fever and a positive slide for malaria have a similar risk of having concurrent bacteraemia and/or bacteriuria as those admitted with fever and a negative malaria slide. Therefore, one should have a high index of suspicion for these infections when faced with a child with fever and no focus of infection, regardless of the slide report. However, the presence of a positive slide does not put the child at a higher risk.

1.0 INTRODUCTION AND LITERATURE REVIEW

Infections and infection related conditions account for 75% all hospital admissions in Africa. Malaria is the single most important infectious disease both in terms of admission and as a cause of death ¹. An estimated 300 - 500 million cases are reported annually, 90% of which are African children below five years ^{2,3}. In Kenya, 25 - 30% of all out-patient consultations are due to malaria, and it is the cause of approximately 26,000 deaths in children below five years annually, which amounts to 72 deaths per day ⁴. Of major concern is that despite good understanding of disease mechanisms in malaria, case fatality from treated severe malaria remains high (5 - 15%) ^{2,5,6}. Some of the contributors to this high mortality include; late presentation to the health facilities, inadequate and/or deteriorating health systems, emergence of multiple drug resistance by the parasite, and possible complicating pathologies ^{2,3,7-9}.

Recently, there has been a resurgence of malaria to previously non -endemic areas¹⁰. This has been attributed to changing climatic and environmental factors. For example, Nairobi, the capital city of Kenya, is a high altitude area that has previously been considered malaria free. However, recent studies indicate that hypoendemic transmission does occur in Nairobi, with population parasite rates of about 6.2 %, and malaria cases are reported throughout the year due to constant in-migration of people from endemic areas ¹¹ The large population of non-immune children in Nairobi are most susceptible, and once infected tend to present with severe forms of malaria ¹².

Except for a few cases of imported malaria, asymptomatic parasitaemia is unlikely in children resident in Nairobi.

Malaria remains a leading cause of morbidity and mortality in Nairobi¹¹. Statistics from Kenyatta National Hospital Records Department for the year 2000 show that 1,592 cases of malaria were diagnosed in children aged 0-13 years. Of these, a total of 132 patients died giving a case fatality rate of 8.3 %¹³. Some cases were diagnosed clinically and some were proven by blood slide examinations though the exact proportions were not evident from the data provided.

Although there are various methods of diagnosing malaria, demonstration of parasites in blood is taken as the gold standard. The thick film is more sensitive than the thin film. Its sensitivity is influenced by among others, the staining methods, level of parasitaemia, competency of the reader, and number of fields examined. An average of less than 4 parasites/ mm³ is likely to be missed even by an experienced microscopist. Increasing the number of fields scanned from 200 (6 minutes) to 600 (19 minutes) raises the sensitivity from 60 to 80%⁶⁴. If the initial film is negative, further films should be examined every few hours until the diagnosis has been established or reasonably excluded (up to a minimum of 6)⁶⁵. Demonstration of parasites in blood confirms infection.

However, diagnosis of malaria in children is difficult even with good laboratory support. This is partly due to varied case definitions of a clinical episode of malaria in

different geographic areas, based on variations in malaria specific immunity in different populations. In holoendemic transmission areas, asymptomatic parasitaemia is a common finding. Therefore, the presence of parasites in blood does not always imply clinical disease. A child may be parasitaemic and well, or parasitaemic but sick due to a different condition (e.g. bacteraemia, meningitis etc) ¹⁴. Although some investigators have defined a case as fever with a high parasite density, it is not possible to provide a uniform case definition under every setting since the etiological fractions of fever and parasite density will be a function of the risks of super infection and immunity by age^{9,15}. However, studies have shown that peripheral parasitaemia is not a reliable measure of total (circulating plus sequestered) parasite load¹⁶. In addition, it has also been shown that the correlation between the clinical severity and the level of parasitaemia is weak; well children may have high peripheral parasitaemia, and occasional cases of cerebral malaria may be slide negative ¹⁷. This implies that a positive slide has to be interpreted in context with the clinical condition of the child. However, a child who is sick enough to require admission is more likely to progress to severe disease and therefore more likely to die.

There has been increasing realization that many children present to hospital with more than one condition, and that there are overlaps in the signs and symptoms of several common infectious diseases. For example, many of the clinical features of malaria closely resemble those of other febrile illnesses, such as sepsis¹⁸⁻²⁰. Respiratory and gastrointestinal signs common in malaria patients are often attributed to the malaria parasite itself ^{19,20}. Likewise, localized infections such as in the urinary tract, or in the

central nervous system may present with systemic manifestations, which mimic malaria²¹. The distinction becomes more difficult in the younger children, a population predisposed to both malaria and bacterial infections²².

Several studies have demonstrated specific disturbances in the immune function associated with the *P. falciparum* malaria. *In vitro* studies have demonstrated impaired opsonization and phagocyte killing by macrophages, following ingestion of parasite-derived haemozoin (malaria pigment) in red blood cells^{23,24}. Alterations in cellular immune function have also been reported in active malaria infections. Gilbreath et al demonstrated deficient spontaneous cell-mediated cytotoxicity in patients with low-level parasitaemia²⁵. They also demonstrated that patients with malaria have a reduction in circulating T-Lymphocyte numbers, presence of antilymphocyte antibodies in their sera, and a decrease in suppressor T-cell generating capability²⁵. The proliferative response of T-cell has been shown to be impaired, resulting in delayed cutaneous reactions, especially to soluble antigens^{26,27,29}. Humoral immunity has also been shown to be impaired. Greenwood et al demonstrated selective immune suppression of body response to the tetanus toxoid and to the “O” antigen of salmonella in all malaria patients, but more so in severe malaria^{28,29}. Activation of complement by the alternative pathway has been reported in children with acute *Plasmodium falciparum* malaria³⁰. However, the clinical significance of these changes has not been defined.

Bacterial infections consisting predominantly of Gram-negative organisms have been documented in children with severe malaria^{31,32}. Phillips et al documented bacterial infections, 9% of which were bacteraemia, in 40% of 169 patients over 5 years old with cerebral malaria³³. In a study of 50 cerebral malaria cases in Nigeria, 8 (16%) had positive blood cultures³¹. Local studies by Berkley et al on children with severe malaria from an endemic area found 7.8% to have bacteraemia³⁴. Mabe et al reported a high frequency of recent malarial infection in 30 out of the 71(42 %) Gambian children treated for non-typhoid salmonella septicaemia. However, the association was with low-level parasitaemia, anaemia and the presence of intraleucocyte haemozoin, rather than with acute severe malaria³⁵. In a study to establish the cause of fever in acutely febrile Nigerian preschoolers without localizing signs, Akpede et al found the incidence of bacteraemia in children who had malaria to be 9.6%, which was comparable to that found in those without malaria (12.2%). They found similar rates of isolation at the different levels of malaria parasitaemia³⁶. However, it has been difficult ascribing a role to the presence of malaria parasitaemia for these infections. The children with bacteremia usually have no obvious focus of infection, but those with double infections (of malaria and other bacterial infection) experience greater morbidity^{32,33}.

