SPECTRUM OF BLOOD BACTERIAL ISOLATES FROM SEVERELY MALNOURISHED CHILDREN AGED 2 TO 59 MONTHS AT MUHIMBILI NATIONAL HOSPITAL, DAR ES SALAAM, TANZANIA

By

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A dissertation submitted in partial fulfillment of the requirement for the degree of Master of Medicine in Paediatrics and Child Health of Muhimbili University of Health and Allied Sciences

Muhimbili University of Health and Allied Sciences

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CERTIFICATION

The undersigned certify that they have read and hereby recommend for acceptance by the Muhimbili University of Health and Allied Sciences a dissertation entitled **"Spectrum of blood bacteria isolates from severely malnourished children aged 2 to 59 months at Muhimbili National Hospital, Dar es salaam, Tanzania"** in partial fulfillment of the requirements for the degree of master of medicine (Paediatrics and Child Health) of the Muhimbili University of Health and Allied Sciences (MUHAS).

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DECLARATION AND COPYRIGHT

I, **Winfred Philemon Kyambile**, declare that this dissertation is my own original work and that it has never been presented and will not be presented to any other university for a similar or any other degree award.

Date ……. Signature……

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DEDICATIONS

This work is dedicated to my grandmother Mariam Kifanga, Mum and Dad for their education foundation and encouragement that I was able to attain this level.

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ABSTRACT

Background

In Tanzania, over 50% of under five deaths are attributed to malnutrition. At Muhimbili national hospital severe acute Malnutrition has the highest case fatality rate (32%) compared to other paediatrics conditions. However septicemia as a cause of death in these patients is not well known.

Routine empirical uses of antibiotics for the treatment of bacterial infections in the first phase of inpatient management of SAM as recommended by WHO is implemented. Changes of aetiologies and susceptibility to antibiotics might have occurred over time. Therefore it is important to have regular updates on the sensitivity pattern of the commonly used antimicrobials. This information is useful in the proper management of bacterial septicaemia in severe acute malnutrition.

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Broad objective: To determine the spectrum and antimicrobial sensitivity pattern of blood bacteria isolates from severely malnourished children aged 2 to 59 months admitted at Muhimbili National hospital.

Methodology: This was a cross sectional hospital based study. One hundred thirty eight (138) children aged 2 to 59 months who met the inclusion criteria were recruited in the study between September 2011 to March 2012. Children were consecutively enrolled in the study after their parents or guardians had given a written consent. Demographic and clinical findings were recorded. Bacterial Isolates were recovered from cultured blood specimens. Antibiotic susceptibility tests were performed using commercial antibiotic disks by the Kirby- Bauer disc diffusion method. Data analysis was done using SSPS program for windows version 16 Software.

Results: Bacteremia among severely malnourished patients admitted at Muhimbili National Hospital was 29%. *Staphylococcus aureus* was the commonest gram positive aerobe (47.5%), followed by *Coagulase negative Staphylococcus* (32.5%) and group D streptococcus (12.5%). The Gram – negative aerobes *Klebsiella* and *Escherichia coli species* constituted 5% and 2.5% of all isolates respectively. Majority of patients (68.1%) had taken antibiotics prior to blood sample collection

All the blood isolates demonstrated an overall low susceptibility to Ampicillin (15%), Ceftriaxone,(50%),Gentamicin(55%), and Chloramphenicol(58%), but were most susceptible to amikacin (90%) and Kanamycin (92%). Only 58% of the blood bacterial isolates were susceptible to the antibiotics as recommended by the WHO empirical regimens.

Forty eight children (34.8%) were HIV positive. Children with HIV infections grew more bacterial isolates compared to those without HIV infections ($p = 0.05$). Moreover, children with HIV infections grew the group D streptococcus (GDS) aerobes more than those who were HIV negative ($p = 0.05$). There was no significant difference in susceptibility to antibiotics between the HIV positive and HIV negative groups. Twenty six (18.8%) children died and 7 (17.5%) of them had bacteremia.

CONCLUSIONS: The prevalence and pattern of blood bacterial isolates in severely malnourished children is the same since it was last reported by Isaac et al in 1990.Bacterial isolates were similar among HIV positive and HIV negative children. However, patients with HIV infection were most likely to have bacteremia than those without.The blood bacterial isolates were highly susceptible to Kanamycin (92%) and Amikacin (90%). There was high level of bacterial resistance to Chloramphenicol (58%), Gentamicin (55%), Ceftriaxone (50%), Ampicillin (15%), and Cloxacillin (10%), and compared to the previous studies done in the same setting. There was no difference in the susceptibility to antibiotics by HIV infection status.

RECOMMENDATION: The use of ampicillin, gentamicin, chloramphenicol, cloxacillin and ceftriaxone in the empirical treatment of bacterial infections in SAM in the paediatrics wards of MNH needs to be re-evaluated. Amikacin or kanamycin should be used initially while waiting for blood culture and sensitivity results. Evaluation of local blood bacterial isolates in severe acute malnutrition (SAM) and detection of any shift in their antimicrobial susceptibilities is very important for management of SAM.

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LIST OF ACRONYMS

AIDS	Acquired Immunodeficiency Syndrome
CCP	Comprehensive chemistry panel
CD	Cluster of differentiation
CDC	Centers for Disease Control
CI	Confidence interval
CONS	Coagulase negative staphylococcus
DNA	Deoxyribonucleic acid
ELISA	Enzyme linked immunosorbent assay
FBP	Full blood picture
HIV	Human Immunodeficiency Virus
IFN	Interferon
JAK-3	Janus Kinase3 (a protein tyrosine kinase associated with cytokine)
MAPK	Mitogen- activating protein kinase
MNH	Muhimbili National Hospital
MUAC	Mid Upper Arm Circumference
MUHAS	Muhimbili University of Health and Allied Sciences
NAIDS	Nutritional Acquired Immunodeficiency
NCCLS	National committee for clinical laboratory standards
NCHS	National centre for Health Statistics
PCR	Polymerase Chain Reaction
SAM	Severe Acute Malnutrition
SD	Standard Deviation
STAT-3	Signal transducer and activator of trascription 3
SPSS	Statistical package for Social sciences
TB	Tuberculosis
TDHS	Tanzania Demographic Health Survey
UNICEF	United Nations Children's Fund
WHO	World Health Organization

CHAPTER ONE

1.0 INTRODUCTION AND LITERATURE REVIEW

Severe acute malnutrition (SAM) affects approximately 13 million children under the age of 5 years worldwide and is associated with 1-2 million preventable child deaths each year. Children with severe malnutrition are at risk of several life threatening problems like hypoglycemia, hypothermia, serious infections and severe electrolyte imbalance. Because of this vulnerability, they need careful assessment, special treatment and management. [1]

Many severely malnourished children die from inappropriate treatment. Case fatality rates of 25-30% commonly occur, and in some hospitals as many as 50-70% dies. This is more than the 5% which is the agreed cut off point by the WHO. Only few of those requiring care actually access treatment.[2 - 8]. Studies across Africa have revealed Case fatality to be high in children with bacteremia compared to those without. [9, 10]

1.1 Immunity in Severe Acute Malnutrition

Diminished immune functions render undernourished patients more susceptible to infections, notably by opportunistic pathogens.[7, 11–14] Immune defense at the epithelial barrier of the undernourished host is compromised due to altered architecture of the gut mucosa, such as flattened hypotrophic microvillus, reduced lymphocyte counts in Peyer's patches, and reduced immunoglobulin A (IgA) secretion. This immunodeficiency has been termed nutritionally acquired immunodeficiency syndrome.[15] Stimulation of an immune response by infection increases the demand for metabolically derived anabolic energy and associated substrates, leading to a synergistic vicious cycle of adverse nutritional status and increased susceptibility to infection. Under inflammatory conditions such as sepsis, mediators increase the catabolic disease state characterized by enhanced Arginine use. Furthermore, Arginase is induced during infection and uses up arginine as substrate. [16] It has been suggested that depletion of this amino acid impairs T cell responses, and exceeding the body's Arginine production leads to a negative nitrogen balance.[17]

Severe protein malnutrition in newborns and small children causes atrophy of the thymus with reduced cell numbers and subsequently ill-developed peripheral lymphoid organs, i.e., lymph nodes and spleen which compromises immunity in children by a long-term reduction of peripheral lymphocyte counts.[18] This causal chain leads to long-lasting immune defects characterized by leucopenia decreased CD4 to CD8 ratio and increased numbers of CD4/CD8 double-negative T cells, and, therefore, the appearance of immature T cells in the periphery.

