THE PREVALENCE OF BACTERAEMIA IN THE SEVERELY MALNOURISHED CHILDREN AGED 2 TO 59 MONTHS AT MBAGATHI DISTRICT HOSPITAL NAIROBI.

A DISSERTATION PRESENTED IN PARTIAL FULFILLMENT FOR THE AWARD OF THE DEGREE OF MASTER OF MEDICINE (PEDIATRICS) IN THE DEPARTMENT OF PEDIATRICS AND CHILD HEALTH, COLLEGE OF HEALTH SCIENCES, UNIVERSITY OF NAIROBI.

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DECLARATION

This dissertation is my original work, and has not been presented for a degree in any university or published anywhere.

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This dissertation has been presented with our approval as the supervisors.

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DEDICATION

I dedicate this work to my grandmother Nyiha who loved me so much and encouraged me to always strive for excellence in everything that I do.

ACKNOWLEDGEMENTS

I wish to express my sincere gratitude to:

1. My supervisors, Prof Fred Were, Dr. Nyambura Kariuki and Dr. Daniel Njai for their guidance, patience and constant support during my study
2. Dr. Sam Kariuki for his valuable advice on the laboratory procedures
3. The Mbagathi Malnutrition study group residents. They include Dr. Kamunya, Dr. Fondo, Dr. Mwinyishee, Dr. Wamalwa, and Dr. Bakalemwa. Together we were able to collect data on childhood malnutrition comprehensively 24 hours 7 days a week during the study period.
4. The Clinical Officers in Mbagathi District Hospital who assisted in data collection.
5. The Medical Superintendent Mbagathi District Hospital, Dr. Sule for facilitating our work.
6. Dr. Mutai, the Consultant Pediatrician and Cardiologist, at Mbagathi District Hospital for her encouragement
7. The PRIME K MNCH linked award for their help and funding of the research.
8. All the parents, caregivers and children who participated in this study.

THANK YOU.

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LIST OF ABBREVIATIONS

WHO	World Health Organization
SAM	Severe acute malnutrition
CONS	Coagulase negative Staph.aureus
MUAC	Mid upper arm circumference
MOH	Ministry of Health
KEMRI	Kenya Medical Research institute
KNH	Kenyatta National Hospital
TMRU	Tropical Metabolic Research Unit
HIV	Human immunodeficiency virus
Kg	Kilogram
KDHS	Kenya Demographic and Health Survey

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ABSTRACT

Introduction:

Severe malnutrition is a common cause of preventable morbidity and mortality among children aged 5 years in developing countries. The prevalence of bacteraemia, urinary tract infection, diarrhea and pneumonia among children with severe malnutrition is high. These, coupled with an atypical clinical presentation of sepsis, justify the routine use of empirical antibiotic treatment in the initial phase of inpatient management of SAM children[1 2] .The choice of antibiotics should be guided by locally prevalent pathogens and their antibiotic susceptibility patterns.

Objectives:

The broad objective of this study was to determine the prevalence of bacteraemia in SAM children at Mbagathi District Hospital and its association with the history and physical examination characteristics of the enrolled children.

The primary objectives of the study were:

- To determine the blood bacterial isolates in SAM children in Mbagathi District Hospital.
- To determine the sensitivities of the bacterial isolates to the WHO recommended antibiotics among SAM children in Mbagathi District Hospital.

The secondary objective was:

- To determine the association of clinical history and examination findings in the bacteraemic and non bacteraemic SAM children.

Design: The study was a hospital based cross-sectional survey conducted at Mbagathi District Hospital over a period of 3 months.

Subjects and setting: A probability sampling was used to recruit 2 to 59 months' old children with SAM in the out-patient pediatric filter clinic and the wards at Mbagathi District Hospital.

Main outcome measures: Blood bacterial isolates by blood culture and their antibiotic sensitivities to WHO recommended antibiotics by disc diffusion method.

Sample size: Using Fishers formula for prevalence studies gave a sample size of 88 children.

Study procedure: Socio- demographic characteristics, clinical history, physical examination findings and anthropometric measurements of the study subjects were taken. In subjects who met inclusion criteria, 3mls of venous blood was aseptically drawn and taken within two hours to KEMRI laboratory for culture and sensitivity testing.

Data management: Data obtained was coded and entered in a preformed Excel data sheet and analyzed using social sciences statistical package version 18

Results:

A total of 90 children seen at Mbagathi District Hospital with severe acute malnutrition were included in this study. The mean age of patients with SAM was 16 months, (SD=8.0) and the age range was 5 to48 months. The presenting features were as follows: Acute diarrhea 40(44.4%), chronic diarrhea 6(6.7%), vomiting everything 31(34.4%), acute cough 19(21.1%), chronic cough 3(3.3%), ability to drink 59(65.6%) fever 56 (62.2%).

The total number of enrolled children was 90. 88(97.7%) were severely malnourished, with weight for height < -3SD the median, and 2(2.2%) were very severely malnourished with a WHO Z score weight for height < -4SD the median. The overall prevalence of bacteraemia was 30 %(27) with *S. aureus* accounting for 21.1 %(19); *S. typhi 4.4* %(4*); S. epidermidis* 3.3 %(3)

and *E. fecalis* 1.1 % (1). There was no difference in the occurrence of bacteraemia between the male and female gender, (p=0.679) and the various age ranges of the severely malnourished children studied (p=0.853). With regard to bacteraemia and clinical history, children with diarrhea and vomiting were more likely to have bacteraemia with p=0.008 and p=0.05 respectively. The physical examination characteristic associated with bacteraemia was the presence of skin lesions with p=0.008 .In the multivariate analysis the independent risk factors for bacteraemia were acute diarrhea (OR = 5.63; 95% CI 1.3-24.45), oedema (OR = 5.92; 95% CI 1.81-19.37) and skin lesions (OR = 5.08; 95% CI 1.54-16.69).

The antibiotic sensitivity profile of the bacterial isolate was as follows; ampicillin and cotrimoxazole showed resistance (resistance to ampicillin ranged from 94.7% to 100% while to cotrimoxazole it was between 63.2% and 100%). Most of the isolates were sensitive to amoxicillin (77.7%), gentamycin, (74%) and chloramphenical (81.4%).

Conclusion

The prevalence of bacteremia in SAM children in Mbagathi District Hospital was 30%.It was associated with diarrhea, oedema and skin lesions. The isolates were generally sensitive to amoxicillin, gentamycin, and chloramphenical. They showed varying resistance to ampicillin and cotrimoxazole.

BACKGROUND

Severe acute malnutrition (SAM) occurs after a relatively short duration of nutritional deficit that is often complicated by marked anorexia and concurrent illness[1]. The prevalence of bacteraemia, urinary tract infections, diarrhea, and pneumonia among children with severe malnutrition is high[2].Globally, co morbidities such as diarrhea, pneumonia, and malaria, which result from relative defective immune status, remain the major causes of death among children with SAM. Children with these co morbidities require hospital care due to the attendant high risk of mortality. The atypical clinical presentation of sepsis in these children justify the routine administration of antibiotic in the initial phase of inpatient management as recommended by WHO [3 4].

In an effort to improve the quality of hospital care for severely malnourished children and reduce case fatality, the WHO developed clinical guidelines with 10 steps that need to be followed in the inpatient care of severely malnourished children. Step five of these guidelines recommends giving routine antibiotic as outlined below[7]:

If the child appears to have no complications, give: Cotrimoxazole for 5 days (20 mg of sulphamethoxazole + 4 mg of trimethoprim per kilogram orally twice daily). A short course of oral antibiotics is also advised for children with uncomplicated SAM children treated in the community.

If there are complications give: Ampicillin (25–50 mg/kg IM/IV 6-hourly for 2 days), then oral amoxicillin (15 mg/kg 8-hourly for 5 days) OR, if amoxicillin is not available, oral ampicillin (25–50 mg/kg 6-hourly for 5 days) and gentamycin (7.5 mg/kg IM/IV) once daily for 7 days.

If the child fails to improve within 48 hours: Add chloramphenical (25 mg/kg IM/IV 8-hourly) for 5 days.

If meningitis is suspected: Do a lumbar puncture for confirmation, where possible, and treat with chloramphenical (25 mg/kg 6 hourly) for 10 days.