Clinicians manning paediatric health care units often find themselves in a dilemma when faced with children presenting with fever without any obvious focus of infection. The W.H.O integrated management of childhood illnesses recommends management with an antimalarial and an antimicrobial agent any child from a low

risk malaria area with danger signs (inability to drink or breast feed, vomiting everything, convulsions, lethargy or unconscious) ³⁷. Most Children requiring admission usually have one or more of these signs. Studies, mainly done in the West, have shown that approximately 3.9% of these children have occult bacteraemia ^{22,38}. However, Urinary tract infection is the most common bacterial infection found in these children, with prevalence rates ranging from 4.7 –7.5% in the developed countries, to 22.2% in local studies ³⁹⁻⁴¹.

Malnutrition and H.I.V infection are associated with an increased risk of community acquired bacterial infections. The increasing frequency of malnutrition and the H.I.V infection amongst children resident in malaria endemic areas is expected to be associated with increase in bacterial infections ^{17,42-44}. This implies that childhood fevers from these areas will often have mixed etiologies ^{45,46}.

It remains unclear whether bacterial infections in children with malaria are merely coincidental, by virtue of the child having other risk factors, or can be attributed to the malarial infection. However, in their presence, greater morbidity and mortality is experienced ^{32, 33,47}. Reducing the morbid and fatal consequences of *P.falciparum* infection, rather than attempts at parasite eradication, represents the most realistic intervention for much of Sub-Saharan Africa ⁴. A description of the relationship between malaria, bacteraemia and U.T.I will go a long way in providing better understanding of this infection and therefore help improve the management of these children.

2.0 STUDY JUSTIFICATION

Mortality and morbidity from malaria remains very high, especially from severe malaria, even with adequate treatment. Various studies done in endemic areas have reported isolation of pathogenic bacteria from various sites in children with severe malaria.^{16, 18, 20, 31-36} However, it has been shown that peripheral parasitaemia does not reflect the total parasite load¹⁶, and therefore does not predict severity of malarial illness¹⁷. It is possible that the risk of bacterial infections is present even with low-level parasitaemia.

There is anecdotal evidence of routine prescription of antimicrobial agents to children admitted with malaria at K.N.H. This is partly due to difficulties in quick establishment of presence or absence of bacterial infections, and because the W.H.O 'Integrated management of childhood illnesses' guidelines recommend management of any child from a low risk malaria area with danger signs (inability to drink or breast feed, vomiting everything, convulsions, lethargy or unconscious) with an antimalarial and an antimicrobial agent. Studies to demonstrate the prevalence of bacterial infection in children with non-severe forms of malaria, especially in non-endemic areas are sparse and non-conclusive. If significant risk of bacterial infections is present, appropriate treatment would reduce morbidity, and mortality, shortens hospital stay, and hence result in economic and time saving. However, if the converse is true, and there is no significant increase in risk in mild and moderate malaria, this practice is uneconomical and subjects the child to unnecessary complications.

In view of this, and scientific evidence of impaired immunity in both severe²³⁻³⁰ and non-severe forms of malaria^{25, 28-30}, it is important to know the prevalence of bacteraemia and U.T.I in children with mild, moderate, and severe forms of malaria.

However, given the increasing incidence of HIV and malnutrition in our set-up, the prevalence of community acquired bacterial infections presenting with fever are also on the rise. In order to establish what proportion of the positive isolates are attributable to the malarial infection, or to the other risk factors, a comparison group of children with fever and no focus of infection from the same population would be imperative.

This study aims at defining the association between malaria, bacteraemia and U.T.I in a non-endemic area, where the proportion of childhood fevers attributable to malaria is lower. The characterization of such a relationship will provide important information, and guidelines for proper management of children admitted with fever and no obvious focus of infection. This is likely to improve the outcome.

3.0 OBJECTIVES

3.1 MAIN OBJECTIVE

To determine if malaria parasitaemia is associated with an increased risk of occurrence of bacteraemia and urinary tract infections in children admitted to Kenyatta National Hospital.

3.2 SPECIFIC OBJECTIVES

1. To compare the prevalence of bacteraemia in children admitted with malaria, and those without malaria.
2. To compare the prevalence of U.T.I in children admitted with malaria, and those without malaria.

4. MATERIALS AND METHODS

4.1 STUDY DESIGN

The study is a hospital based cross sectional survey, in which two groups of children with and without the exposure of interest (malaria parasitaemia) are investigated for presence of the outcome (bacteraemia and/or bacteriuria).

4.2 STUDY SITE

The study was carried out at K.N.H, the national tertiary referral hospital for Kenya, which also serves as a first level hospital for Nairobi and its environs. An average of 40 children are admitted daily to the five general paediatric wards.

4.3 STUDY POPULATION

This was drawn from children aged between 1 month and 12 years exclusively, admitted to the general paediatric wards at K.N.H with an acute febrile illness.

4.4 INCLUSION CRITERIA

4.4.1 MALARIA CASES

A malaria case was defined as any child admitted with fever, and had no obvious focus of bacterial or viral infection, and in whom asexual forms of malaria parasites were demonstrated in blood.

For purposes of this study, fever with no obvious focus is defined as: an axillary temperature of $\geq 37.5^{\circ}\text{C}$, in an otherwise normal child whose clinical findings reveal no obvious infective focus, with the exception of a non-bloody diarrhoea, or tachypnoea. Any child with a positive slide was regarded as having malaria.

4.4.2 NON-MALARIA CASES.

This was defined as any child admitted during the study period with fever and no obvious focus of bacterial or viral infection and who had a negative slide for malaria parasites. No matching was done for cases.

For the purposes of this study, any child with a negative slide was regarded as not having malaria.

4.5 EXCLUSION CRITERIA

Children with the following conditions were excluded from the study:

1. Previously diagnosed or suspected chronic illnesses.
2. Diagnosed septic conditions such as meningitis, pneumonia, abscesses, otitis media, or tonsillitis.
3. Clinical A.I.D.S (Acquired immune deficiency syndrome).
4. Severe malnutrition.
5. Failure of the parent / guardian to consent.

4.6 SAMPLE SIZE

This was obtained using the EPI INFO Version 6 (WHO and CDC approved)

programme. The assumptions made were as follows:

1. 95% confidence limits ($1-\alpha$)
2. 80% power of the study ($1-\beta$) in a cross sectional survey where the ratio of exposed to the non-exposed was 1: 1
3. The expected frequency of bacteraemia in the non- malaria group was 3% as found by Teele D.W. et al. as the prevalence of bacteraemia in children under 2 years³⁸.
4. The expected frequency of bacteraemia in the malaria group was 15% as found in African studies, which reported prevalence of between 7.8% and 16%^{31, 34, 36}. 15% was considered a reasonable estimate given lack of similar studies in non-severe malaria and in non-endemic areas.
5. Odds Ratio = 5.71

The minimum sample size calculated was 104 malaria cases and 104 non-malaria cases.