Malnourished children suffer in greater proportion from respiratory infections, infectious diarrhea, measles, and malaria, characterized by a protracted course and exacerbated disease. These malnourished children present with diminished functional T cell counts, increased undifferentiated lymphocyte numbers, and depressed serum complement activity. The restricted availability of complement components affects the capacity of professional phagocytes to engulf and eliminate pathogens.[19] Reduced antibody responses to polysaccharide antigens of encapsulated bacteria such as *Streptococcus pneumoniae* and *Haemophilus influenzae* exacerbate susceptibility to these pathogens. [11, 13, 20]

1.2 Malnutrition in HIV/AIDS

In Kenya Malnutrition was found to be the commonest cause of admission (40.8%) for children with HIV/AIDS as was reported by Wamsele *et al* (2006).[21] This rose concern on co morbidity of NAIDS, HIV- 1 and TB.[22-24] Deterioration of immunity against HIV and TB has increased the prevalence of these infections and the associated mortality among children in sub-Saharan Africa. [23, 25-26] It has also been associated with increased case fatality rates among children with severe acute malnutrition.[24, 26]

The coexistence of HIV and TB in children with severe acute malnutrition could expedite deterioration and death. However, there is little information about the extent of immunological alteration caused by co-existence of the double immunological burden (NAIDS and AIDS) in these children.

There is a need to document the contribution of HIV to the high case fatality rate of children with severe acute malnutrition in African health facilities, including those with adequate intensive services.[27-28]

The study conducted by Wamsele *et al* (2006) in Kenya reported bacteremia to be common in HIV positive children and more frequently observed among children with malnutrition. *Bacillus spicies* and *Staphylococcus epidermidis* were the commonest isolates from blood culture.[21] Several other studies have reported Coagulase negative Staphylococcus microbes to be a common blood isolates though there are arguments on its clinical importance.[30 - 37]

1.3 Treatment of bacterial infections in SAM

For resource-poor settings, the option of empirical antibiotic coverage has been recommended. This is because the usual signs of infection such as fever are often absent, yet multiple infections are common. Hypoglycemia and hypothermia are often signs of severe infections.[1] [38] the recommended antibiotic regimen for the treatment of infection in severe malnutrition at Muhimbili National Hospital is to give routinely broad spectrum antibiotics to all patients when first admitted as per WHO guidelines. [1, 39].

1.4 Blood bacterial isolates and sensitivity pattern in SAM

Small bowel bacterial overgrowth occurs in all children with severe malnutrition. These enteric bacteria frequently are the source of systemic infection by translocation across the bowel wall. They also cause malabsorption of nutrients; failure to eliminate substances excreted in the bile, fatty liver, intestinal damage and can cause chronic diarrhoea. Because children with kwashiorkor have free iron in their blood, bacteria that are not normally invasive, such as *Staphlococcus epidermidis* and "exotic bacteria" can cause systemic infection or septicaemia.[40]

The role of bacterial translocation across the bowel wall in the pathogenesis of systemic sepsis is supported by the spectrum of organisms (i.e. *K. pneumonia, E. coli, Salmonella species* and *P. aeroginosa*) associated with septicaemia in SAM.[41]

The prevalence of bacteremia varies from one country to another and from one region to another. In East Africa the prevalence ranges between 9.2 to 36 %, [9-10, 42-44] 8.6 to 70% in West Africa [45-46], and 7.7 to 13% in South Africa. [47, 48-49] The causative agents for bacteremia also vary from one country to another. Studies from Kenya, Uganda, Ethiopia and South Africa reported preponderance of Gram negative microbes. [9, 42-43, 47-48, 50] Other studies showed predominance of Gram positive organism.[29, 37, 45-46, 48, 51-55] Of the gram negative microbes, *Enterobacteriacea* (*Nontyphoid salmonella, Klebsiella species, and E.coli species*) are the commonest as sited in studies from Kenya and Uganda.[42-43] Staphylococcus aureus has been reported by several studies to be the commonest Gram positive blood isolates.[37, 43, 53-57]

A study done by Nooran *et al* (2005) at Kenyatta National Hospital in Nairobi showed nearly a third (28.9%) of children admitted with severe malnutrition to have concomitant severe bacterial infections; primarily manifesting as bacteremia. Gram-negative agents were responsible for most severe bacterial infections in children, regardless of their HIV serological status. About 1/3 of the gram positive isolates were Coagulase negative staphylococci, largely resistant to commonly used antibiotics such as Erythromycin, Ampicillin, Cotrimoxazole, Chloramphenicol and even Oxacillin. More than half demonstrated resistance to commonly used oral antibiotics. About 80% of all gram positive and negative isolates were sensitive to Ciprofloxacin. Aminoglycosides, Gentamicin and Amikacin. Third generation Cephalosporins, Ceftriaxone and Ceftazidime, were found to be effective against most gram-negative isolates. [42]

Babirekere-Iriso *et al* (2006) in a study to determine bacteremia in severely malnourished children in an HIV endemic setting in Uganda found a prevalence of bacteraemia to be 22%. The predominant organisms isolated were gram-negative enteric bacilli (77%) with Salmonella species and E. coli contributing to 67% of the isolates. Hypoglycemia was significantly associated with bacteraemia (p=0.007). Most organisms were resistant to cotrimaxazole (93.3%), ampicillin (76.7%), gentamicin (66.7%) and chloramphenicol (60%). All isolates were sensitive to ceftriaxone. Sensitivity to ciprofloxacin was 97%.