If other specific infections are identified (such as pneumonia, dysentery, skin- or soft-tissue infections): Give antibiotics as appropriate.

Data from the KDHS show the nutritional status of children in Kenya has not improved much since the last survey. Thirty five percent of children under 5 years are stunted, 14% severely stunted, 7% are wasted, 2% severely wasted, 16% are underweight, and 2% are severely underweight.[6]

Few studies have been done to evaluate the emerging resistance patterns of the common bacterial isolates to the antibiotic protocols in use among children with severe malnutrition in Kenyan District Hospitals. The few studies available show high prevalence of bacterial resistance to the antibiotics currently used in empiric management of severe malnutrition. One such study done in Kenyatta National Hospital, Nairobi, showed high prevalence of resistance of bacterial isolates to the antibiotics commonly used in the ministry of Health (Kenya) Basic Pediatric protocols.[8]

LITERATURE REVIEW

Severe malnutrition is defined as the presence of oedema of both feet, or severe wasting (<70% weight-for-height/length or <-3SD), or clinical signs of severe malnutrition .[7]

Bacteraemia is a common occurrence in children with severe acute malnutrition, a finding that has led to the current recommendation for empiric antibiotic cover in all children with SAM. Its prevalence among children with severe malnutrition is variable across sub-Saharan Africa. It ranges from 8.6% to 70% in West Africa.2% to 36% in East Africa and 7.7%to 13% in South Africa. [8, 9, 11] The responsible bacteria types, however, vary geographically with most studies reporting a predominance of gram-negative enteric bacteria while a few report gram-positive aerobes, mostly staphylococcus species.

Globally available studies have reported varying findings as to the resistance patterns of bacterial isolates to the current WHO antibiotic for empiric treatment of children with SAM.

Lazzerini M, and Tickell D, from Institute of Maternal and Child Health, Trieste, Italy did a systematic review of evidence in support of WHO guidelines recommending broad-spectrum antibiotics for children with severe acute malnutrition. They reviewed two randomized controlled trials (RCTs), together with 18 pharmacokinetic studies. They found weak evidence to support recommendations for administration of antibiotic in children with SAM. Their conclusion was that large RCTs were needed to define optimal choices of antibiotic in the treatment of children with SAM with and without complications. They recommended further research into gentamycin and chloramphenical toxicity and pharmacokinetics of ceftriaxone and ciprofloxacin.[12]

Thame. *et al* conducted a retrospective audit of antimicrobial sensitivities of bacteria isolated from children admitted with a diagnosis of malnutrition to the Tropical Metabolism Research Unit (TMRU), University of the West Indies, between January 1995 and December 1999. There

were 150 admissions for severe malnutrition to the TMRU during this period, which was approximately 50% fewer than in a previous TMRU study done ten years earlier, between 1984 and 1989. In the 1995-1999 study, bacteraemia was documented in 10% of 150 severely malnourished children aged between 1 and 31 months of age. The most common organisms isolated were coagulase-negative staphylococci, which represented 40% of the total isolates. The micro-organisms grown were found to be sensitive to amoxicillin/clavulanic acid. The current TMRU treatment protocol for severe malnutrition recommends use of crystalline penicillin plus gentamycin as empirical antibiotic therapy. In this study the researchers concluded that this empiric antibiotic therapy may be inappropriate[13].

In a study done to determine bacterial isolates and antibiotic sensitivities among 140 Gambian children with SAM, Okomo *et al.* found that 38 children had a positive isolate for a pathogen, 60% of which were considered contaminants. Coagulase negative staphylococcus was the predominant contaminant, while the major causes of bacteraemia were non-typhoidal salmonella (13%), *S. pneumonia* (10%), and *E. coli* (8%).All isolates *of H. influenza* in this study were non-sero-typable, and the researchers attributed this to the nearly complete coverage of *H. influenza* type b (Hib) vaccine in the Gambia[14].Though considered a contaminant, coagulase-negative staphylococcus (CONS) was the predominant blood isolate in this study accounting for 50% of isolates. Studies from several different regions have reported CONS rates in blood cultures ranging from 26.7 to 40%. The high CONS in these studies may have been due to the use of 70% alcohol alone to clean the skin prior to veno-puncture, rather than using it in combination with 10% povidone iodine as in other studies[15]. The CONS are prominent component of the microbial skin flora, so that any interruption in the normal skin defense barrier as may occur in severe malnutrition facilitates entry of these organisms into blood stream with resultant bacteraemia[15].

Moreover, CONS is well recognized as a significant cause of sepsis among critically ill immune-suppressed children.[16]. In vitro sensitivity by disc diffusion method showed that 87.5% of isolates were sensitive to ampicillin and or gentamycin. Okomo *et al.* concluded that a combination of ampicillin and gentamycin provided adequate cover among the SAM children in the Gambia[17].

In a study to determine septicemia in kwashiorkor, in blood and stool cultures from 90 black children in South Africa, Scragg *et al.* found the commonest organisms isolated were gram-negative aerobic rods. The mortality rate was highest in the group which developed septicemia, while in patients with negative blood culture, the outcomes were much more favorable, although the majority of them showed evidence of respiratory and /or bowel infection, Scragg *et al.* concluded that routine antibiotic therapy is advisable in the management of kwashiorkor[18].

In a study to determine bacteraemia among severely malnourished children infected and uninfected with HIV-1 in Kampala, Uganda, Bachou *et al*, reported bacterial isolates in 76 blood specimens out of 450 blood specimens. Of the 76 bacterial isolates, 58% were gram negative, *S. typhimurium* (27.6%) and *S. enteritidis* (11.8*). S. aureus* (26.3%) and *S. pneumoniae* (13.2%) were the main gram positive isolates. There was no difference in the risk of bacteraemia by HIV status, age<24 months, male sex or edema except for oral thrush (OR 2.3 95% CI 1.0-5.1) and hypoalbuminemia (OR 3.5 95% CI 1.0 -12.1) More than 80% of isolates were susceptible to ciprofloxacin, ceftriaxone and gentamycin. There was low susceptibility to chloramphenical, ampicillin (<50%) and co-trimoxazole,(<25%)The prevalence of bacteraemia of 17% among severely malnourished children in Bachou et al. study was about the same as the 13% reported by Philips and Wharton[19] in the same hospital in the pre-HIV/AIDS era, and comparable to the 28.7% recently reported from Nairobi by Noorani *et al*.[8] Gram negative organism especially,

non-typhoidal salmonella species, were the predominant cause of bacteraemia in severely malnourished children, supporting early results from Uganda and recent studies from Kenya, Malawi and Ethiopia[8,19,23]. Bachou *et al* also found a high proportion of Gram positive organism particularly staphylococcus aureus. The reason for the predominance of *S. aureus* is not clear as there was no associated skin ulceration. It is possible that vitamin A deficiency in severely malnourished patient might have contributed to this. Several studies have suggested vitamin A deficiency predisposes to *S. aureus* through causing phagocyte dysfunction and decreased compliment activity.[20, 21]Bachou *et al*. study demonstrated high bacterial resistance to commonly used antibiotics such as co-trimoxazole, ampicillin and chloramphenical among both HIV negative and positive children[25]. These findings raise great concern as ampicillin, in combination with gentamycin, is routinely given to all children admitted with severe malnutrition.

In a study done in Mulago Hospital, in Kampala, Uganda to determine the rate of bacteraemia in SAM children in a HIV endemic setting, Babirekere-Iriso *et al*. found that sixty-one (45.5%) had edematous malnutrition and 73 (54.5%) had severe wasting. Fifty-nine (44.0%) were HIV-infected. The prevalence of bacteraemia among the study subjects was 22%. The predominant organisms isolated were gram-negative enteric bacilli (77%) with Salmonella species and *E. coli* contributing 67% of the isolates. Hypoglycemia was significantly associated with bacteraemia (p=0.007). Most organisms were resistant to cotrimoxazole (93.3%), ampicillin (76.7%), gentamycin (66.7%) and chloramphenical (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. In the absence of culture and sensitivity, the

researcher recommended that, ciprofloxacin or ceftriaxone should be considered as first-line antibiotics for severely malnourished children in this setting[10].