The lower estimated prevalence of bacteraemia was used rather than that of U.T.I in the calculation, as this would provide an adequate sample to give the study enough power to determine the prevalence of both bacteraemia and of U.T.I. A total of 158 children with malaria and 106 without malaria were however recruited.

4.7 PROCEDURES

4.7.1 PATIENT RECRUITMENT

Recruitment was done from January to March 2001. The investigator visited the admitting wards on weekdays between 8a.m and 10 p.m. All the eligible children were identified with the assistance of the primary ward doctors within 1 hour of admission. A detailed semi-structured questionnaire (Appendix II) was then administered to the parent or guardian where the following information was sought: socio-demography, relevant medical history and nutritional state assessment.

4.7.2 SPECIMEN COLLECTION

4.7.2.1 BLOOD SPECIMEN COLLECTION

The skin at the site of venepuncture was disinfected by swabbing consecutively with 3 different surgical spirit swabs, and then iodine applied. It was then punctured with a gauge 23 hypodermic needle and approximately 1.1mls of blood drawn into a 5ml plastic syringe. While observing strict aseptic technique, a new sterile disposable needle was used to inoculate 1ml of blood into a blood culture bottle containing 5mls of liquid medium. 'Brain heart infusion broth' was the culture medium used in this study. The samples were transported to the hospital's microbiology laboratory within 1 hour of collection. Samples taken in the night were refrigerated at temperatures below 8⁰ C until the following morning.

A thick blood slide was prepared at the bedside using the remaining 0.1mls of blood. This was air dried before transportation to the hospital's haematology laboratory.

4.7.2.2 URINE SPECIMEN COLLECTION

A clean catch midstream specimen of urine (MSSU) was the method used for urine collection in all the children. This was the preferred method of urine collection as it is the least invasive and therefore acceptable to most mothers. In order to eliminate any differences in yield rates arising from method of urine collection, MSSU was obtained in all the children.

In toilet- trained children who could follow instructions, the child was asked to pass the first urine after admission into a wide mouthed sterile bottle. In the younger children, a sterile urine collector was applied to the perineum after swabbing the perineum with savlon swabs. This was left *in-situ* until the child passed urine. The urine was transferred into a sterile urine bottle avoiding any contamination. All samples were transported to the hospital's microbiology laboratory within 1 hour of collection. Samples taken in the night were refrigerated at temperatures below 8^o C until the following morning.

5.0 LABORATORY PROTOCOLS

5.1 PERIPHERAL BLOOD FILMS

The thick blood films were stained using Field's stains before being examined for asexual forms of *P. falciparum*. The thick film was preferred to the thin film because of its high sensitivity. Minimum of 200 high power fields were examined, before a slide was declared negative.

All the slides were read by one laboratory technician throughout the study period. At the end of the study, all the slides were sent for a second slide reading by a different laboratory technician at the same laboratory. This was done to provide a quality control of the first slide reading. Both technicians were experts in malaria parasitology with at least ten years experience. Where their findings were not in agreement, the slide was picked out by the investigator and given to a third slide reader who was a haematologist, and who was aware of the conflicting results, and who's verdict was taken as final.

A definite diagnosis of malaria was established on finding malaria parasites in blood.

5.2 BLOOD CULTURE METHOD

All culture bottles were incubated at 35- 37°C for 48 hours. The bottles were inspected daily for evidence of microbial growth. Growth was indicated by a floccular deposit on top of the blood layer, turbidity, haemolysis, coagulation of the broth, a surface pellicle, production of gas or formation of granules as in the case of

staphylococci. Whenever there was evidence of growth, it was subcultured on 5% sheep blood agar, chocolate agar and MacConkey's media and incubated at 35- 37⁰C for a further 24 hours. The plates were examined the following day for any evidence of growth. In those with growth, the isolates were processed and identified by standard bacteriological techniques like gram stain morphology, catalase and oxidase tests, and other biochemical tests when indicated.

5.3 URINE CULTURE METHOD

A platinum wire loop calibrated to deliver 0.001 ml of urine was used to inoculate uncentrifuged urine onto Cystein-Lactose- electrolyte deficient (CLED) agar and incubated at 37⁰C for 24 hours. Colony count was done after 24 hours to determine significant bacteriuria. This depended on whether the child had previously been on antibiotics or not. Presence of Urinary tract infection was considered when there was:

- a. Isolation of more than 10⁵ microorganisms / ml of urine from any patient.
- b. A pure colony growth of 10³ microorganisms / ml of urine isolated from a patient who was already on antibiotics.

Mixed growth required a repeat sampling of the urine. The respective organisms were processed and identified by standard bacteriological techniques like gram stain morphology, catalase and oxidase tests, and other biochemical tests when indicated.

6.0 DATA MANAGEMENT

- Data was entered daily in a computer using Statistical packages for Social Sciences (SPSS) software.
- Analysis was performed at the end of the study using SPSS. Prevalence of bacteraemia and U.T.I were determined amongst cases and controls.
- Prevalence between cases and controls was compared using Mann-Whitney test for continuous variables and Chi-square (or Fisher's exact test where relevant) for dichotomous or categorical variables.
- Results are presented in bar graphs and tables.

7.0 ETHICAL CONSIDERATIONS

Approval was sought from the K.N.H ethical and research committee (KNH-ERC) before embarking on the study. Parents/guardians of all eligible children were given a full explanation of the study, and a verbal consent sought for inclusion into the study. Children whose parents declined to give consent were excluded.

Clinical management of these patients was the responsibility of the attending clinician. All patients' reports were treated confidentially, but were made available to the patients' primary ward doctors, for the patients' daily management. All children were managed according to the accepted standard practice, and no interference was made in the patients' day-to-day management.

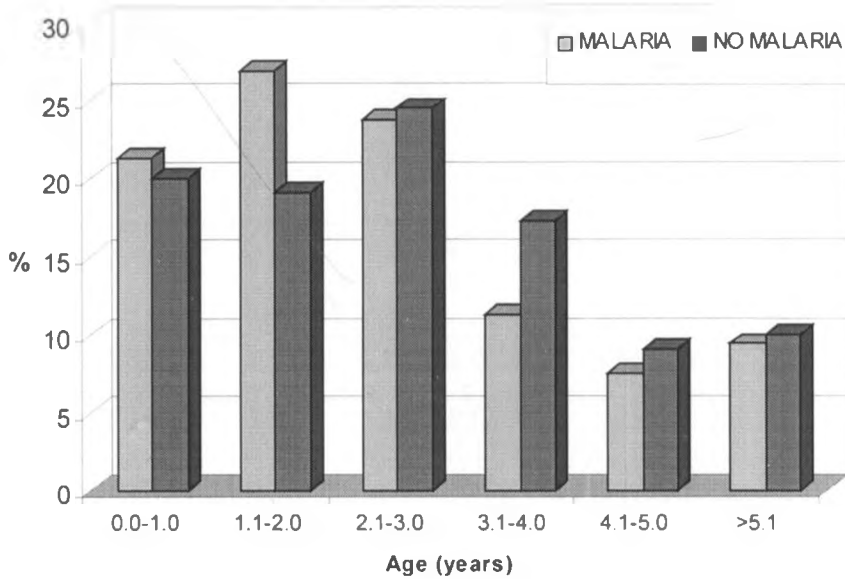
8.0 RESULTS

8.1 GENERAL DESCRIPTION OF THE STUDY POPULATION

A total number of 264 children were recruited into the study between January and March 2001. The first technician found 160 slides to be smear positive for malaria parasites whereas the second found 149 of the slides to be smear-positive. The 11 slides that were conflicting were referred to the third slide reader whose decision was considered final. Two of the slides read by the first technician were reported to be artifacts and were therefore regarded as negative. The remaining 9 slides were reported as scanty parasitaemia.