There was no strong association between HIV infection and bacteraemia.
The relative risk of death in malnourished children with bacteraemia was ten times higher than in those without bacteraemia.[9]

In a study done in Uganda by Bachou *et al* (2006) 17.1% of blood specimen grew bacterial isolates; 58% were Gram negative - *S. typhimurium* (27.6%) and *S. enteriditis* (11.8%). *Staphylococcus aureus* (26.3%) and *Strep. pneumoniae* (13.2%) were the main Gram positive organisms. There was no difference in the risk of bacteraemia by HIV status, Isolates from severely immune-suppressed children (CD4% <15%) were more likely to grow Salmonella enteriditis (OR 5.4; CI 1.6 - 17.4). The isolates were susceptible (> or = 80%) to ciprofloxacin, ceftriaxone and gentamicin; with low susceptibility to chlorampenicol, ampicillin (< 50%) and co-trimoxazole (<25%). Among bacteraemic children, mortality was higher (43.5% versus 20.5%) in the HIV-positive; OR 3.0 (95%CI 1.0, 8.6).[56]

Reed *et al* (1996) in a study to determine bacteremia in malnourished rural South African children, the incidence of bacteraemia in severely malnourished children was 11.8%. The predominant organisms retrieved were gram-negative enteric bacilli (48.5%). Amongst the severely malnourished, who empirically receive intravenous ampicillin and gentamicin, 95.8% of all isolates were sensitive to this antibiotic combination. The case fatality rate of severely malnourished bacteraemic children was 20.8%. In malnutrition of all categories, the case fatality rate for bacteraemic children was (22.6%) significantly greater than in those without bacteraemia (9.3%).[47]

The results of a prospective study done by Shimeles *et al* (1994) [(10)] on the clinical profile and pattern of infection in Ethiopian children with severe protein-energy malnutrition (PEM) showed that Over 80% of the patients were infected and the lungs were the commonest sites. Bacterial pathogens, predominantly Gram negative enteric organisms were isolated from 36% of blood specimens. Septicemia, gastroenteritis, pneumonia and disseminated tuberculosis accounted for an overall case fatality rate of 32%.[10]

Bernal *et al* (2008) [(58)] in a study done in Colombia to evaluate the implementation of world health Organization guidelines for the treatment of children with severe acute malnutrition overall, mortality during the 5 years was 5.7%, with sepsis the most common cause. The mortality rate was significantly higher in children with edema. Children with moderate acute malnutrition had similar complications and mortality when compared to children with severe acute malnutrition (5.3%).[58] Ashworth *et al* (2004) in a study done in South African to assess feasibility and effectiveness of WHO case management guidelines for severe malnutrition in resource poor hospitals also reported mortality rate to be higher in children with edema.[59]

1.5 STATEMENT OF THE RESEARCH PROBLEM

Trends in the nutritional status of children under five years in Tanzania show an increase of severe malnutrition from 3% (2004 – 05 TDHS) to 4% (2010 TDHS). Over 50% of under five deaths in Tanzania are attributed to malnutrition. At Muhimbili National Hospital (MNH) the case fatality rate was 32% (102/320).[60] This is the highest case fatality rate compared to other paediatrics conditions. The contribution of bacteremia in these deaths is not clear.

There are 72,000 children born to HIV infected mothers each year (TDHS 2004 - 2005). A study done at MNH by Sunguya *et al*(1995) showed malnutrition to be one of the commonest diagnosis (38.1%) in HIV – 1 infected children compared to 16.1% in uninfected children.[61]

Isaac *et al* (1990) at MNH reported septicemia to be the commonest bacterial infection in severe acute malnutrition, with a prevalence of 35.6%. The commonest organism was *Staphylococcus aureus* and was highly sensitive to Cloxacillin, Erythromycin, and Gentamycin.[62] Blomberg B et al (2005 - 2007) at MNH reported bacteremia in children aged between 0 to 7 years to be 13.9% (255/1828) of admissions, despite two thirds of the study population having received antimicrobial therapy prior to blood culture. One third (34.9%) of children with bacteremia died. The mortality rate from Gram-negative bacteremia (43.5%) was three times that of Gram-positive bloodstream infection (16.7%). He also reported high rates of resistance to common inexpensive antibiotics such as Ampicillin, and Cotrimoxazole. There was also high rate of fatal cases of paediatric septicemia caused by Gram – negative bacteria with extended-spectrum beta-lactamases.[64, 65]

Whether over the years during this HIV/AIDS pandemic the blood bacterial isolates and their sensitivity to commonly used antibiotics has changed, it remains unknown.

1.6 RATIONALE OF THE STUDY

The case fatality rate in severe acute malnutrition at Muhimbili National Hospital has remained very high despite using the WHO protocol for the management of SAM.

Bacteremia cases in severe acute malnutrition are associated with higher mortality rates. Different studies from across Africa have shown high prevalence of bacteremia in SAM with causative agents varying from one country to another.

The last study to determine blood bacteria isolates and their susceptibility to commonly used antibiotics at MNH was conducted more than twenty years ago. However, current studies have suggested increasing level of resistant to the commonly used antibiotics including those recommended by WHO for empirical use.

This study aimed at providing updates of the blood bacterial isolates and their susceptibility to antibiotics in use. The study also assessed the appropriateness of WHO antimicrobials recommendations for treatment of infections in SAM. This information is important in rational choice of antibiotics and will help in managing children presenting with SAM at our setting. It also aimed at assessing the contribution of bacteremia on mortality in HIV infected and HIV uninfected children presenting with severe acute malnutrition.

Study hypothesis

Blood bacteria isolates and sensitivity pattern in severely malnourished children at Muhimbili National Hospital have remained the same since last reported.

1.7 OBJECTIVES OF THE STUDY

1.7.1 BROAD OBJECTIVE

To determine the spectrum and antimicrobial sensitivity pattern of bacterial blood isolates in severely malnourished children aged 2 to 59 months admitted at Muhimbili National Hospital.

1.7.2 SPECIFIC OBJECTIVES

The specific objectives of the study were to determine:-

1. Blood bacterial isolates among severely malnourished children by age and sex.

2. Blood bacterial isolates among severely malnourished children by type of severe acute malnutrition.

3. Antimicrobial sensitivity pattern among severely malnourished children by HIV infection status.

4. WHO recommended antimicrobials sensitivity pattern for empirical treatment of infections in SAM.

CHAPTER TWO

2.0 METHODOLOGY

2.1 Study design

This was a descriptive hospital based cross-sectional study.

2.2 Study setting

This study was conducted in the Paediatrics wards at Muhimbili National hospital (MNH), Dar es salaam, Tanzania. The MNH is a tertiary national hospital as well as a referral hospital for the Coast, Lindi, Mtwara, Morogoro and Dar es salaam regions. MNH is also a teaching hospital for Muhimbili University of Health and Allied Sciences (MUHAS). The Paediatrics wards have a total of 124 beds with bed occupancy rate of 40.4% per annum. It is the only hospital which has a malnutrition ward in the region which receives about 320 children with SAM per year. All the patients are admitted as referrals from the Municipal hospitals for the management of SAM and other medical conditions. Patients are admitted through the emergency medical department (EMD) where emergency triage, initial investigations and treatment are done. Majority of SAM patients receives their first dose of broad spectrum antibiotic at EMD before being admitted in Paediatrics wards. Samples for Cultures were taken at admission in the Paediatrics wards. The blood culture and antimicrobial testing were done at MUHAS microbiology laboratory. Serology for HIV and HIV DNA PCR tests was done at the MNH microbiology and immunology laboratory.

Throughout the study duration, the principal investigator worked in malnutrition ward and was fully involved in managing all the participants from time of admission to the discharge.

2.3 Study duration

The study was carried out in a period of seven months starting from September 2011 to March 2012.

2.4 Study population

All severely malnourished children admitted at the MNH, aged 2 to 59 months, with or without HIV infection during the study period were eligible.

2.5 Sample size and sampling

The following formula was used to calculate the sample size.

$$n = \frac{z^2.p(1-p)}{\varepsilon^2}$$

Where Z = 1.96 for 95% confidence interval corresponding to 5% significance level

n = Estimated sample size

P = Prevalence of severely malnourished children with bacteremia at Mulago Hospital in Uganda = 22%.[9]

ε= Margin of error (desired precision) = 7 %

Therefore, n = $(1.96)^2$ x 22 (100 – 22)/ 49 = 134, so the sample size was 134.

Every eligible patient admitted in Paediatrics wards during the study period was consecutively enrolled until the sample size was reached. The enrollment into the study was after the parents/guardians had provided a written consent. An average of 20 patients per month were enrolled per month.