In a study to determine the prevalence of bacteraemia among severely malnourished children in Jimma University Hospital, Ethiopia, Shimeles *et al*, found that, bacteraemia could be caused by both gram positive and gram negative bacteria. Among the gram positive bacteria *Coagulase negative staphylococci* species and *S. aureus* were the most common, were as *Enterobacteriaceae* were the most common among gram negative isolates. In this study Shimeles *et al* found, 48.2% of the severely malnourished children had edematous malnutrition and 51.8% severe wasting. This was consistent with similar studies done in Ethiopia in 1992, and in Uganda in 2001[23]. They found the prevalence of bacteremia to be 21%. In this study Gram positive organisms, especially *Staphylococcus* species, were the predominant cause of bacteraemia (68.6%) in severely malnourished children. This was in contrast with previous findings in Ethiopia, Uganda, Kenya and South Africa, were gram negative organisms predominated. The reason for the predominance of *staphylococcus aureus* in this study was not clear and warrants further study. CONS species were the second leading gram positive bacteria following *staphylococcus aureus.* The finding shows CONS species are becoming a great health problems and this agrees with von Eiffel *et al*. observation that the proportion of all bloodstream infections caused by CONS and the overall incidence of true CONS bacteraemia is increasing[26]. These bacteria are normal inhabitants of human skin and mucous membranes and patients with CONS infections are usually immune-compromised, with suppressed immunological response to bacterial infections [27 28]. In Shimeles study, from the overall tested isolates, 86.7% were sensitive to ciprofloxacin, 81.5% to gentamycin, 81.2% to ceftriaxone, 76.9% to cephalothin, 51.7% to trimethoprim-sulphamethoxazole, 33.3% to tetracycline, 21.2% to ampicillin and 15.2% to

chloramphenical. There was increased antimicrobial resistance to septrin, ampicillin and chloramphenical, which might have been related to the higher prevalence of self medication in Jimma town and its surroundings as documented in previous studies [30]. The high rate of resistance to the routinely prescribed antimicrobials such as amoxicillin raised great concern as amoxicillin, in combination with gentamycin, was routinely given to children admitted with severe malnutrition to Jimma University Specialized Hospital [23]. The best combination of antimicrobials in this study was gentamycin and ciprofloxacin, although safety of quinolones was of concern. Hampel *et al* however, reported that the safety profile of ciprofloxacin in children is not substantially different from that of adults [31]. Shimeles *et al.* concluded that bacteraemia constitutes about 21% of the overall severely malnourished in this settings. They recommended further studies to determine the most feasible combination of antibiotics for the management of bacteraemia in severely malnourished children in Ethiopia.

A hospital based cross-sectional survey to identify bacterial isolates and determine antibiotic sensitivity pattern in children with severe Protein Energy Malnutrition (PEM) presenting at the Pediatric Filter Clinic (PFC) of Kenyatta National Hospital (KNH) was done by Noorani *et al*, in 2 to 59 months old children .Ninety-one children, were recruited for the study. There were 30 bacterial isolates from 26 subjects. Ten bacterial isolates were gram positive and twenty gram negative. Isolation rates did not vary by HIV serological status. Twenty one out of the 30 isolates were from blood culture. About 1/3rd of the gram positive isolates were coagulase negative staphylococci, largely resistant to commonly used antibiotics such as erythromycin, ampicillin, cotrimoxazole, chloramphenical and oxacillin. More than half of isolates demonstrated resistance to commonly used oral antibiotics while 80% of all gram positive and negative isolates were sensitive to ciprofloxacin. Aminoglycosides; gentamycin and amikacin, and third generation

cephalosporin such as ceftriaxone and ceftazidime, were found to be effective against most gram-negative isolates. The researchers concluded that, nearly a third (28.9%) of children admitted with severe malnutrition at KNH have concomitant severe bacterial infections; primarily manifesting as bacteraemia. Gram-negative agents were responsible for most severe bacterial infections in children admitted at the KNH, regardless of their HIV serological status. The researchers recommended then that blood culture should be included in the initial septic screening of severely malnourished children at KNH. In the absence of culture and sensitivity information, ciprofloxacin be considered among the first line options in the empirical treatment of severe bacterial infections among these children. They noted that further clinical trials were needed to evaluate in-vivo effectiveness of various single or combination antibiotics[8].

These studies demonstrate that bacteraemia is a common occurrence in severely malnourished children.

STUDY JUSTIFICATION

Establishing the pattern of infection and antimicrobial sensitivities in local environment is critical to rational use of antibiotics and development of management algorithms. Severely malnourished children have a depressed immune status and it is critical to give the correct antibiotic combination in order to facilitate their quick recovery. Available evidence from other parts of the world show high prevalence of bacteraemia among SAM children and bacterial resistance to current WHO antibiotic protocols. There is a need to gain knowledge on the local pattern of antibiotic sensitivities. This study is will inform rational use of antibiotic among the severely malnourished children in Kenyan District Hospitals.

STUDY QUESTION

What is the prevalence of bacteraemia in severely malnourished children in Mbagathi District Hospital?

What bacteria are isolated in blood and what is their sensitivity pattern to current WHO recommended antibiotics in the SAM children?

OBJECTIVES:

Broad objective

To determine the prevalence of bacteraemia in SAM children at Mbagathi District Hospital and its association with the clinical and examination characteristics

Primary objective

- To determine the specific blood bacterial isolates in SAM in Mbagathi district hospital.
- To determine the sensitivities of the bacterial isolates to the WHO recommended antibiotics in Mbagathi District hospital.

Secondary objective

- To determine the association of clinical history and examination findings in the bacteraemic and non bacteraemic SAM children.

STUDY METHODOLOGY

The study design:

This was a cross sectional hospital based survey.

Setting: Mbagathi District Hospital in Nairobi Kenya.

The study was conducted at Mbagathi District Hospital that has a pediatric ward with a bed capacity of 45. The paediatric unit at the hospital is run by two paediatricians and 5 paediatric clinical officers. The monthly average admission and outpatient attendance for children aged less than 5 years of age at the hospital is approximately 340 and 2600, respectively. The catchment area for the hospital is the informal settlements of Kibera and Golf Course within Dagoretti division.

Study population

It comprised 2 to 59 months old children with severe malnutrition seen at Mbagathi District Hospital.

Sample size

The sample size was calculated using Fisher's formula for prevalence studies.

$N= (z1-\alpha/2)^2 \times p\ (1-p)/d^2$

N=minimum sample size

α =level of significance set at 5%

p = estimated proportion of bactaraemia in severely malnourished children in East Africa (9.2% to 36% Babirekere-Iriso *et al.*[10] – The upper bound of the reported range (36%) was used in the

sample size calculation because it yields the maximum possible sample size to allow estimation of the population prevalence of bacteraemia with the specified precision (d).

$Z1-\alpha/2 = 1.96$ and is the value for standard normal distribution curve at a significance of 5%

d = degree of precision. Value used is plus or minus 10%.

$n= (1.96^2 \times 0.36 \times 0.64)/0.1^2=88$

Thus the minimum required sample size was 88 severely malnourished children.

INCLUSION CRITERIA

- Children aged 2 to 59 Months seen at Mbagathi District Hospital meeting the criteria for severe acute malnutrition as defined.

EXCLUSION CRITERIA

- Children on follow up after discharge from ward and still on antibiotics.
- Children that were in the ward and receiving antibiotics.
- Known HIV positive children that were on cotrimoxazole prophylaxis.
- Children on penicillin prophylaxis.
- Children with length less than 49cm because there is no standard WHO Z SCORES.