A total of 158 children had a positive slide for malaria and 106 had a negative slide. The median age of the malaria cases was 2.3 years (range 3 months to 11 years), and that of the non- malaria cases was 2.5 years (range 6 months to 12 years). Most of the children recruited were aged below 3 years, 113 / 158 (71.5%) with malaria, versus 66 / 106 (62.3%) without malaria. This reflects the age distribution of population of children admitted to the paediatric wards. The age distribution of the population studied is presented in figure 1. The male: female ratio in both the malaria and non-malaria groups was 3: 2.

FIGURE 1: AGE DISTRIBUTION OF THE STUDY POPULATION



We compared the baseline and socio-demographic characteristics of the groups in order to assess the suitability of the non-malaria cases as a good match for the malaria cases. The characteristic assessed included age, sex, nutritional status, area of residence, room density, the type of wall their house was made of, mother's level of education, and previous use of antimalarial and antimicrobial agents. The comparison of these characteristics in the study patients is presented in table 1. The malaria cases were similar to the non-malaria cases in all the characteristics assessed except room density. Room density was used as a measure of crowding. This was calculated using the formula:

$$\text{Room density} = \frac{\text{Number of people in the house}}{\text{Number of rooms in the house}}$$

TABLE 1: BASELINE AND SOCIO-DEMOGRAPHIC CHARACTERISTICS OF THE STUDY POPULATION.

VARIABLE		MALARIA N= 158 No. (%)	NO MALARIA N = 106 No. (%)	P VALUE OR (95% CI)
MEAN AGE (years)		2.8	3.1	0.20
SEX	Male	98 (62.0)	58 (54.7)	0.24 0.74 (0.45 - 1.22)
	Female	60 (38.0)	48 (45.3)	
NUTRITION STATUS	Good nutrition	130 (82.3)	83 (78.3)	0.42 0.78 (0.42 – 1.44)
	Malnourished	28 (17.7)	23 (21.7)	
RESIDENCE	Low	123 (77.8)	78 (73.6)	0.43 0.79 (0.45 – 1.41)
	Medium	35 (22.2)	28 (26.4)	
ROOM DENSITY	≤4	125 (79.1)	75 (70.8)	0.02 0.64 (0.36 – 1.13)
	>4	33 (20.9)	31 (29.2)	
TYPE OF WALL	Stone	118 (74.7)	83 (78.3)	0.50 1.22 (0.68 – 2.20)
	Others	40 (25.3)	23 (21.7)	
MOTHER'S EDUCATION	≤ Primary	91 (57.6)	48 (45.3)	0.06 0.61 (0.37 – 1.00)
	≥Secondary	67 (42.4)	58 (54.7)	
ANTIMALARIAL USE	Yes	34 (22.7)	18 (18.0)	0.37 0.75 (0.40 – 1.41)
	No	116 (77.3)	82 (82.0)	
ANTIMICROBIAL USE	Yes	37 (25.9)	16 (16.5)	0.09 0.57 (0.30 – 1.10)
	No	106 (74.1)	81 (83.5)	

Majority of the study subjects, 82.3% with malaria and 78.3 without malaria, were of good nutrition status. Only 30 (18.7%) of malaria cases and 27 (24.5%) of the non-malaria cases were underweight (weight between 60th and 80th percentile of the Harvard standard and without oedema). Of the malaria cases, 74.5% resided in stone walled houses, compared to 78.3% of those without malaria. Most of the children studied (77.8% and 73.6% for malaria and non-malaria cases respectively) resided in the low- income areas of the city.

Among the malaria cases, 37 (25.9%) and 16 (16.5%) of the non-malaria cases had been on antimicrobial therapy before recruitment into the study. This was based on evidence from a health record card or the mother showing the bottle containing the drug used. Likewise, 18 (18%) of those without malaria parasitaemia had used antimalarial drugs in the preceding week, compared to 34 (22.7%) of those with malaria. These differences were however not statistically significant (see table 1).

8.2 PREVALENCE OF BACTERAEMIA.

All the children recruited had blood cultures done. There were 26 isolates from blood cultures of the malaria cases, of which 2 were diphtheroid spp, and 6 coagulase-negative staph, which were considered contaminants. There were 22 isolates from blood cultures of the non-malaria group, of which 2 were micrococcus, 1 diphtheroid spp, and 5 coagulase-negative staph, which were considered contaminants. Thus, pathogenic bacteria were grown from the blood cultures of 18 (11.4%) out of the 158 children with malaria, compared to 14 (13.2%) out of the 106 children without malaria. This difference was however not shown to be statistically significant (P value = 0.66, OR= 0.85, 95% CI = 0.40 – 1.78). The isolation rates in the blood of the study population are presented in table 2.

TABLE 2: BLOOD CULTURE ISOLATION RATES IN CHILDREN WITH AND WITHOUT MALARIA.

	BACTERAEEMIA No. (%)	NO BACTERAEEMIA No. (%)	TOTAL No. (%)
MALARIA	18 (11.4)	140 (88.6)	158(100.0)
NO MALARIA	14 (13.2)	92 (86.8)	106(100.0)

P value = 0.66

There was no difference in blood isolation rates between the sexes in both the malaria group (P values = 1. 00, OR = 1.05, 95% CI = 0.381 – 2.86) and in the non-malaria group (P value = 0.40, OR = 1.73, 95% CI = 0. 56 – 5.40).

8.3 PREVALENCE OF U.T.I

Significant bacteriuria was found in 21/ 158 (13.3%) of the malaria cases, and 17 / 106 (16.0%) of the non-malaria. This difference was not however statistically significant (P value = 0.53, OR = 0.80, 95% CI = 0.40 –1.60). The urine isolation rates in the study population are shown in table 3.

TABLE 3: URINE CULTURE ISOLATION RATES IN CHILDREN WITH AND WITHOUT MALARIA.