2.6 Inclusion criteria:

Children Aged 2 to 59 months admitted at MNH with severe forms of malnutrition (i.e. marasmus, kwashiorkor, and marasmic-kwashiorkor) with or without HIV infection with parental/guardians consent.

2.7 Exclusion criteria:

- Not granting assent,
- Age below 2 months and above 59 months,
- Mild to moderate malnutrition and
- Those who died before taking the necessary investigations.

2.8 Study procedures

2.8.1 Data Collection

A Structured Questionnaire (Appendix I) designed for the purpose of the study was used to record data including age, sex, relevant clinical findings such as weight, height/length, MUAC, oedema and laboratory investigations. Information was extracted from patient file after the principal investigator had completely attended the patient.

2.8.2 Research assistants

Internship doctors rotating in malnutrition and diarrhea wards were research assistants. All were oriented to study objectives and study procedures while joining the wards because this study was part of the normal procedures for managing patients with severe acute malnutrition in the wards. The principal investigator practically demonstrated to research assistants on how to take anthropometric measurements and collect blood samples and observed them while practicing. The research assistants also facilitated the completion of other investigations and treatments for the patients.

2.8. 3 Participant recruitment and data collection

All patients aged 2 to 59 months with diagnosis of SAM were consecutively recruited in the study as they arrived in Paediatrics wards. Recruitment was done daily. At admission all patients were assessed and treated for emergency signs, and then detailed history of the illnesses and physical examinations were done as a routine procedure. During the discussion of types of investigations for each patient, the principal investigator/research assistants explained about the study to the parents/guardians and requested for informed consent.

Blood culture and sensitivity is a routine investigation to all patients with SAM, therefore blood was collected from all the patients and sent to MUHAS microbiology and immunology laboratory for culture and sensitivity. Pretest counseling was done and consent obtained for HIV/AIDS screening, this was done by the principal investigator/research assistants or nurses in the wards. Random blood glucose was checked at EMD by using a glucometer. The principal investigator participated in the above mentioned activities and personally filled the questionnaires.

2.8.4 Anthropometric measurement

Weight, length/height and Mid-Upper Arm Circumference (MUAC) were determined from each study participant.

Weight

Weight was determined using Solar cell SECA® infant weighing scale for infants and Solar SECA® beam balance for children aged 12 to 59 months. All children were weighed without clothes and shoes. The weight was estimated to the nearest 100 grams. Before being used, the weighing scale and the beam balance were checked for accuracy and consistency by using a known standard 2 kg weight (weighing scale standardization).

Length / height

Length / Height were determined using the length/height measurement board available in the ward. Children less than 85cm or those who could not stand up, the length were taken using a length board placed on flat surface. Children were placed, lying supine along the middle of the board. The assistant held the sides of the child's head and positioned it firmly against the fixed headboard with the hair compressed. The measurer pressing his hands on the child's knees gently stretched the child and then kept one hand on the knees to prevent flexion. While positioning the child's legs straight, the sliding foot-piece was pushed firmly against the bottom of the child's feet. To read the measure, the foot-piece was fixed perpendicular to the axis of the board and vertical. The length was read to the nearest 0.1 centimeter. Children with more than 85 cm and those who could stand, the height measuring board was put upright on flat surface. The child stood upright in the middle, against the measuring board. The child's head, shoulders, buttocks, knees, heels were held against the board by the assistant. The measurer positioned the child's chin straight at 90 degrees. A headpiece was slowly placed on the head at 90 degrees. The height was read to the nearest 0.1 centimeter.

The interpretation of weight for length/height was done using the WHO- 2005 weight – for-height reference tables for African region (Appendix IV).

Weight for length/height equal or less than minus 3 Z score or – 3SD was interpreted as severe wasting implying severe acute malnutrition.

Mid Upper Arm Circumference

The Mid Upper Arm Circumference is as an alternative measure of "thinness" to weight-for-height, particularly in children from six months to fifty nine months. The mother/guardian was asked to remove clothing that covered the child's left arm. The midpoint of the child's left upper arm was first determined. The child's left elbow was bent to make the right angle. The tip of the shoulder (Cricoids' process) and Elbow joint (Olecranon process) were palpated.

The tape was placed at zero, on the tip of the shoulder and pulled straight down past the tip of the elbow. The number at the tip of the elbow was read to the nearest centimeter, and then divided by two to estimate the midpoint. The midpoint was the Mid Upper Arm. The child's arm was then straightened and the tape wrapped around the arm at the midpoint. The tension of the tape on the child's arm was inspected, making sure that the tape was not too tight or too loose. The MUAC was read to the nearest 0.1cm. A reading equal or less than 11.5 centimeters was consistent with severe wasting indicating severe malnutrition.

Blood specimen collection

Blood specimens for culture and sensitivity were collected using the BacT/Alert PF (Pediatric) Bottles. Due to financial constraint, anaerobic blood isolates were not determined, and therefore only blood for aerobes was collected.

After location of the antecubital vein or femoral vein in some cases, the venopuncture site was thoroughly cleaned with a cotton swab soaked in 70% alcohol for a minimum of 30 seconds, Iodine solution (10% Povidone Iodine) was then applied for another 30 seconds in a concentric circle away from the puncture site covering a circular area of 1 to 2 inches in diameter. The puncture site was left to air dry for one minute before venopuncture to give time for complete disinfection. Sterile Needle and Syringe were used to draw 3mls of blood. The protective flip top over cap of the sample collection bottle was removed, the rubber stopper was cleansed by a cotton swab soaked in 70% alcohol or iodine solution and allowed to dry for 1 minute before inoculation. The needle used to draw the blood from the vein was discarded, a new needle was fixed to the syringe outlet, then using the syringe markings as a guide for correct volume, 2mls of blood was inoculated in the BacT/Alert PF (Pediatric) bottle, and the remaining 1 ml was put in a plain 5ml vacutainer tube for HIV testing for those participants whose HIV infection status was not known.

Bottles were labeled with Patient's name, Medical Record number, date, and time of specimen collection. Care was taken not to cover bottles barcode labels and lot numbers. Bottles were sent to the laboratory immediately without refrigerating it before.

Blood culture and Microbial identification

At the laboratory specimens were immediately incubated in an Air-Jacketed, DH Auto flow Automatic CO_2 incubator at 37 °C for 24 hours, after which they were sub cultured on Blood agar (BA),chocolate agar(CA) and MacConkey agar (MCA) plates. The plates were then incubated at 37°C for 24 hours and readings were being done at 48 hours of incubation. For cultures that showed positive bacterial growth, identification of culture isolates was done by colonial characteristics, gram stain and biochemical tests according to the standard methods.[66] Samples with negative bacterial growth were sub cultured in CA, MCA and BA at 48 and 72 hours if continued to show no bacterial growth. Specimen was reported negative if no bacterial growths after 96 hours had elapsed. All negative bottles were discarded after a 5 days incubation period and a negative report was issued.

Susceptibility Testing

The susceptibility test was performed using the Kirby- Bauer disc diffusion method as per the NCCLS recommendations.[67] The antimicrobials that were used in determining the sensitivity pattern included : Ampicillin (AMP,10µg) ,Gentamicin (CN,10 µg) , Chloramphenicol (C, 30µg) Cloxacillin (1µg) , Augmentin (20µg) , Ceftriaxone (CRO,30µg), and Metronidazole which are recommended by the WHO in the treatment of infections in SAM. The other less commonly prescribed antibiotics such as Amikacin (AK, 30µg), Kanamycin 10µg, Erythromycin (E, 15µg), and Cotrimoxazole (STX, 25 µg) were also tested. All the antimicrobial disks were products of Liofilchem s.r.l, Roseto (TE) Italy.