DATA COLLECTION PROCEDURE

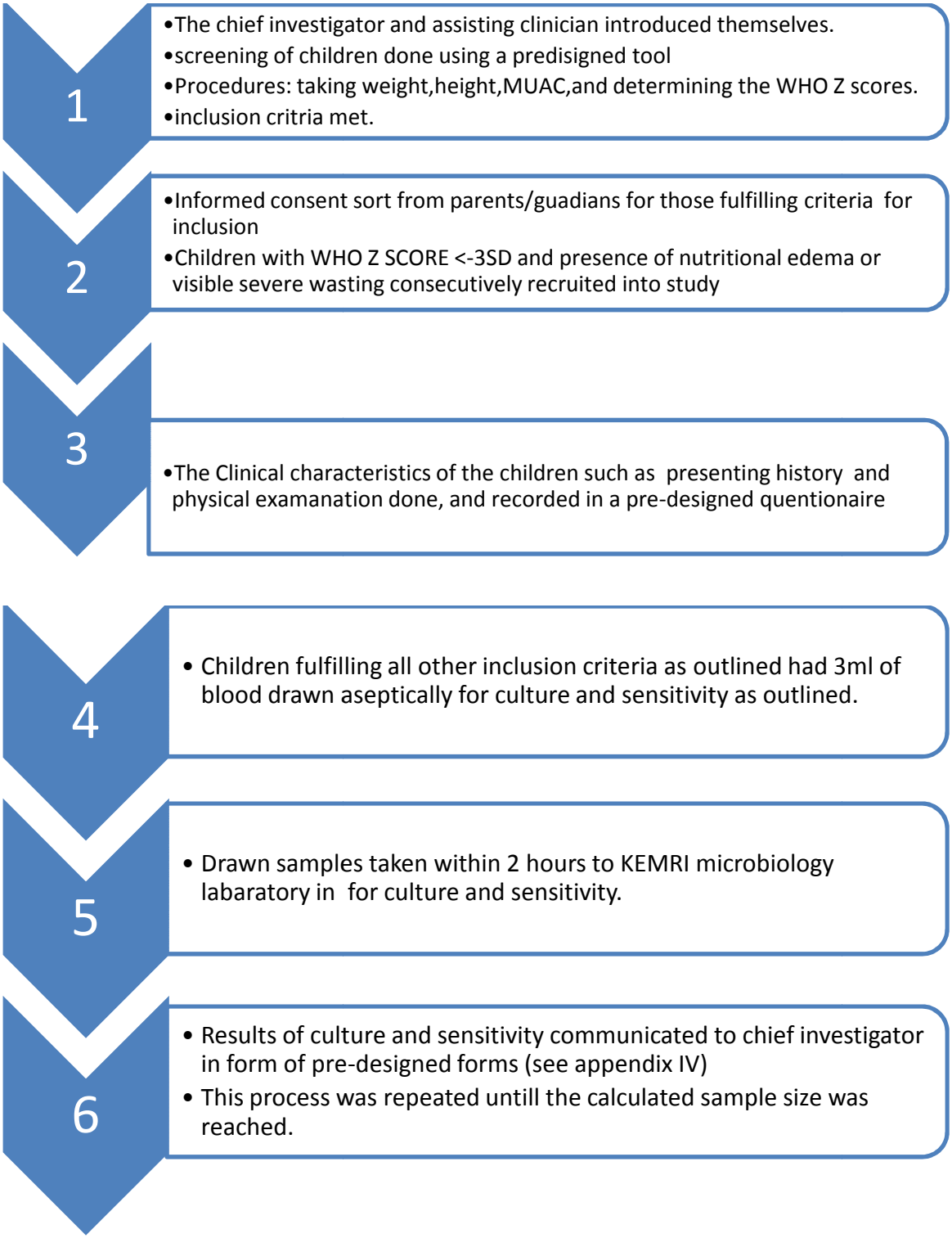
Prospective data collection was done by the principal investigator or a clinical assistant during admission of severely malnourished children at the paediatric filter clinic and those already in ward but not yet on antibiotics. The principal investigator was based at the clinic daily, including weekends from 8 am to 6 pm. Between 6 pm and 7 am, a clinical officer trained in management of malnourished children examined all children presenting to the hospital and recruited those meeting study criteria.

Sampling

A probability based sampling method was used to enroll patients into the study. A sampling frame was compiled from all SAM patients seen at the outpatient clinic and pediatric ward and meeting the study criteria. After the compilation of a sampling frame, each day, a sample was drawn from the population of malnourished children attending Mbagathi District Hospital using simple random sampling. All children registered at pediatric clinic and those admitted and not already on antibiotics had their weight, height, and length taken. These data was entered into a screening tool (appendix 111). From these data the weights for height Z score were determined using the standard WHO table appropriate for age and gender. The children were then screened to determine whether they were eligible for the study.

For the consecutively screened children who met the inclusion criteria; an informed consent was sought from the parents/guardian. For parent that consented to be in the study a pre-designed questionnaire was administered to record the clinical history and physical examination findings (appendix II)After taking the clinical history and doing the physical examination, 3mls of blood was drawn from the peripheral vein aseptically as outlined in the laboratory methods section.

A FLOW CHART ILLUSTRATING THE SEQUENCE OF RECRUITING SAM CHILDREN INTO THE STUDY



The WHO measuring technique

All patients were weighed and had height measured to determine eligibility for inclusion in the study based on the main WHO anthropometric indices – WAZ, HAZ and WHZ.

Weight:

Body weight measurements were conducted using a Salter scale (maximum capacity-25 kg). Daily calibration of the scale was done by checking the scale against a known weight of 10 kg or less each morning before use. The weighing pants were attached to the lower hook of scale, and the instrument was adjusted to zero. The clothes of the child were removed and the pan was put on. The weight was read to the nearest 0.1 kg with the scale at eye level. The measurer read the value out loud; the assistant repeated it and recorded it on the recording form.

Height:

A measuring board was used for measuring length in children who were less than two years of age (less than 85 cm in length). The child was placed gently on the board with head against the fixed vertical part. The soles of feet was placed near the moving part(cursor)The child was made to lie straight in the middle of the board, looking directly up. The assistant held the feet firmly against the feet board and placed one hand on the knees of the child. The measurer gently held child head, placed the cursor against the crown of the head and read out the length to the nearest 0.1 cm. The assistant repeated the reading and recorded it in the record form. Length is slightly more (0.5cm) than height due to the effects of gravity. In view of this 0.5cm was subtracted from all lengths taken.

For children 2 years of age and above (over 85 cm in length), height was taken using a stadiometer. The barefoot child was made to stand straight on a horizontal surface of stadiometer with the heel, buttock and occiput against vertical board of stadiometer. The fixed head board of stadiometer was then lowered onto the child's crown of the head. The length was read to the nearest 0.1cm. The measurer read out loud; the assistant repeated it and recorded it on the recording form.

Study recruitment was done at the pediatric outpatient clinics after obtaining consent by the chief investigator and a trained clinical officer based at Mbagathi District Hospital. The children who met the selection criteria were consecutively recruited.

Specification of equipments for anthropometric measurement:

- Stadiometers
- Infant weighing scales(salters)
- Standard weighing scales(salters)

BLOOD SAMPLE COLLECTION PROCEDURE

The clinician washed hands with soap and water for 15 sec as per WHO guidelines and wore sterile gloves for this procedure. A Blood sample was aseptically drawn from a peripheral vein after thoroughly cleaning the skin with 70% alcohol swab and 10% povidone iodine for 30 seconds on dry skin and 2 minutes on a wet skin. 3ml of blood was drawn using a 10ml cc syringe and a 23-gauge needle. Needles were changed. The drawn blood was injected into the culture bottles (aerobic and anaerobic) after swabbing the cap with spirit/povidone iodine solution. The labeled samples (serial number, sex and age) were taken to the KEMRI Centre for

Microbiology Research based for culture and sensitivity within two hours. Samples were transported while in cold boxes.

BLOOD CULTURE

Three mls of venous blood was obtained from each child and cultured in 25 ml of brain heart infusion broth containing para-aminobenzoic acid and incubated in 5% $C0_2$ at 37^oC in a BACTEC automated incubator. Blood cultures were sub-cultured after a positive signal from the incubator onto blood, chocolate and MacConkey agar plates. An optochin disc was placed onto the blood agar plate to detect any pneumococcal. The blood cultures were subsequently observed for a further 7 days for signs of bacterial growth (gas production and/or turbidity). A final subculture was performed for all blood cultures on the 8^{th} day regardless of the state of bacterial growth. Routine bacteriology and identification of the species of bacterial isolates was done using a Gram stain examination, biochemical tests for Gram positive and Gram negative pathogens and typing for confirmation of species.

ANTIMICROBIAL SUSCEPTIBILITY TESTING

Using Isosensitest (Oxoid, Basingstoke, UK) Initial sensitivity tests of bacterial isolates were performed using the disk diffusion technique for all commonly used WHO antimicrobials for empiric treatment of SAM. These included; amoxicillin ,ampicillin 10µg, trimethoprim 5µg, sulphamethoxazole 100µg, chloramphenical 30µ and gentamycin 10µg. Minimum inhibitory concentrations (MICs) were done using the E-test strips (AB BIODISK, Solna, Sweden). Results were interpreted according to the guidelines provided by the Clinical Laboratory Standards Institute (2010) and reported as sensitive, intermediate or resistant.