	U.T.I No. (%)	NO U.T.I No. (%)	TOTAL No. (%)
MALARIA	21 (13.3)	137 (86.7)	158(100)
NO MALARIA	17 (16.0)	89 (84.0)	106(100)

P value = 0.53

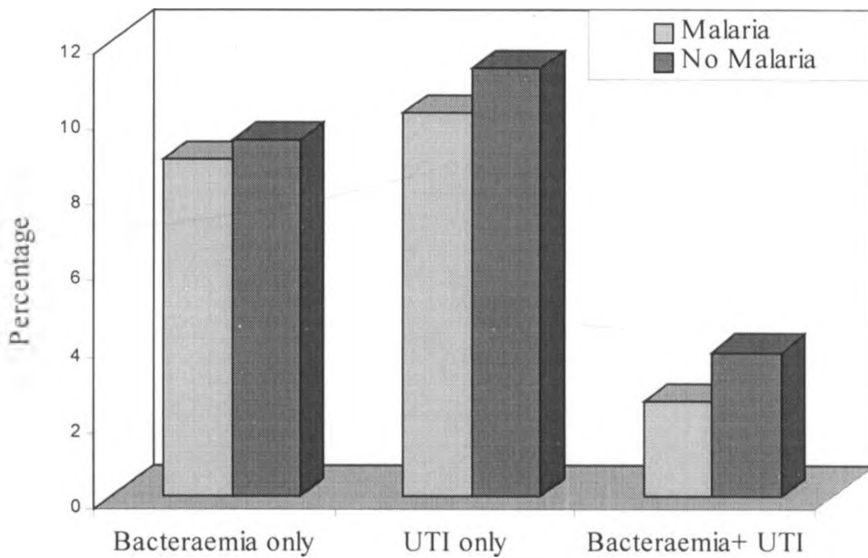
Among the malaria cases, 52% of those with positive isolates were males and 48% were females, whereas in the controls, 47% were males and 52% females.

However, the difference in urine isolation rates between the sexes was not significant in both the malaria group (P values = 0.34, OR = 1.58, 95% CI = 0.63 – 3.97) and in the non-malaria group (P value = 0.11, OR = 2.58, 95% CI = 0.88 – 7.59).

8.4 THE OVERALL ISOLATION RATES FROM BLOOD AND URINE OF THE STUDY POPULATION

Out of the 158 children with malaria, 35 (22.2 %) had pathogenic bacteria isolated from either blood or urine, compared to 27(25.5%) out of the 106 without malaria. Four children from each of the groups had isolates in both blood and urine. Therefore, the rate of dual isolation was 2.5% in the malaria cases and 3.8% in non-malaria. All the children with both infections were less than 3 years old. Amongst the children with both infections, 2 with malaria, and 3 without malaria had the same organism isolated from both blood and urine. The overall rates of isolation are as presented in figure 2.

FIGURE 2: THE OVERALL ISOLATION RATES FROM BLOOD AND URINE IN CHILDREN WITH AND WITHOUT MALARIA.



8.5 AETIOLOGICAL ORGANISMS ISOLATED

TABLE 4: A COMPARISON OF THE SPECIFIC ORGANISMS ISOLATED FROM BLOOD AND URINE OF CHILDREN WITH AND WITHOUT MALARIA.

ORGANISM	BACTERAEMIA		U.T.I	
	Malaria No.	No malaria No.	Malaria No.	No malaria No.
Staph aureus	3	1	-	-
Coagulase negative staph	6	5	2	3
Strep. Pneumonie	-	1	-	-
Enterococcus	-	4	1	1
Acinetobacter	2	1	-	-
Citrobacter	3	2	4	2
Proteus	-	-	-	1
Klebsiella	-	1	1	3
E. coli	1	-	12	6
Pseudomonas	1	-	-	1
Salmonella typhi	1	1	-	-
Salmonella typhimurim	7	3	-	-
Candida albicans	-	-	1	-
TOTALS	24	19	21	17

The aetiological organisms isolated in the blood and urine of the study patients is presented in table 4. *Salmonella typhimurium* was the commonest blood isolate among the malaria cases, identified in 7 /18 (38.9%) of the pathogenic isolates, while Enterococcus was the commonest pathogenic blood isolate in the non-malaria group, comprising 4 /14 (28.6%) of the isolates. *E. coli* was the most frequent isolate in urine for both the malaria 12 (57.1%), and the non-malaria 6 (35.3%) groups. The organisms isolated were further grouped into those that were gram-positive or gram-negative. This was done because the numbers of children grouped by specific organisms were too few for any meaningful analysis to be done, and also because this grouping had more meaningful clinical application in terms of choosing the most suitable antimicrobial therapy. Although there were more gram-negative organisms isolated in both blood and urine of children with malaria compared to those without malaria, the differences were not statistically significant. The sub-analysis of type of organisms isolated is shown in table 5.

TABLE 5: A COMPARISON OF ISOLATION RATES OF GRAM- POSITIVE VERSUS GRAM- NEGATIVE ORGANISMS IN MALARIA AND NON- MALARIA GROUPS.

i. Blood isolates.

	BLOOD	
	Gram positive No. (%)	Gram negative No. (%)
MALARIA (N = 18)	3(16.7)	15(83.3)
NO MALARIA (N = 14)	5(35.7)	9(64.3)

P value = 0.62, OR = 1.20, 95% CI = 0.17 – 8.38.

ii. Urine isolates.

	URINE	
	Gram positive No. (%)	Gram negative No. (%)
MALARIA (N = 21)	3 (14.3)	18 (85.7)
NO MALARIA (N = 17)	4 (23.5)	13 (76.5)

P value = 0.40, OR = 0.49, 95% CI = 0.07 – 3.34.

8.6 THE EFFECT OF DENSITY OF MALARIA PARASITAEMIA ON ISOLATION RATES IN BLOOD AND URINE.

We compared the rates of positive isolates at the different levels of malaria parasitaemia. The prevalence of bacteraemia and significant bacteriuria did not appear to be related to the degree of malaria parasitaemia. However, no meaningful analysis was possible because our study was not powered to do such stratified analysis. The isolation rates at different levels of malaria parasitaemia are presented in table 6.

TABLE 6: VARIATION OF ISOLATION RATES IN BLOOD AND URINE WITH DENSITY OF MALARIA PARASITAEMIA.

MALARIA PARASITES	BACTERAEMIA No. (row%)	U.T.I No. (row%)
+ (N =32)	4 (12.5)	4 (12.5)
++ (N = 62)	5 (8.1)	9 (14.5)
+++ (N =64)	9 (14.0)	8 (12.5)
TOTAL (N = 158)	18 (11.4)	21(13.3)

Key:

+ = 1 - 20 parasites/ 100 WBCs.

++ = 21- 50 parasites/100 WBCs.

+++ = > 50 parasites/100 WBCs.