HIV testing

HIV tests were done after counseling and obtaining consent from parents/guardians. In children older than 18 months HIV status was determined by serology tests using AXSYM machine after centrifuging the blood sample and obtaining the serum.

Positive antibody tests in patients younger than 18 months were verified by using HIV-DNA PCR assay testing. Children with known documented HIV infection status were not re-tested.

The principal investigator and research assistants facilitated completion of all indicated investigations and follow up of results in order to facilitate patient management and complete data collection. On admission each patient had blood collected for FBP, CCP and HIV serology for those whom their HIV infection status was not known. The other investigations routinely done in children with SAM in addition to blood for culture and sensitivity are chest x rays, urinalysis, and urine for culture and sensitivity.

The principal investigator collected files once a week to check whether the results other than the blood culture are ready and also to check for the final diagnosis reached and the management outcome. HIV positive patients and those diagnosed to have TB disease were respectively enrolled into CTC and TB programs as required for proper management.

The principal investigator participated in doing procedures such as venipuncture, taking samples to microbiology laboratory, incubating the samples, sub culturing of blood samples, reading the results, identification of microbes and doing antimicrobial testing. Each patient was followed up until all the investigations were completed, definitive diagnosis was reached and patient discharged.

2.9 Data management and analysis

All filled questionnaires were checked and coded by the investigator and any missing data or information was actively searched from patients' files. Data analysis was done by using the Statistical Package for Social Sciences (SPSS) program for windows version 16. Descriptive cross tabulations were performed to examine for associations. Continuous variables were expressed as median and interquantile range. Differences in proportions were tested using the chi-square test and Fishers test where applicable. Odds ratio (OR) and 95% confidence intervals (CI) were calculated to determine the associations between dependent variables on other variables.

A *p – value* equal to or less than 0.05 was a significance level.

Ethical clearance

Ethical clearance to carry out this study was obtained from the MUHAS Research and Publication Committee. Permission to use MNH facilities for the study was sought from MNH management.

2.10 Ethical consideration

Information about the study was given to all parents/guardians before a written informed consent (Appendix III) was obtained from individuals who agreed to participate in the study. The information was given to the parents/guardians to make sure that they have the right information for making a well informed choice, including; aim of the study, blood collection procedures, risks and advantages, confidentiality of the results and other obtained information. Treatment was provided as per recommended guidelines and results of blood culture. All parents/ guardians who did not grant consent to participate in the study, their children were not denied the rights to treatments. HIV testing was done after doing pre test counseling to parents or caretakers, and post test counseling was done when the results were available. HIV positive patients were managed as per guidelines of HIV/AIDS care.

CHAPTER THREE

3.0 RESULTS

Basic characteristics of the study population

A total of 138 patients were recruited in this study. Majority of the patients 105 (76.1%) were 24 months old or younger. The median age at enrollment was 13 months, with interquartile range of 12 to 24 months, 72 (52.2%) were females. One hundred and fourteen (114) patients (83%) presented with fever, 86 (75%) of these had fever of more than seven days. Seventy two (72) patients (52%) presented with cough, 37(51%) had cough of more than 14 days. There were 55 (40%) patients who had diarrhea, and of these 38% had persistent diarrhoea. Eighty five patients (61.6%) of those recruited had marasmus, 35 (25.4%) had marasmic-kwashiorkor and 18 (13%) had kwashiorkor.

Ninety four (68.1%) patients had already received one or two of the commonly prescribed antibiotics such as Penicillin, Ampicillin, Gentamicin, Ceftriaxone and Chloramphenicol before being referred to MNH.
(Table 1)

Table 1. Basic characteristics of the study population. (n=138)

Variable		Number of participants (%)	
Age group in months			
≤ 24 months		105	76.10%
> 24 months		33	23.90%
Median age	13moths		
Interquantile range	12-24months		
Sex			
Male		66	47.80%
Female		72	52.20%
History of fever (n = 114)			
< 7 days		28	24.60%
> 7 days		86	75.40%
History of cough (n =72)			
< 14 days		35	48.60%
> 14 days		37	51.40%
History of diarrhoea (n =55)			
<14 days		34	61.80%
> 14 days		21	38.20%
Previous treated with antibiotics		94	68.10%
Marasmus		85	61.60%
Kwashiorkor		18	13.00%
Marasmic-kwashiokor		35	25.40%

Blood bacterial isolates

Out of 40 blood specimens which grew bacterial isolates, 19/40 (47.5%) grew *Staphylococcus aureus*, 13/40 (32.5%) grew Coagulase negative staphylococcus, all being *Staphylococcus epidermidis*, 5/40 (12.5%) grew group D *streptococcus*, 2/40 (5%) were *Klebsiella spicies* and 1/40 (2.5%) grew *Eschelichia coli.* Gram positive organisms were more predominant than Gram negative organisms. (Table 2)

Table 2: Type and proportion of bacterial isolates

	Number(n)	Percent (%)
S. aureus	19	47.5
CONS	13	32.5
GDS	5	12.5
Klebsiella species	2	5
E .coli species	1	2.5
Total	40	100

CONS = Coagulase negative Staphylococcus, GDS = Group D Streptococcus

There were thirty two blood samples (30.2%) of children aged 24 months or younger which grew bacterial isolates compared to 8 (24.3%) in children aged above 24 months. This was not statistically significant. There was also no significant difference in the proportion of bacterial isolates by sex, though bacteremia was higher among females (36.1%) than males (21.2%). Children with kwashiorkor had higher proportion of bacteremia (39%), followed by marasmus (31%) and marasmic- kwashiorkor (20%), however, this difference was not statistically significant. (Table 3)

Table 3: Bacterial isolates by Age, Sex, and Type of SAM

	Blood bacterial isolates				
	Present	Absent	Total	Odds ratio(95%CI)	P-Value
Age ≤ 24mo	32(30.5%)	73(69.5%)	105		
> 24mo	8(24.2%)	25(75.8%)	33		
Total	40(29%)	98(71%)	138	1.37(0.56 - 3.36)	0.660
Sex Male	14(21.2%)	52(78.8%)	66		
Female	26(36.1%)	46(63.9%)	72		
Total	40(29%)	98(71%)	138	0.48(0.22-1.00)	0.062
Type of SAM					
Marasmus	26(31%)	59(69%)	85		
Kwashiorkor	7(39%)	11(61%)	18		
Marasmic-kwashiokor	7(20%)	28(80%)	35		
Total	40(29%)	98(71%)	138		0.311

Chi – square test. P-value ≤ 0.05

Out of 40 patients who grew bacterial isolates, 19/48 (39.6%) were from HIV positive group compared to 21/90 (23.3%) in HIV negative group, and this was statistically significant (OR, 2.15, 95% CI 1.01- 4.59). (Table 4).