CONTROL FOR POSSIBLE CONTAMINATION IN THE LABORATORY

The laboratory employed the use of a biphasic culture system for blood cultures. Both liquid and solid media were in the same bottle. The inoculum was added to the liquid media and when subcultures were to be made, the bottle was simply tilted to allow liquid to flow over the solid media.

Participating laboratory

Culture and sensitivity testing was done at the KEMRI centre for microbiology research based at KNH. Dr.Sam Kariuki, the chief research scientist at the centre supervised the culturing and sensitivity testing during the entire study.

Maintaining confidentiality and sharing of laboratory results with the clinicians at Mbagathi.

The laboratory received consecutively numbered sample with no names and after processing, those results with bacterial isolates were communicated using the laboratory record form (see appendix 4) to chief investigator, who upon receipt of these results informed the pediatrician at Mbagathi. The chief investigator was the only one who had the names of children under investigation and only he could link these names to serial numbers of samples.

DATA MANAGEMENT

Data collection

A data collection form was be used to record anthropometric measurements, the socio demographic data, the history and physical examination findings of the study subject. A pre-designed form was used to record laboratory data.

Data analysis

Data obtained was coded and entered into Microsoft access data base. Data cleaning was done prior to analysis and any inconsistencies in data were verified against the original questionnaires before amendments were made. Data were then transferred to Statistical Package for Social Sciences (SPSS) version 18 for analysis. Descriptive statistics were used to summarize data using means, standard deviation and median for continuous variables including age and Z scores. Categorical data like patients' gender, proportions with specific clinical features were summarized by calculating percentages which were presented as frequency tables, and charts. The main outcome was prevalence of bacteraemia determined by calculating the percentage of severely malnourished patients with any bacterial isolate on blood culture. The Chi square test and Fishers exact test were used to compare categorical data among children with and those without bacteraemia. Similar comparisons for continuous data were conducted using the student t test.

ETHICAL CONSIDERATION

APPROVAL

The research proposal was submitted for review to the Ethics and research committees of University of Nairobi and Mbagathi District hospital. The study only commenced after ethical approval had been granted.

CONSENT

Patients who were willing to participate in the study were required to provide consent in writing.

No names were disclosed in the study report and any personal information obtained was held in strict confidentiality.

PROCEDURES

All procedures performed as part of the study did not interfere with the standard of patient care within these institutions. No patient was subjected to additional procedures not specified in the proposal.

RESULTS

All laboratory results that were required by the patient and/or physicians were made readily available to them in form of written reports. All findings were readily availed for scrutiny by the institutional review boards of participating hospitals. Laboratory results with bacterial isolates were immediately communicated to patients and /or pediatrician.

RESULTS

A total of 90 children seen at Mbagathi District Hospital with severe acute malnutrition were included in this study. The demographic characteristics, clinical features, prevalence of bacteraemia and correlates of bacteraemia in this group of children are presented in the following sections.

Demographic characteristics

The mean age of the patients with severe malnutrition was 16 months (SD = 8.0), and the age range was 5 to 48 months. As shown in table 1 most (69.66%) children with SAM were between the ages 12 and 35 months. There were 47 (52.22%) males and 43(47.78) females with SAM in the study.

Table 1: Demographic characteristics of severely malnourished children

		Frequency (N = 90)	Percent
Age in months	2 to 5 months	1	0.01
	5 to 11 mo	23	25.84
	12 to 35 mo	62	69.66
	36 mo and above	4	4.49
sex		90	100
	Male	47	52.22
	Female	43	47.78

The overall prevalence of bacteraemia among SAM patients was 30% (27 out of the 90 children enrolled). As shown in figure 1, *S. aureus* was the most common isolate 19 (27), followed by *S. typhi* 4 (27), *S. epidermidis* 3 (37) and *E. fecalis* 1(27).

Figure 1 shows the total number of bacterial isolates in severely malnourished children at Mbagathi Hospital. Twenty-seven out of the 90 children sampled had a bacteria isolated in blood. *S. aureus* and *S. typhi* were the predominantly isolated bacteria in the study.

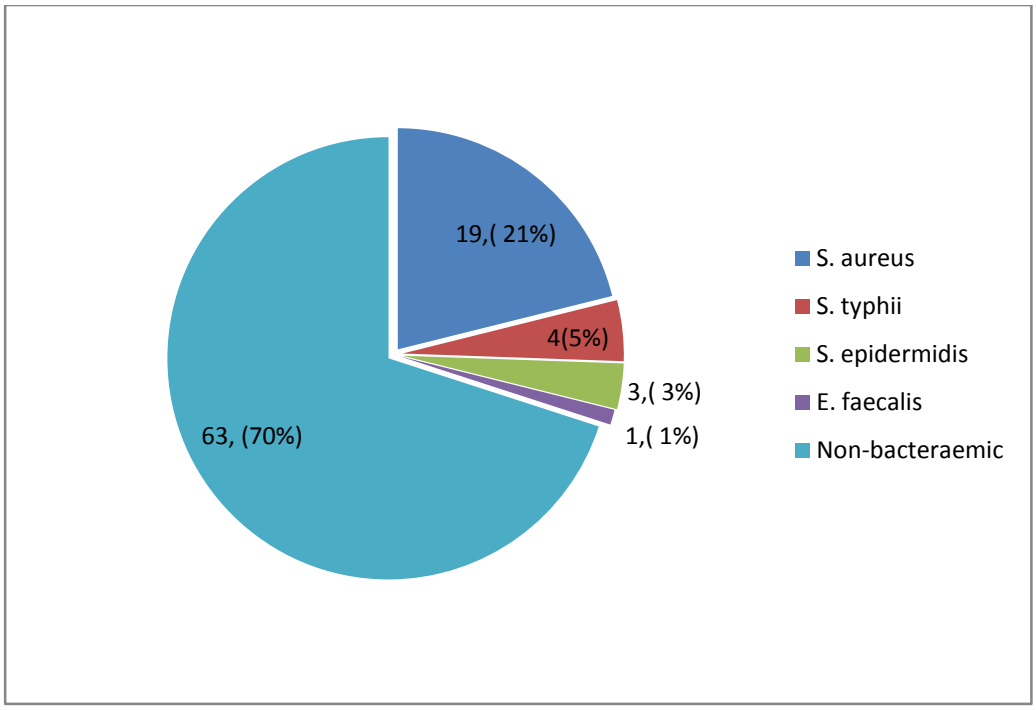


Figure 1: Proportion of bacterial isolates in SAM children at Mbagathi District Hospital

Table 2 compares demographic characteristics of bacteraemic and non-bacteraemic severely malnourished children. There was no statistically significant difference in gender and occurrence of bacteraemia in SAM children (p = 0.679). There also was no difference found among different ages of children with SAM and the prevalence of bactaraemia (p = 0.853).

Table 2: Bacteraemia and demographic characteristics

	Proportion of bacteraemic N=27		**Proportion of Non bacteraemic N=63**		
	n/N	**%**	**n/N**	**%**	**P value**
Male	15/27	55.6	32/63	50.8	0.679
Age					
5 to 11 mo	8/27	29.6	15/63	24.2	0. 853
12 to 35 mo	18/27	66.7	44/63	71.0	
36 mo +	1/27	3.7	3/63	4.8	

As shown in this table 3 there was a statistical significant difference in occurrence of bacteraemia in children with diarrhea and vomiting compared to those without bacteraemia p=0.008 and p=0.05 respectively. Diarrhea was more common among bacteraemic (77.8%) compared to non-bacteraemic (47.6%) children. Similarly 88.9% of bacteraemic children presented with vomiting compared to 69.8% of non bacteraemic children.