8.7 ASSOCIATION BETWEEN CO-VARIATES AND ISOLATION RATES IN BLOOD AND URINE.

Higher age-specific isolation rates were observed from blood in children below 3 years in both the malaria (15.9%) and non-malaria (22.7%) groups, than those above three years. However, this difference was not significant (P value = 0.53, OR = 0.69, 95% CI = 0.21 – 2.22, and P = 0.45, OR = 0.62, 95% CI = 0.18 – 2.14 respectively). Similarly, although higher age-specific isolation rates were observed from urine in children less than three years in the malaria (14.2%) and non-malaria (19.7%) groups, the difference was not significant (P = 0.61, OR = 0.76, 95% CI = 0.26 – 2.21, and P = 0.19, OR = 0.45, 95% CI = 0.14 – 1.50 respectively).

Although room density was noted earlier to differ between malaria and non-malaria subjects (refer table 1), it was not shown to influence the isolation rates in both blood (P value = 0.58, OR = 1.54, 95% CI = 0.51 – 4.68 for malaria, and P value = 0.11, OR = 2.83, 95% CI = 0.90 – 8.92 for non-malaria) and urine (P value = 1.00, OR = 0.88, 95% CI = 0.27 – 2.3 for malaria, and P value = 1.00, OR = 1.01, 95% CI = 0.32 – 3.15 for non-malaria subjects).

Lower isolation rates were observed in blood and urine of children who had previously been on antibiotics for both malaria (10.5% in blood and 28.6% in urine) and non-malaria subjects (7.1% in blood and 26.3% in urine), compared to those who had not been on antibiotics (74% in blood and 71.4% in urine for malaria, and 78.6% in blood and 63.2% in urine for the non-malaria cases). However, these differences in

isolation rates were not statistically significant for both bacteremia (P value = 0.34, OR = 2.45, 95% CI = 0.53 – 11.40 for malaria, and P value = 0.68, OR = 2.36, 95% CI = 0.28 – 19.67 for non-malaria subjects) and U.T.I (P value = 0.76 OR = 0.85, 95% CI = 0.30 – 2.39 for malaria, and P value = 0.71, OR = 0.75, 95% CI = 0.18 – 3.05 for non-malaria subjects).

Given all the baseline (age, sex, nutrition status, previous use of antimalarial and antimicrobial agents) and socio-demographic characteristics (residence, type of walls of house, mother's level of education) were similarly distributed between the malaria cases and controls, except room density, then the non-malaria subjects were a reasonable match to the malaria cases. This means that none of these factors (except room density) was likely to confound any association between malaria and the outcomes of interest (bacteraemia and U.T.I) in this data. Room density was also shown not to influence the occurrence of both bacteraemia and U.T.I on univariate analysis and therefore not a confounder. Given no association was observed on univariate analysis, further logistic analysis was deemed not necessary.

9.0 DISCUSSION

The majority of children recruited into this study were below the age of 3 years (71% malaria cases and 62.2% without malaria), and resided in the low-income areas of the city (77.8% with malaria and 73.6% non-malaria). This is a reflection of the catchment areas of K.N.H. Both groups had comparable age profiles, nutritional status, previous drug use, and sociodemographic characteristics. Thus, the two groups were similar in their predisposing factors to bacteraemia.

Out of the 158 malaria cases, 18 (11.4%) had pathogenic bacteria isolated from blood. Akpede et al in Nigeria evaluating children with severe and non-severe forms of malaria in an endemic area in Nigeria reported a similar rate of 9.6%, whereas Berkley et al in Kilifi, Kenya found a prevalence of 7.8% in children with severe malaria^{33,34}. One explanation for the lower prevalence by the latter group may be due to differences in the risk profiles for bacteraemia such as age and nutrition status, which were not reported. Secondly, lack of consensus on what criterion is used to define a contaminant in blood culture reports may contribute to the differences observed.

The overall contamination rate of blood cultures in this series was 8.9% (14 / 158), compared to 16% in the Kilifi study. The Nigerian study did not report on their rates of contamination. Contamination may arise either during collection, or processing of the sample⁴⁷. Isolates are considered as contaminants if they are polymicrobial, take a longer duration (72 hours) to grow, or comprise of species normally colonizing the

skin or air-borne organisms, or are considered as low-virulence organisms. For example, most previous surveys have excluded coagulase negative staphylococcus as a contaminant, except in children with indwelling catheters, malnourished children, H.I.V positive patients and in the neonates,^{47,48, 50}. This organism comprised 20.1% and 28.5% of the positive isolates in the malaria and non-malaria groups in this study, respectively. It has been observed that some of the low-virulence organisms, including coagulase negative staphylococcus, are becoming pathogens with increasing clinical significance⁴⁹. Given the prevalence of H.I.V in this series was unknown, and assuming appropriate quality control measures eliminates most of the sources of contamination, it is possible that some of these isolates in this study may have been true pathogens. Similarly, some of the isolates regarded as contaminants in the Kilifi study may have been pathogens.

Due to low parasite rates in a hypoendemic area, any symptomatic child with a positive slide for malaria is usually regarded as a case of malaria and is treated accordingly. The fraction of childhood fever attributable to malaria is much lower in a hypoendemic area, than would be observed in an endemic area¹⁵. Therefore, in the presence of malaria parasitaemia, the risk of co-morbidity would be higher in a child in a non-endemic area.

There was no significant difference in isolation rates from blood between those with or without malaria. This means that malaria parasitaemia is not associated with higher risk of bacteraemia compared to those without malaria. Akpede et al in Nigeria

observed a similar pattern. Other studies did not have comparative groups, and therefore presence of bacteremia cannot be ascribed to the malaria parasitaemia per se, given other associated risk factors to bacteraemia were not assessed.

In this study, differences in occurrence of bacteraemia were noted to exist by age groups, with highest rates observed in children less than 3 years. The Kilifi team in Kenya, as well as in the Nigerian studies, observed similar findings. This may be due to the fact that both infections have their peak in this age group, due to impaired functional immune responses^{22,53}. Most of our study subjects were of good nutrition status. Rates between 8-31% have been documented in malnourished children^{43,54}.

Higher rates of bacteraemia were observed in the non- malaria group (13.2%), compared to that reported in previous surveys of community acquired bacteraemia, done in Western countries, which found rates ranging between 3 - 8%^{22,37}. Akpede et al found however found a similar rate (12.2%) in children presenting with fever and no obvious focus and a negative slide³⁵. Fever per se is known to be associated with bacteraemia, as it may be a transient phase before the development of localized disease such as pneumonia, meningitis, or septic arthritis. Presence of fever was a denominator in our inclusion criteria, as well as in the Nigerian study, unlike community surveys. This may have contributed to the higher rates observed.

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Immunocompromised states including malignancies, diabetes mellitus, sickle cell disease, severe malnutrition, ARC, AIDS, etcetera, may enhance the risk of bacterial

infection. Due to a limitation of funding, we were not able to exclude all immuno-compromising conditions in this series. However, the author attempted to exclude all children presenting with diagnosed chronic illness such as renal or liver disease, severe malnutrition, and clinical AIDS, which are associated with significant immune-suppression.