Table 4 : Bacterial isolates by HIV status

	HIV Status			
Bacteria isolates	HIV +ve n/total (%)	HIV -ve n/total (%)	Odds ratio(95% CI)	P - value
Straphylococcus aureus (n= 19)	7/19(37)	12/19(63)		
Coagulase negative (n=13)	6/13 (46)	7/13 (54)		
Group D streptococcus (n= 5)	3/5 (60)	2/5 (40)		
Klebsiella spicies (n=2)	2/2 (100)	0/2 (0)		
Eschelichia coli (n = 1)	1/1 (100)	0/1 (0)		
Total	19/48(39.6)	21/90(23.3)	2.15 (1.01-4.59)	0.05

Chi – square test. P-value ≤ 0.05

Blood bacterial isolates susceptibility to antibiotics

There were no significant differences of isolates to antibiotics by HIV status. In both HIV positive and negative patients,isolates had higher susceptibility to Amikacin and Kanamycin. (Amikacin 90 and 91% respectively and for kanamycin 92 and 92% respectively) (Table 5)

Table 5 : Blood bacterial isolates Susceptibility to antibiotics by HIV status

	HIV status			
	positive	negative		
Antibiotics	N/total (%)	N/total (%)	Odds ratio (95%CI)	P-Value
ampicillin	3/19(16)	3/21(14)	1.1 (0.2-6.4)	1.00
Amikacin	17/19(90)	19/21(91)	0.9 (0.1-7.1)	1.00
Augmentin	2/19(11)	1/21(5)	2.4 (0.2-28.1)	0.60
Cloxacillin	3/19(16)	1/20(5)	3.8 (0.4-39.6)	0.30
Chloramphenicol	12/19(63)	11/21(52)	1.6 (0.4-5.5)	0.50
Cotrimoxazole	1/19(5)	1/21(5)	1.1 (0.1-19.1)	1.00
Ceftriaxone	12/19(63)	8/21(38)	2.8 (0.8-10.0)	0.20
Erythromycin	4/19(21)	4/20(20)	1.1 (0.2-5.1)	1.00
Gentamycin	9/19(47)	13/21(62)	0.6 (0.2-2.0)	0.50
Kanamycin	11/12(92)	11/12(92)	1.0 (0.1-18.1)	1.00
Metronidazole	0/19(0)	0/21(0)		

Chi – square test. P-value ≤ 0.05

The bacterial isolates had low susceptibility to the WHO recommended antibiotics for treatment of bacterial infections in SAM. This was reflected as follows Ampicillin (15%), Cloxacillin (10%), Chloramphenicol (58%), Gentamicin(55%), Ceftriaxone (50%), the other commonly used antibiotics tests reflected the following susceptibility; Amikacin (90%), Kanamycin (92%) Erythromycin (21%), Augmentin (8%) and Cotrimoxazole (5%). (Table 6)

Table 6: Blood bacterial isolates susceptibility to WHO recommended antibiotics

Antimicrobials	S.aureus n/total (%)	CONS n/total (%)	GDS n/total (%)	kebsiella spp n/total (%)	E.coli n/total (%)	overall N/total(%)
Ampicillin*	3/19(16)	1/13(8)	2/5(40)	0/2(0)	0/1(0)	6/40(15)
Amikacin	17/19(90)	11/13(85)	5/5(100)	2/2(100)	1/1(100)	36/40(90)
Augmentin	1/19(5)	1/13(8)	1/5(20)	0/2(0)	0/1(0)	3/40(8)
Cloxacillin*	3/19(16)	0/13(0)	1/5(20)	0/2(0)	0/1(0)	4/40(10)
Chloramphenicol*	9/19(47)	10/13(77)	3/5(60)	1/2(50)	0/1(0)	23/40(58)
Cotrimoxazole	2/19(11)	0/13(0)	0/5(0)	0/2(0)	0/1(0)	2/40(5)
Erythromycin	4/18(22)	1/12(8)	3/5(60)	0/2(0)	0/1(0)	8/39(21)
Gentamycin*	10/19(53)	8/13(62)	3/5(60)	0/2(0)	1/1(100)	22/40(55)
Kanamycin	13/14(93)	2/3(67)	4/4(100)	2/2(100)	1/1(100)	22/24(92)
Ceftriaxone*	11/19(58)	5/13(39)	2/5(40)	1/2(50)	1/1(100)	20/40(50)
Metronidazole	0/19	0/13	0/5	0/2	0/1	0/40(0)

CONS = Coagulase negative Staphylococcus, GDS = Group D Streptococcus

*Antibiotics recommended by WHO for empirical use in SAM.

CHAPTER FOUR

4.0 DISCUSSION

One hundred thirty eight patients with severe acute malnutrition were prospectively enrolled in this study between September 2011 and March 2012. Majority of the patients 105 (76.1%) were 24 months or younger. The median age at enrollment was 13 months. The predominance of SAM in this age group parallels the high prevalence of HIV positive children which was 83.3 % in children aged 24 months or younger.

The prevalence of bacteremia of 29% among severely malnourished patients in this study is similar to that reported across East Africa in which the prevalence ranges between 9.2% to 36%.[9-10, 42-44] It is also within the ranges reported in West Africa where the prevalence lies between 8.6% to 70%.[45-46] In South Africa, studies have shown a prevalence that ranges between 7.7% to 13%.[47-49] The predominance of causative agents for bacteremia varies from one geographical region to another. In this study, the Gram – positive aerobes were the most common isolates accounting for 92.5% (37/40) followed by the Gram – negative aerobes 7.5% (3/40). This finding is similar to a previous study done at MNH.[62] It is in keeping with the results of studies done in South Africa and West Africa and Ethiopia.[45-46,48-49,51-54] Studies from Kenya, Uganda and Malawi demonstrated predominance of Gram – negative organisms as the cause of bacteremia.[10,42,47-48,50] Most recent studies of bacteremia in SAM have revealed predominance of Gram- Positive organisms. [37,53-55] Whether this suggests a change in the epidemiology from the predominant Gram – negative organisms described in the previous reports warrants further studies.

Staphylococcus aureus was the leading Gram positive bacteria in this study, a finding similar to other studies from Uganda in 2004, Ethiopia in 2010, and Gambia in 2008.[42,53-54] *Staphylococcus aureus* bacteremia can be due to community acquired pathogens or nosocomial pathogens.

Isaac *et al* (1990) demonstratred Staphylococcus aureus to be the leading cause of nosocomial bacteremia in severely malnourished children admitted in MNH paediatric wards.

[62] Whether the high prevalence of Staphylococcus aureus in this study was community acquired or pre referral hospital acquired it was not clear. Several studies have suggested vitamin A deficiency to be a predisposing factor to *Staphylococcus aureus* infections through phagocyte dysfunction and decreased complement activity.[19, 57] Other risk factor that could have contributed to the high prevalent of *Staphylococcus aureus* includes prior hospitalization as majority of the study participants were referred from municipal hospitals.

Coagulase negative Staphylococcus (CONS) was the second leading cause of bacteremia in this study. This has been a commonest blood bacterial isolates in several studies across Africa and Jamaica with proportions ranging between 26 to 40 %.[29-30, 36, 53-54] In the current study the proportion of CONS isolates was 32.5% despite of using 70% alcohol and 10% Povidone-Iodine to disinfect the skin prior to venopuncture. This makes judging the clinical significance of CONS very important before considering them as contaminants. CONS are normal inhabitants of human skin and mucus membranes, but in immunocompromised patients infection may result.[37] In the interruption in the normal skin defense barrier as may occur in severe acute malnutrition, entry of organisms into the blood may be achieved and lead into bacteremia.[29] Despite of controversy in the clinical significance of CONS, they are well recognized as a significant cause of sepsis among critically ill and immunosuppressed patients.[31-32]

Group D Streptococcus bacteria were another Gram – positive blood bacterial isolates in this study. It accounted for 12.5% of all isolates. A similar finding was reported by Isaac et al (1990) at MNH as nosocomial infection.[62] *Group D Streptococcus* are normal inhabitants of the gastrointestinal tract of humans. They are usually not aggressive invasive organisms. They usually cause disease in children with damaged mucosal surfaces or impaired immune response as may occur in SAM. Their dramatic emergence as a cause of nosocomial infection is predominantly due to their resistance to antibiotics commonly used in hospital setting.