Table 3: Bacteraemia and clinical history

	Bacteraemic (n = 27)		**Non bacteraemic (n = 63)**		
	n/N	**%**	**n/N**	**%**	**P value**
Diarrhea	21/27	77.8	30/63	47.6	0.008
Vomiting	24/27	88.9	19/63	69.8	0.050
Cough	11/27	40.7	34/63	54.0	0.250
Difficult breathing	9/27	33.3	20/63	31.8	0.883
Fever	19/27	70.4	38/63	60.3	0.364
Convulsions	2/27	7.4	6/63	9.5	0.746
Inability to drink	15/27	55.6	44/63	69.8	0.191

Table 4 compares physical examination findings of bacteraemic and non-bacteraemic severely malnourished children. There was higher likelihood of bacteremia in children with skin lesion p=0.008.A significant statistical difference was also found in the occurrence of oedema between the bacteraemic and non-bacteraemic children p=0.02

Table 4: Bacteraemia and Physical examination

	Bacteraemic (n = 27)		**Non bacteraemic (n = 63)**		
	n/N	**%**	**n/N**	**%**	**P value**
Tachypnea	19/27	70.4	41/63	65.1	0.626
Lymphadenopathy	10/26	38.5	30/62	48.4	0.394
Skin lesions	19/27	70.4	25/63	39.7	0.008
Jaundice	6/27	22.2	14/62	22.6	0.970
Pallor	26/27	96.3	53/62	85.5	0.138
Edema	8/27	29.6	35/62	56.4	0.020
Oral thrush	17/27	63.0	31/62	50.0	0.259

Findings of the multivariable logistic regression analysis to identify independent predictors of bacteraemia are shown in table 8. Three out of the five characteristics that showed significant associations with bacteraemia in the univariate analysis, namely edema, skin lesions and diarrhea were significantly associated with bacteraemia in the adjusted analysis. The odds of bacteraemia in severely malnourished children was five-fold higher in children with edema (OR = 5.92; 95% CI 1.81-19.37), skin lesions (OR = 5.08; 95% CI 1.54-16.69) or diarrhea (OR = 5.63; 95% CI 1.3-24.45) compared to children without these features.

Table 5: Multivariable regression analyses of predictors of bacteraemia in SAM children

	Odds ratio (95% CI)	Std. Error	Z statistic	P value
Age (in months)	0.98(0.92-1.04)	0.03	-0.66	0.509
Edema present	5.92(1.81-19.37)	3.58	2.94	0.003
Skin lesions present	5.08(1.54-16.69)	3.08	2.68	0.007
Diarrhea	5.63(1.3-24.45)	4.22	2.31	0.021
Vomiting	0.88(0.16-5.01)	0.78	-0.14	0.887

Bacterial isolates and antibiotic sensitivities

Penicillin sensitivity

All the bacterial isolates were strongly sensitive to amoxicillin (Figure 2). *S. aureus* in-vitro sensitivity to ampicillin was below 25%. The single *E. faecalis* isolate was resistant to ampicillin but sensitive to amoxyl. All three S.epidermidis isolates were sensitive to amoxyl while two of these isolates were resistant to ampicillin (figure 3).

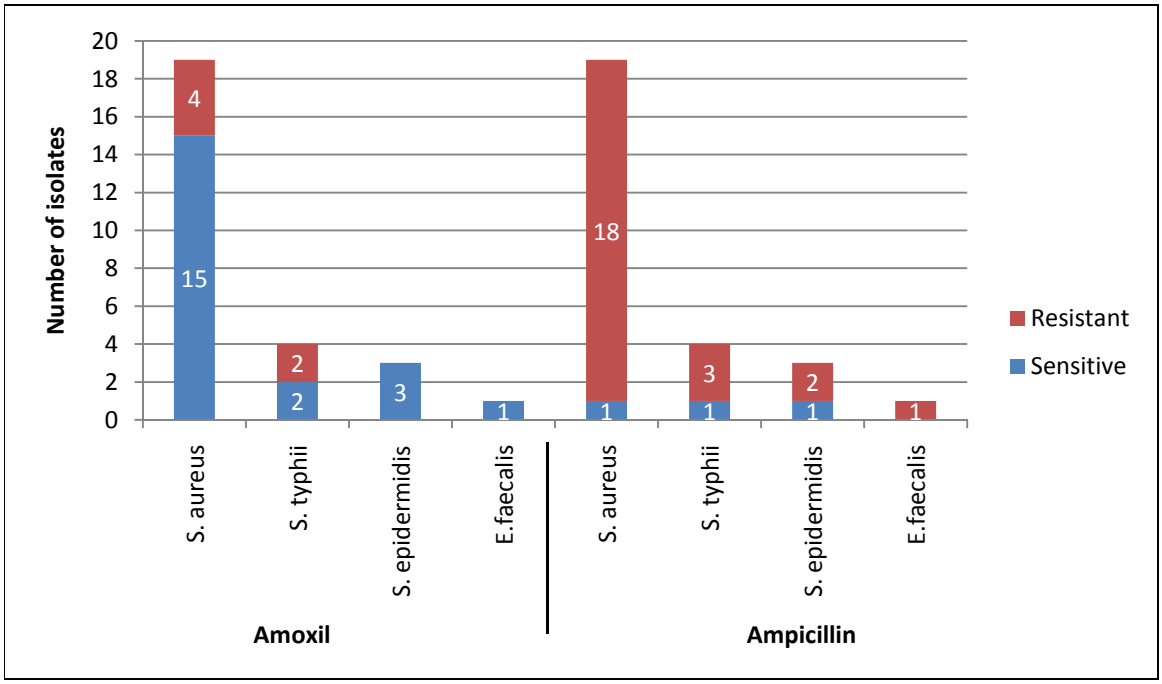


Figure 3: Bacterial isolate sensitivity to amoxicillin and ampicillin

Figure 3 shows isolate sensitivity to additional WHO recommended antibiotics. *S.aureus* isolates were sensitive to gentamycin and chloramphenical but significant resistance to Septrin was documented. The single *E.fecalis* was resistant to gentamycin and Septrin and only sensitive to chloramphenical. Three out of the 4 *S.typhi* were resistant to both gentamycin and Septrin (figure 4). *S.epidermidis* isolates (n = 3) were sensitive to Gentamycin.

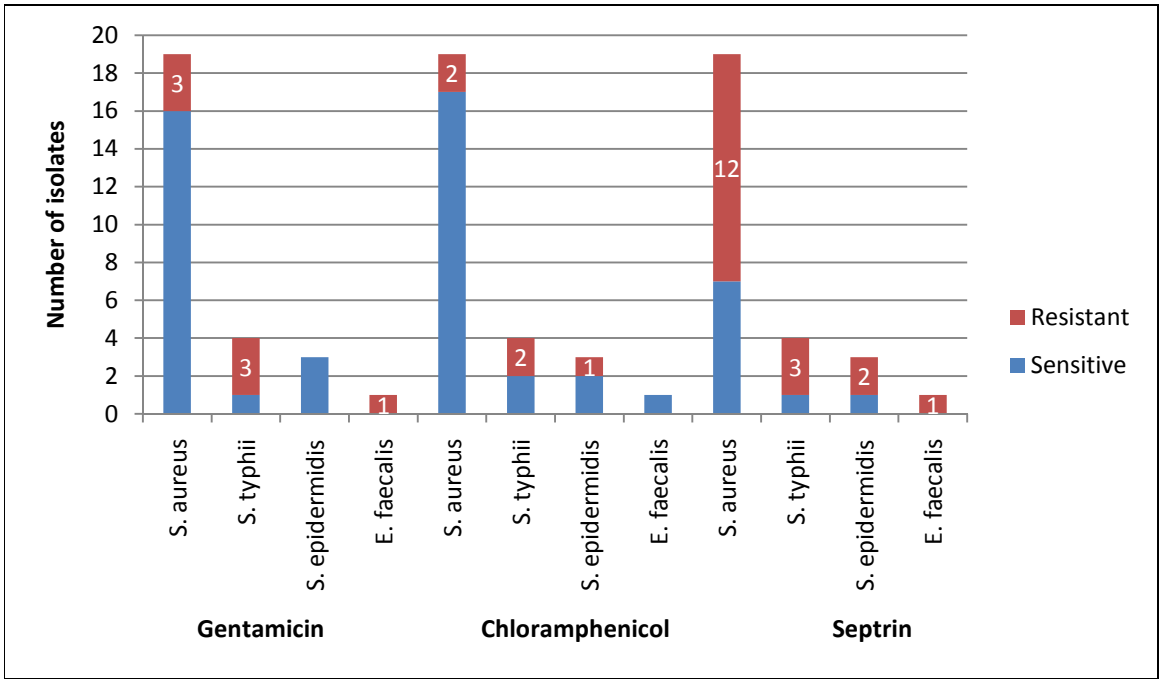


Figure 3: Bacterial isolate sensitivity to Septrin, gentamycin and chloramphenicol

THE OVERALL SENSITIVITY PATTERN OF BACTERIAL ISOLATES

The overall sensitivity pattern of the isolates was 77.7% to amoxicillin, 33.3% to septrin, 74% to gentamycin, 81.4% to chloramphenical and 11.1% to ampicillin.