The prevalence of HIV in the hospital population is has been shown to be on the rise, and is estimated to be between 20 - 40% (anecdotal evidence). In paediatric H.I.V, 'percentage CD 4 lymphocyte' level (percentage of total lymphocytes that are of the CD 4 lineage) has been employed to monitor immune depletion as the disease progresses. The risk of bacterial infections is not enhanced until the 'percentage CD 4 lymphocyte' ratio falls below 25% (ARC stage), and becomes severe below 15% (clinical AIDS stage). Most children at these stages of the disease can be identified by presence of typical clinical signs. There has been no association described between malaria and HIV infection, except in rare cases when recurrent anaemia from malaria may increase the risk of transfusion related HIV transmission. Since the study subjects were drawn from the same source population, we do not think that the prevalence of HIV infection was different in the malaria and non-malaria groups, and therefore HIV infection was not a potential confounder. However, a few children in both malaria and non-malaria groups, with a 'percentage CD 4 lymphocyte' between 15-25% may have been missed if asymptomatic. Although this could have resulted in higher isolation rates in blood and urine, the direction of the association between malaria and these bacterial infections would not be changed.

Blood culture is the gold standard diagnostic tool for bacteraemia⁴⁷. Although being highly specific, it has a low sensitivity and the yield is affected by prior antibiotics use. Thus, the prevalences reported are really under-estimates, and the true prevalence of bacteraemia in both groups is likely to be much higher.

Of the specific organisms isolated from blood, there was no significant difference in isolation rates of gram- positive and gram-negative organisms both in those with or without malaria. *Salmonella typhimurium* was the highest single isolate in the malaria cases. Prada et al in Nigeria and Mabey et al in Gambia reported a similar pattern³⁰,³⁴. Although higher rates of Gram-positive organisms (mainly *staphylococcus aureus*) was reported by Akpede et al and *streptococcus pneumoniae* by Berkley et al, the proportion of Gram-negative organisms isolated was still higher than that reported from studies done in the West⁵¹. Our findings support the idea that microorganisms causing disease in the tropics are different from those causing the same infections in the West. This has been demonstrated for bacteraemia and U.T.I, as well as other wound infections⁵⁵.

Reasons for the increasing predominance of salmonella species from African studies remains unclear. Several hypotheses have been advanced to explain this trend. Firstly the fact that seasonal variations of both conditions peak at the same time, may contribute to their association. Mabey et al observed that 74% of the cases of non-typhoid salmonella septicaemia, and 91% of malaria illness occurred in the rainy

season³⁴. Haemolysis, a prominent feature in certain conditions that predispose to salmonellosis, such as sickle cell disease is also present in malaria. This suggests that haemolysis might be a predisposing factor. Haemolysis leads to increased saturation of iron-binding protein, which increases the susceptibility to bacterial infections⁵⁶. Thirdly, complement abnormalities, which have been documented in children with malaria, are associated with defective bactericidal activity against salmonella species⁵⁷. Opsonization by macrophages is impaired by erythrophagocytosis, through interaction between erythrocyte components and reactive products of oxygen metabolism^{23,24}. Erythrophagocytosis has been observed in malarial spleens. Circulating immune complexes, which occur in sera of malaria patients, also impairs macrophage function⁵⁸. Lastly, there has been an association noted between H.I.V positivity and salmonellosis. The increasing prevalence of H.I.V among patients resident in malaria endemic areas may explain the observed trend.

There was no correlation observed between the level of malaria parasitaemia and occurrence of bacteraemia in this study. However, this study was not powered to allow for this sub-analysis. Nevertheless, the possible explanations for this trend include the fact that slide parasitaemia is not a true reflection of the total parasite load due to parasite sequestration and severity of malarial illness does not correspond to the degree of parasitaemia,^{16,17}. Secondly, previous antimalarial usage may lower the level of parasitaemia without altering the risk of parasitaemia. Lastly, fever due to a coexisting viral illness such as influenza, may lower malaria parasitaemia yet increase the risk of invasive bacterial disease⁵⁶.

Although the prevalence of significant bacteriuria was lower in the malaria cases (13.1%), than in those without malaria (17.3%), this difference was not statistically significant. This implies that malaria parasitaemia is not associated with an increased risk of occurrence bacteriuria. No comparative studies have been done on the prevalence of U.T.I in malaria. However, a lower rate of 17% was registered among those with a negative slide as compared to 22.2% reported by Abdullah ⁴⁰. This may partially be attributed to differences in ages of the children recruited, where they only recruited children less than 5 years, while our study also included older children. However, a higher rate of contamination would be expected with MSSU, which was the method of urine collection in this study, compared to suprapubic aspiration or catheter specimens employed by Abdullah in some subjects. However, this is unlikely to influence the direction of any association between malaria and U.T.I, as it would be of similar magnitude in both groups. On the other hand, whilst any level of bacteriuria is considered significant with the other methods of urine collection, some of our low-colony isolates may have been considered insignificant. Prior antibiotic use may also have contributed to the lower isolation rates observed.

Like bacteraemia, a higher prevalence of significant bacteriuria occurred in children from low-income residence and with higher room density, but this was not statistically different. Higher rates of crowding and poor sanitation common in these environments and may predispose to U.T.I, resulting from infrequent bathing and change in underclothing. This theoretically increases the risk of ascending infection

by bacteria, which arise from faecal flora, colonize the perineum and enter the bladder via the urethra, especially in girls. Mwaura (1976) reported a lower prevalence of 17% in children with kwashiorkor⁶⁰. The difference may be due to our recruitment criteria, where presence of fever was the denominator, a symptom common in U.T.I, whereas they also included asymptomatic children.

E. coli was the commonest organism isolated from both the malaria cases, 12 (57.1%), and 6 (35.3%) of those without malaria. Many investigators have demonstrated similar findings^{60,61}. *E. coli* has been shown to account for up to 75% of U.T.I in all paediatric age groups, followed by other enterobacteria especially *klebsiella*, *proteus* and *pseudomonas*. Gram-positive organisms are rare except *staph saprophyticus*, which occurs in adolescent girls. *Staph epidermidis*, a coagulase negative staph, is usually a contaminant.

This study was powered to detect a 5-fold difference in the prevalence of bacteraemia between the malaria and non-malaria subjects, which was not shown to be present. Our sample size was calculated based on the assumption that the prevalence of bacteraemia in non-malaria subjects was about 3%, whilst that in the malaria group was 15%, based on previous African studies. However, we found the prevalence's of bacteraemia and U.T.I to be similar in children with malaria and those without malaria. Our findings suggest that malaria parasitaemia does not increase the risk of bacteraemia five fold, as suggested by previous surveys. Infact, presence of malaria

parasitaemia seems to reduce one's risk of having bacteraemia and bacteriuria in this set-up.