Klebsiella and *E.coli species* were the Gram – negative isolates that were demonstrated by this study. They accounted for 5% and 2.5% of all isolates respectively.

This finding is similar to that of Alem *et al* (2011) in Ethiopia[54] and Christie *et al* (1992) in Jamaica.[29] They are *Enterobacteriaceae* which their presence in blood may be a result of their translocation across the bowel wall, a phenomenon that can occur in severely malnourished patients.[41]

In the current study, the proportion of bacteremia was higher (30.4%) in patients aged 24 months or younger compared to 24.2% in patients aged more than 24 months. Females had higher (36.1%) proportion of bacteremia compared to 21.2% in males. These findings were not statistically significant, and are similar to the findings reported by Bachou et al in Uganda[43] and Oduak et al in Gambia[53].

In the current study proportion of blood bacterial isolates was higher (39%) in patients with kwashiorkor compared to 31% and 20% in marasmus and marasmic-kwashiorkor respectively. This finding was not statistically significant. Similar findings were reported by Bachou et al in Uganda[43] and Sunguya et al (2006) at MNH, Tanzania .[61]

The absence of significant differences in the proportion of blood bacterial isolates by age, sex and by type of severe acute malnutrition could be explained by the pathophysiology of severe acute malnutrition which is also does not differ by age, sex and type of severe acute malnutrition. [11-15]

A positive HIV test in this study was significantly associated with high proportion of bacteremia ($p = 0.05$). This finding is similar to the result of the studies done by Berkley *et al* (2005) in Kenya[63] and Wamsele *et al* (2006) in Tanzania.[21] Noorani *et al* (2005) in Kenya[42] and Bachou *et al* (2006) in Uganda[43] found no influence of HIV positive test in bacteremia. The differences observed in the current study to the previous studies could be due to study designs and the difference in the prevalence of HIV infections in the study areas in the study periods. Patients with HIV positive in this study were also more likely to have *group D streptococcus* (GDS) bacteremia ($p = 0.05$). A finding which is in keeping with occurrence of GDS bacteremia in immunocompromised patients.

This study demonstrated high bacterial resistance to the commonly prescribed antibiotics such as Ampicillin, Gentamicin, Chloramphenicol and Ceftriaxone. The overall susceptibility of blood bacterial isolates in this study was 15% for Ampicillin, Amikacin (90%), Augmentin (8%),Cloxacillin(10%),Chloramphenicol(58%),Cotrimoxazole(5%),Erythromycin(21%),Gentamycin (55%), Kanamycin(92%) and 50% for Ceftriaxone. Similar finding was reported by Babirekere *et al* (2006) in Uganda.[9] Bachou *et al* (2006) in Uganda [43] and Alem *et al* (2011) in Ethiopia [54] also reported high resistance of blood bacterial isolates to Chloramphenicol, Cotrimoxazole and Ampicillin but more than 80% susceptibility was seen to Ceftriaxone and Gentamicin. A study done by Uduak *et al* (2008) in Gambia[53] by excluding patients who had taken any antibiotics within two weeks prior to presentation found 87.5% of isolates to be susceptible to ampicillin and/or gentamicin and 84.4% to penicillin and/or gentamicin. The difference in the results between this study and a study done in Gambia by excluding patients who had taken antibiotics prior to blood collection, calls for a similar study to be done in our setting.

The current study shows that there has been a change in the blood bacterial isolates susceptibility to antibiotics by showing low susceptibility to commonly used antibiotics. Isaac *et al* (1990) in the same setting found high susceptibility of blood isolates to Erythromycin, Gentamicin and Cloxacillin.[62]

The findings of this study are from the in vitro sensitivity test by disk diffusion. The high proportion of positive blood culture from patients who had already taken one or two of the commonly prescribed antibiotics prior to blood sample collection may be a reflection of in vivo resistance to these antibiotics. In this study 23/40 (57.5%) of the positive blood culture grew from patients who had taken antibiotics prior to blood sample collection. Twelve (12) patients grew bacterial isolates after had used Penicillin and Gentamicin, six (6) after receiving Ampicillin and Gentamicin, and five (5) after they had taken Ceftriaxone.

The high susceptibility to uncommonly prescribed antibiotics Amikacin and Kanamycin in this study, may probably explain the high resistance to commonly used antibiotics. This may be attributed to easy accessibility of the commonly used antibiotics and their improper use of in the community and at health facilities. There was no difference in the susceptibility tests by HIV status, a finding which is in conformity with other previous studies.[9, 42-43]

The results of this study raises great concern because the bacterial isolates revealed very low susceptibility to the antibiotics (Ampicillin, Gentamicin, Chloramphenicol, Cloxacillin and Ceftriaxone) that are currently recommended by WHO for the treatment of presumed bacterial infections in SAM.[1,39] The high susceptibility to Amikacin and Kanamycin should suggest these antibiotics to be used in SAM at our set up. However this calls for further studies to find out the most feasible antibiotics for the treatment of bacterial infections in severely malnourished patients in this setting.

In the current study, mortality among patients with SAM and bacteremia was 17.5%. This is comparable to findings from other studies done across Africa.[43, 47-48] In this study, the proportion of mortality was higher (19.4%) in patients without bacteremia compared to (17.5%) in patients with bacteremia. This difference was not statistically significance.

Two studies have shown higher mortality in the bacteremic group compred to non bacteremic group. However it was not document if the difference was of statistical significance. [9, 47] The lack of statistical significance in the finding of this study could be a reflection of other co - morbidities other than bacteremia to be the cause of deaths, or could be due to the predominance of less fatal Gram positive microbes. Of the 26 deaths in the current study 8(30.8%) had PTB, 6 (23%) had Persistent diarrhoea, 5 (19.2%) had cerebral palsy, 4(15.4%) severe pneumonia, 2(7.7%) had Hydrocephalus and 1 (3.8%) had congenital heart disease.

Mortality among children with bacteremia in the HIV positive group and those who tested HIV negative was 21% and 14.3% respectively.

However, the difference was not statistically significant. This finding is not similar to that of Bachou *et al* (2006) in Uganda who found mortality to be higher in HIV positive group with bacteremia.[43] This difference can be due to the differences in the predominating organisms. i.e. the most fatal Gram negative organisms in Uganda versus the less fatal Gram positive in this study.

STUDY LIMITATIONS

1. Many patients had already taken one or two of the commonly used antibiotics prior to recruitment. This may have lowered the detection rate of blood bacterial isolates and sensitivity pattern. .

2. This being a cross sectional hospital based study at tertiary referral hospital, its finding might reflect selection bias and the results cannot be generalized countrywide.

3. Isolation of anaerobic microbes was not done due to financial constraints.

CHAPTER FIVE

5.0 CONCLUSIONS

- Bacteremia among severely malnourished patients admitted at Muhimbili National Hospital constituting was 29%. Gram – positive organisms were the predominating causative agents, with high proportion of *Staphylococcus aureus* (47.5%), followed by *Coagulase negative Staphylococcus* (32.5%) and group D streptococcus (12.5%). The Gram – negative aerobes *Klebsiella* and *Escherichia coli species* constituted 5% and 2.5% respectively.
- Majority of patients (68.1%) had taken antibiotics prior to blood sample collection
- Bacterial isolates were similar in HIV positive and HIV negative. However, patients with HIV infection were most likely to have bacteremia than those without.
- The blood bacterial isolates were highly susceptible to Kanamycin (92%) and Amikacin (90%).
- There was high level of bacterial resistance to the commonly used antibiotics such as Ampicillin (15%), Gentamicin (55%), Cloxacillin (10%), Chloramphenicol (58%) and Ceftriaxone (50%) compared to the previous studies done in the same setting.
- There was no difference in the susceptibility to antibiotics by HIV infection status.