Table 6: The overall sensitivity pattern of the bacterial isolate in SAM

	amoxicillin	septrin	gentamycin	chloramphenical	ampicilin
S.aureus	15(19)79%	7(19)36.8%	16(19)84.2%	17(19)89.5%	1(19)5.3%
S.typhi	2(4)50%	1(4)25%	1(4)25%	2(4)50%	1(4)25%
S.epidermidis	3/(3)100%	1(3)33,3%	3(3)100%	2/(3)66.7%	1/(3)33.3%
E.fecalis	1(1)100%	0(1)0%	0(1)0%	1(1)100%	0(1)0%
SENSITIVITY	21/27(77.7%)	9/27(33.3%)	20/27(74%)	22/27(81.4%)	3/27(11.1%)

Discussion

The overall prevalence of bacteraemia was 30 %(27 out of 90) among the severely malnourished children in Mbagathi District Hospital. This figure is slightly higher than that of a similar study done at Kenyatta National Referral hospital by Noorani *et al* who reported a prevalence of bacteraemia of 28.9%[8]. Though statistically insignificant the slight difference may be attributed to the fact that most severely malnourished children seen at KNH are often referrals from the District Hospitals were they may already have been on antibiotics.

Regionally this figure is still higher compared to 22% reported by Babirekere –Iriso *et al* in their study of bacteraemia in children with SAM in HIV endemic setting in Kampala Uganda[10]. The 21% reported by Shimeles *et al* in Ethiopia [23] and 27% reported by Okomo et al in the Gambia[17] .Elsewhere in the world, Thame *et al*. in West indies reported a prevalence of 10% [13].

In Mbagathi coagulase positive organisms, mainly S. aureus were the predominant isolates (*S. aureus* 21%); others included *S. typhi* (4.4%), *S. epidermidis* (3.3%) and *E. fecalis* (1.1%).This contrast with recent studies in Kenya by Noorani *et al* who found that 8.67 % of isolates were CONS. It's however comparable to Ethiopian study by Shimeles *et al*. who reported a predominance of *staphylococcus aureus*. In Uganda, Babirekere-iriso et al reported high prevalence of gram negative bacteria mainly *S. typhimurium* (27.6%) and *S .enteritidis* (11.8%). Mbagathi study also found *S. typhi* bacteraemia though at lower percentage (4%). It was also lower than that found in Uganda by Bachou *et al.* of 27.6% [25]. Green SD *et al*. in their study reported mortality occurred significantly more often when children fell ill with Salmonella bacteremia in the late rainy season, coinciding with the peak of malnutrition, than in the dry season (RR = 2.62).Chloramphenicol-resistant S. typhi isolated were significantly associated with increased mortality (RR = 3.19)[35].

Our study and that of Shimeles *et al*. suggest a change in epidemiology from the predominant gram negative etiologies to gram positives. Other bacteria isolated in this study were *S. Epidermidis* and *E.fecalis*. In a study done by Richards MJ, *et al* they found the top 3 pathogens in bloodstream infections were coagulase-negative staphylococci (38%), *Enterococcus* (11%), and *S aureus* (9%)[33].

Most of the children seen at Mbagathi District Hospital had an intravenous catheter already fixed as part of the routine standard of triage for the very sick children. Studies done on hospital acquired infection have shown strong association between presence of catheter and blood stream infection [34].

The reason for *S. aureus* predominance in this study needs further study. It is known that this bacterium is ubiquitous and may be a part of human flora found in the axillae, the inguinal and perinea areas, and the anterior nares. Von Eiffel *et al* described 3 patterns of carriage: those who always carry a strain, those who carry the organism intermittently with changing strains, and a minority of people who never carry *S. aureus* **[26]**.Persistent carriage is more common in children than adults. Nasal carriers may be divided into persistent carriers with high risk of infection and intermittent or no carriers with low risks of infection.

The odds of bacteremia in SAM children was fivefold higher in children with skin lesions (OR=5.08; 95% CI 1.54-16.69) Given the fact that S. aureus was the predominant isolate and also the fact that it's found in the skin it is possible that the portal of entry was the skin. Other studies have reported different association. Bachou *et al*. study in Kampala reported an association between bacteraemia and presence of oral thrush and hypoalbunemia**[25]**.They reported no association in social demographic characteristics, HIV status and oedema. In our study at

Mbagathi we found there was a fivefold odds ration of SAM children with oedema having bacteraemia (OR5.92 CI 95 1.81-19.37). Other studies have suggested that vitamin A deficiency that is common in severely malnourished children may predispose *to S. aureus* infection[19]. It's thought vitamin A deficiency predisposes to staphylococcus aureus through phagocyte dysfunction and decreased compliment activity[21].

The odds of bacteremia in the SAM at Mbagathi was fivefold higher in children with diarrhea (OR=5.63; 95% CI 1.3-24.45) than the non bacteraemic ones. Talbert et al in their study on diarrhea complicating SAM found that bacteraemia and diarrhea increased the risk of death.[32]This association coupled with the predominance of *S. aureus* bactaraemia in this study is significant. It is known that *S. aureus* elaborates toxins that can cause specific diseases or syndromes and likely participate in the pathogenesis of staphylococcal infection[32]. Enterotoxin-producing strains of *S. aureus* cause one of the most common food borne illnesses. The most common presentation is acute onset of vomiting and a watery diarrhea 2-6 hours after ingestion. As to whether the diarrhea found in this study was primarily due to S. aureus or the other bacterial isolates requires further investigation.

This study found high bacterial resistance to co-trimoxazole and ampicillin. Cotrimoxazole resistance profile was as follows: To *S. aureus* (63.2%), *S. typhi* (75*%), and S. epidermidis* (66.7%) *E. fecalis* (100%). Ampicilin resistance profile was as follows: To *S. aureus* (94.7), *S. typhi* (75%) *S. epidermidis* (66.7%) and *E. fecalis* (100%)These findings are consistent with earlier studies in KNH, Kenya and Mulago Hospital Uganda [8,25].In Kampala study Bachou *et al,* reported low susceptibility to ampicilin (<50%)and cotrimoxazole (<25%) .In another study, Babirekere-Iriso *et al* showed the following resistance pattern to bacterial isolates: cotrimoxazole (93.3%), ampicilin (76.7%) gentamycin (66.7%) and chloramphenical (60%). In our study the

sensitivity pattern of chloramphenical (81.4%), gentamycin (74%) and amoxicillin (77%) was high. Our study and that of similar studies point to an increasing resistance of bacterial to the current antibiotics recommended in the empiric treatment of bacteraemia in SAM children. This raises great concern as their combination is routinely given to all children admitted with SAM.

Limitations

A limitation of this study was the uncertainty of information given on prior use of antibiotics and prior history of hospitalization that may be associated with bacterial resistance and types of isolates. Large sample size will be required to conclusively define the relationship between clinical history, examination findings and bacteremia in SAM.

Strength

The strength of this study was in the aseptic technique of swabbing the skin with 70% alcohol and povidone iodine and the reliability of the culturing process at KEMRI laboratory.

Conclusions

The prevalence of bacteraemia in severely malnourished children in this setting was 30 %. A multivariate regression analysis showed the independent risk factors for bacteraemia were: acute diarrhea, oedema and severe skin lesion. This study found a predominance of coagulase positive *staphylococcal aureus* among the bacterial isolates. Other isolates included *S. typhi*, *S.epidermidis* and *E. fecalis*. These isolate showed general in-vitro sensitive to amoxicillin, chloramphenical and gentamycin and resistant to both ampicillin and cotrimoxazole.