Our findings show that the prevalence of bacteraemia and bacteriuria in children admitted with fever no obvious focus of infection is increasing. It also shows that a significant number of children (11.4%) admitted with fever and no focus of infection, and a positive slide for malaria have dual diagnosis, with either bacteraemia or significant bacteriuria. Hence, apart from suggesting possible resistance to antimalarials used, persistence of fever and shock in children admitted with malaria may indicate bacterial superinfection. Therefore, attempts should be made to exclude these infections in all children admitted with fever and no obvious focus of infection, regardless of the malaria slide report.

10.0 CONCLUSIONS

1. Bacteraemia occurs with similar prevalence in children admitted with fever and a positive slide for malaria (11.4%), compared to those admitted with fever without an obvious focus of infection and a negative slide for malaria (13.2%).
2. U.T.I occurs with similar prevalence in children admitted with fever and a positive slide for malaria (13.3%), compared to those admitted with fever without an obvious focus of infection and a negative slide for malaria (16%).

11.0 RECOMMENDATIONS

For any child admitted with fever without an obvious focus of infection in this set-up, regardless of the malaria slide report, one should have a high index of suspicion for bacteraemia and/ or bacteriuria, and prompt measures taken to exclude these infections. The presence of a positive slide for malaria does not put the child at a higher risk for these infections.

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APPENDIX I

QUESTIONNAIRE FOR THE STUDY ON THE ASSOCIATION BETWEEN BACTERAEMIA AND URINARY TRACT INFECTION IN CHILDREN ADMITTED TO KENYATTA NATIONAL HOSPITAL WITH MALARIA

A. SOCIO-DEMOGRAPHIC DATA

1. Date
2. Hospital Number
3. Study Number
4. Sex Male = 1, Female = 2.
5. Age of child in years
6. How many rooms does your house have (excluding toilets)?
7. How many people live in your house?
8. What are the walls of your house made of?

1= Stone/brick

2= Corrugated iron

3= Wood

4= Mud

5= Plastic/Cardboard

6= Other (specify)

9. Residence

1= Low income area^{*}

2= Middle income area[◆]

3= High income area[▲]

10. Number of completed years of mother's / guardian's education.

1= None, 2 = Primary, 3 = Secondary, 4 = Beyond secondary.

*Kibera slums, Kawangware, Mathare, Korogocho, Dandora, Mukuru, Kariobangi .

◆ Kayole, Umoja, Tena, Langata, Highrise, Eastleigh, Ayani, Jericho, Pumwani, Komarock.

▲ Buruburu, Upperhill, Kileleshwa, Lavington, South B, South C, Akiba, Ngei, Westlands, Nairobi West, Upper hill, Parklands.

B. HISTORY

Recent drug use for the presenting complaint. Yes = 1, No =2.

- a. Antimalarials
- b. Antibiotics

C. Nutritional State assessment

1. Patients weight in Kilograms.
2. Expected weight at 50th percentile on the “Road to health chart” in kg.
3. Calculate the Harvard standard by using this formula:
$$\frac{\text{Patient's weight}}{\text{Expected weight}} \times 100\%$$
4. Is this child malnourished? [] (Harvard standard < 80%) Yes = 1, No = 2.
5. If yes, classify according to the Welcome classification

Harvard Standard	Oedema absent	Oedema present
60 – 80%	Underweight = 1	Kwashiorkor = 3
< 60 %	Marasmic = 2	Marasmic - Kwashiorkor = 4

D. LABORATORY FINDINGS

1. Peripheral blood film:

Malaria parasites.

Absent = 0, Scanty (+) = 1, Moderate (++) = 2, Heavy (+++) = 3.

2. Microbiology findings.

Blood culture: Organism isolated

Urine culture: Organism isolated

Colony count/ ml

Code:

- | | |
|-----------------------------|----------------------------|
| 1. Staph aureus | 11. Citrobacter spp |
| 2. Staph albus | 12. Candida albicans |
| 3. Coagulase negative staph | 13. Proteus mirabilis |
| 4. Strep pneumonie | 14. Klebsiella pneumonie |
| 5. Strep pyogenes | 15. Escherichia coli |
| 6. Enterococcus | 16. Pseudomonas aeruginosa |
| 7. Strep agalactiae (GBS) | 17. Hemophilus influenza |
| 8. Neisseria meningitidis | 18. Salmonella typhi |
| 9. Neisseria gonorrhoea | 19. Salmonella group D |
| 10. Acinetobacter spp | 20. Others. Specify |

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APPENDIX II

CONSENT FORM FOR THE STUDY ON THE PREVALENCE OF BACTERAEMIA AND U.T.I IN CHILDREN ADMITTED WITH MALARIA.

Hospital Number _____

Study Number _____

I Dr. Okwara F.N. of the Department of Paediatrics, University of Nairobi is conducting a study on children admitted to KNH with fever and/or malaria to establish whether they could have bacterial infections complicating their illness. This will involve asking you questions, examining your child, and I will also need to draw out a sample of 1.1 mls of blood, and obtain a sample of urine that will assist in making the correct diagnosis.

All samples will be examined in the laboratory, and results will be communicated back to your primary doctor to assist in correct management of your child.

All children will receive appropriate treatment for any conditions found. Any information obtained regarding you and your child will be treated with strict confidence. You are free to choose not to participate in the study and the management of your child will not be interfered with in the least.

I am willing to participate in this study.

NAME AND SIGNATURE _____ **Date** _____
(Parent/guardian)

WITNESS SIGNATURE _____ **Date** _____

Tel: 726300 - 19
726550 - 9
726562 - 6
726450 - 9
726581 - 2
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Ref: KNH-ERC/01/1108

30 July 2001

Dr. F.N. Okwara
Dept. of Paediatrics & Child Health
Faculty of Medicine
University of Nairobi

Dear Dr. Okwara,

RE: RESEARCH PROPOSAL "THE ASSOCIATION BETWEEN BACTEREMIA & URINARY TRACT INFECTIONS AND MALARIAL INFECTION IN CHILDREN ADMITTED TO KENYATTA NATIONAL HOSPITAL" (P33/4/2001)

This is to inform you that the Kenyatta National Hospital Ethical and Research Committee has reviewed and approved the revised version of your above cited research proposal.

On behalf of the Committee, I wish you a fruitful research and look forward to receiving a summary of the research findings upon completion of the study.

This information will form part of data-base that will be consulted in future when processing related research study so as to minimize chances of study duplication.

Kindly ensure that a copy of the approval letter is included in your final dissertation as official evidence of approval of your study.

Yours sincerely,

PROF. A.N. GUANTAI
SECRETARY, KNH-ERC

cc Prof. K.M. Bhatt, Chairperson, KNH-ERC

Deputy Director (C/S), KNH

Supervisors: Prof. Wafula E.M., Dept. of Paed. & Child Health, UON
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The Chairman, Dept. of Paediatrics & Child Health, UON

The Dean, Faculty of Medicine, UON