5.1 RECOMMENDATION

- The use of ampicillin, gentamicin, chloramphenicol, cloxacillin and ceftriaxone in the empirical treatment of bacterial infections in SAM in the paediatrics wards of MNH needs to be changed.
- Amikacin or kanamycin should be used as an initial therapy while waiting for blood culture and sensitivity results.
- Evaluation of local blood bacterial isolates in severe acute malnutrition (SAM) and detection of any shift in their antimicrobial susceptibilities is very important for proper management of SAM.

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ANNEXES

ANNEX I: DATA COLLECTING TOOL

A. Identification

Serial No…… Date of admission…… ……

Name ……

Hospital No……. ward……..

Date of birth……. Age in months……..

Sex: 1. Male ( ) 2. Female ( )

B. History : **Duration**

1. Fever YES/NO
2. Cough
3. Diarrhoea
4. Weight loss
5. Previous treatment with Antibiotic Yes/No , if Yes

   Name of drug (s) Duration

……

……

Anthropometric measurements

Body weight……

MUAC…….

Length/Height in centimeters……..

Weight – for height/length……..

Oedema YES/NO

Type of severe malnutrition

1. Marasmus
2. Kwashiorkor ( )
3. Marasmic – Kwashiorkor

C. Investigations

6. Random blood glucose on Admission……
7. (i). HIV Elisa test ≥ 18months Reactive/ None Reactive
   (ii).HIV DNA PCR < 18 months Reactive / None Reactive

D. **Bacteria Isolated**…….

E. **Antimicrobial sensitivity tests**

. Antimicrobial	Sensitive	Resistant
Ampicillin……..		
Amoxycillin……		
Cloxacillin…….		
Chloramphenicol……		
Gentamicin…….		
Amikacin……		
Kanamycin…….		
Erythromycin…….		
Cotrimoxazole……		
Ciprofloxacin……..		
Ceftriaxone……..		
Metronidazole……		

F. Final Diagnosis……...

G. **Outcome of a patient of the patient at discharge:**

8. Recovered
9. Death ( )

ANNEX II: Consent Form

Consent form for participation in the study to determine the Blood bacterial isolates and their antimicrobial sensitivity patterns in severely malnourished children aged 2 to 59 months admitted at Muhimbili National hospital. Dar es salaam, Tanzania.

My name is Dr .Winfred Kyambile

I am a resident in the department of Pediatrics & Child Health at MUHAS. I am doing research study to determine the Blood bacterial isolates and their sensitivity patterns in severely malnourished children aged 2 to 59 months admitted at Muhimbili National hospital. Dar es salaam, Tanzania

I would like to ask you for your permission that your child can participate in this study

I will first explain to you about the study and answer any question you have.

Study aim

This study will determine the Blood bacterial isolates and their antimicrobial sensitivity patterns in severely malnourished children aged 2 to 59 months admitted at Muhimbili National hospital.

How to Participate in the study

Demographic and brief history of present illness questions will be asked and physical examination will be done to your child. Child's weight, height and MUAC will be taken.

A small amount of blood will be taken using a sterile needle from your child's vein after you have have to participate in the study.

The blood will be cultured to see if there are bacterial growth, and if present, they will be determined and their sensitivity to the commonly used antibiotics tested. HIV infection status will also be checked if the status is not known. Also random blood glucose will be checked on admission.

Participation in this study will not delay or discontinue your child from receiving the same service like other children in the ward.

Confidentiality

Your Child's name and other particulars will not be made public in any way. Only the chief investigator and laboratory staff will handle the specimens and information obtained.

Those who are found to be HIV positive will be referred to a comprehensive infectious disease clinic within the department of pediatric & Child health for further management and care.

Risks

The procedure that will be done in this study is a common procedure which is routinely done to all children who are admitted to this ward and is very safe. We don't expect your child to experience any problem as a result of this study.

Now having explained to about the study, I am ready to answer any question you wish to ask concerning the study.

For further question or problems you may contact the following persons:

1. The principal investigator ; Dr .Winfred kyambile
   Departiment of pediatrics & Child Health
   Tel: +255 784 651 832

2. Prof Abood
   Chairman of MUHAS Research and Publication Committee
   P.O.BOX 65001 Dar es salaam.
   Telephone 2150302 - 6

I….. ……..have read or been told the content of this form and understood,and my questions have been answered .I agree my Child to take part in this study.

Date Signature of parent/Guardian Researcher's Sign

ANNEX III: Fomu ya ruhusa ya kushiriki utafiti

Mimi ninaitwa Winfred Kyambile, ni daktari mkazi katika idara ya magonjwa ya watoto na afya ya mtoto katika chuo kikuu cha Muhimbili. Ninafanya utafiti wa kuangalia vimelea vya aina ya bakteria ambavyo vinaweza kuwepo kwenye damu ya watoto wenye utapiamlo na unyafuzi na kuangalia aina ya dawa inayoweza kutibu vimelea hivyo kwa ufanisi mkubwa.Ninaomba ruhusa/kibali cha mwanao kushiriki kwenye utafiti huu.lakini kabla hujakataa au kutoa kibali cha kuruhusu nitakupa ufafanuzi wa utafiti huu.

Namna ya kushiriki

Utaombwa kutoa maelezo ya jinsi mtoto anavyougua ikiwemo utambulisho wake. Mtoto atachunguzwa na daktari na kisha uzito, urefu na upana wa mkono wake juu ya kiwiko utapimwa. Kiasi kidogo cha damu kitachukuliwa kwa ajiri ya kuchunguza vimelea aina ya bacteria kwenye damu,kutambua hali ya maambukizi ya virusi vya UKIMWI kama hajawahi kupima,na kisha kiasi kidogo kitatumika kuangalia kiasi cha sukari kwenye damu. Ushiriki wa mtoto katika utafiti huu hautasababisha asipewe huduma kama wengine e waliopo hapa wodi wenye tatizo kama la kwake,atapata matibabu sawa na wengine . Na uchunguzi wote anaofanyiwa mwanao katika utafiti huu ni ule ambao kila mtoto mwenye tatizo hili hufanyiwa katika kutafuta tiba sahihi. Utafititi huu hauna madhara yeyote. Usiri katika matokeo ya uchunguzi utazingatiwa kama ilivyo kwa magonjwa yeyote. Ni mimi na mtaalamu wa maabara tu ndiye tutakua tukijua matokeo ya uchunguzi na kutoa kwako kama mrejesho.

Baada ya kutoa maelezo ya utafiti huu kwako,nipo tayari kujibu swali au kutoa maelezo ya ziada pale ambapo utakua hujaelewa vizuri au unatia shaka.

Kama umeelewa na kuridhia ushiriki wa mwanao katika utafiti huu,nitaomba ujaze na kuweka saini katika nafasi hapa chini.

Mimi …….. ……..Nimesoma /nimesomewa maelezo yote yaliyomo kwenye fomu hii na nimeelewa.Maswali yangu yote nimejibiwa na kuyaelewa majibu yake.

Nimekubali / Sikubali mototo wangu ashiriki katika utafiti huu.

Tarehe Sahihi ya Mzazi/Mlezi Sahih ya Mtafiti