Recommendation

The bacterial isolates in this study were susceptibility to gentamycin, amoxyl and chloramphenical. We recommend the continued use of these antibiotics but tailored to current WHO guidelines. Given the strong association between presence of skin lesions and bacteraemia in SAM found in this study, proper management of skin infection could affect morbidity. *S. aureus* almost never is a contaminant when isolated from blood cultures.

It is evident from this study and other reviewed studies that bacteraemia is common among the SAM children. District hospitals should therefore be facilitated to have the capacity to do routine blood cultures in the severely malnourished children .There should be continual review of the antibiotic protocols to ensure effective treatment.

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APPENDIX 1

Consent form information sheet

Title:' The blood bacterial isolates in severely malnourished children and their antibiotic sensitivity to WHO recommended antibiotics'

Investigator: Dr.Wycliffe Kimani Ngaruiya

P.o. box 38078-00623 Nairobi

University of Nairobi-Department of pediatrics and child health

Mobile: 0723511013

Introduction:

I am a medical doctor and a postgraduate student in pediatrics. As part of my research dissertation, I am investigating the bacterial isolates in severely malnourished children and their antibiotic sensitivity to the WHO recommended antibiotics' wish to request for your child's participation in this research project. You do not have to give and immediate response. Please feel free to ask any questions regarding the research or seek any clarification now or later.

The Purpose of research:

Severe malnutrition is associated with significant mortality and this may be attributable to bacterial pathogens that have become resistant to the current recommended antibiotic protocols. The reason I intend to do this research is to find out what bacterial pathogens are common in blood of severely malnourished children and if they are sensitive to the current WHO recommended antibiotics.

Participant selection:

The reason your child has been chosen for this research is that he or she has been noted to have signs of severe malnutrition based on very low weight for height by visible severe wasting or by presence of nutritional edema.

Voluntary participation:

It is up to you to decide whether your child will participate in this study or not. This research will not interfere with the care that your child is receiving from this hospital and you are free to withdraw from the research at any time.

Procedures and protocols:

If you agree to your child participating in this research, we will request to:

- take history of your child
- Do a physical examination of your child
- Take weight, length or height of your child.
- Withdraw only once 3 mls of blood from the forearm vein of your child for culture and sensitivity.
- The child will feel some pain from needle prick, but this should last only for a few minutes.

Duration

This research project will go on for 3 months, but we will meet your child only once in the outpatient clinic.

Benefits from the study

During the history taking and physical examination, any new information found will be relayed to the ward doctor with your permission so that he or she can give the appropriate treatment. Knowing what bacterial pathogens could be present in your child's blood and their antibiotic sensitivity will also help in making your doctor choose the best antibiotic to give your child.

Cost

I will do the blood tests on your child at no cost but no money will be paid to you for taking part in the study.

Risk

The research will not involve any treatment that is not part of what the doctor will be giving. There is no risk to the care, which your child will be receiving from your doctor.

Confidentiality

All the information that we will gather about your child will be kept highly secret. Your name or that of the child will not be used at any time in the report of this

Research

Sharing of the results:

The results, which will come from this research, will be used broadly and may be sent to medical journals to be published.

Right to refuse or withdraw:

You may refuse your child to participate at any time or even withdraw after agreeing to consent.

WHO TO CONTACT:

Prof A N Guantai

Secretary, KNH/UON-ERC

Kenyatta National Hospital

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Tel: 726300-9

Fax: 725272

To indicate that you understand the conditions of this study and that you consent your child to participate in it, please sign or put your thumb print in the space provided in the consent certificate.

ENGLISH CONSENT FORM

A study to determine the blood bacterial isolates and their antibiotic sensitivity to the WHO recommended protocols.

ENGLISH CONSENT CERTIFICATE:

I----------voluntarily consent to my child participating in this research study. All the procedures and details of the study have been explained to me and will involve having a blood sample taken for culture and sensitivity testing to WHO recommended antibiotics. I understand that the identity of my child in this study will be treated as confidential. The results of this study, including laboratory or any other data, may be published for scientific purposes but will not give my name or that of my child or include any identifiable reference to me.

Name of the child----------

Parent or guardian signature----------

Date: ----------

Investigators signature: ----------

Date: ----------

Signature of person obtaining consent: ----------

SWAHILI CONSENT CERTIFICATE

MAELEZO KWENYE CHETI CHA RIDHAA

Utangulizi:

Mimi ni daktari katika chuo kikuu cha Nairobi kule ambako ninajifunza taluma ya matibabu ya watoto .Ninahitajika kufanya utafiti kama njia moja itakayopeleka mimi kuhitimu kwa taluma hii.Ningependa kufanya utafiti kwa watoto walio na ugonjwa wa utapiamlo.Lengo langu ni kubaini ni viini vipi vinapatikana kwa damu ya hawa watoto vivavyoweza kuzababisha magonjwa.Pia ningependa kubaini kama viini hivi vinaweza kutibiwa na dawa zilisopendekezwa na shirika la afya ulimwenguni.Ningependa kuomba kushiriki kwa mtoto wako kwa utafiti huu.Uko na uhuru wa kuuliza maswali yeyote yale yanoyoambatana na utafiti huu.

Kusudi la utafiti huu.

Utafiti huu utazaidia kufahamu ni viini vipi vinasababisha magonjwa kwa watoto wilio na shida ya utapiamlo.Hii itabelekea kuwepo kwa utumizi bora wa madawa.

Uchaguzi wa washiriki.

Watakao shiriki kwa utafiti hii ni wale ambao baada ya kutoa ridhaa kwa hiari yao watakuwa wamepimwa uzani na urefu na kuthibitishwa kuwa na shida ya utapiamlo.

Kujitolea kushiriki.

Kukubali mtoto Kushiriki kwa utafiti huu ni kwa hiari yake mtu mwenyewe.Hakutakwepo na kulazimishwa ama kushurutishwa.Ni haki ya kila mshiriki kujiodoa kwenye utafiti huu wakati

ule wowote.kujiondoa kwa mshiriki kwenye utafiti huu hakutapelekea yeye kunyimwa matibabu anayostahili.

Yale ambayo mtoto atafanyiwa:

Mtoto yeyote ambaye atashiriki kwenye utafiti huu atafanyiwa yafuatayo.

- Kuulizwa maswali ili kufahamu ni shida ipi iliteta mtoto hospitali.
- Kupimwa uzito
- Kupimwa urefu.
- Kutolewa kiwango kidogo cha damu kwa minajili ya kuchunguza viini visababishazo magonjwa.
- Mtoto atahisi uchungu kwa muda mfupi tu.

Muda wa utafiti:

Utafiti huu unakuzudiwa kufanyika kwa muda wa miezi mitatu tu.Mtoto wako atakutana na mtafiti mkuu mara moja tu.

Je mtoto wangu atanufaika vipi kwa kushiriki kwa utafiti huu

Katika ile hali ya kueleza shida za mtoto wako na pia pale nitakapo mpima mtoto wako kama kuna mambo mapya nitapata ,nitamfahamisha muuguzi wako ili mtoto afaidike.haya nitafanya tu pale unipeapo ruhusa.

Hapatakwepo na malipo yeyote kwa kushiriki kwa mtoto wako,lakini nitagharamia malipo yote ya kupimwa damu kama ulivyo elezewa.

Je kuna uwezekano wa madhara yeyote kwa mtoto wangu?

Hapatakwepo na madhara yeyote kwa mtoto wako.Utafiti huu umeidhinishwa baada ya kugaguliwa na baraza la ubora wa utafiti kwa binadamu la hospitali ya kenyatta na chuo kikuu cha matibabu cha Nairobi.

Hakikisho la Siri kwa mhuzika:

Yale yote ambayo yatanakiliwa kuhusu mtoto wako yatabaki kuwa siri na hakuna majina ambayo yatatumika ambayo yanaweza kukutabulisha wewe ama mtoto wako.

Utumizi wa matokeo ya utafiti huu:

Matokeo ya utafiti huu yanaweza kuchapichwa kwa majarida ya kisayansi lakini siri ya mshiriki itadumishwa.

Haki yako ya kujiondoa kwa utafiti huu:

Una haki ya kujiondoa kwenye utafiti huu wakati wowote ule.

Cheti cha ridhaa:

Mimi…….. kwa hiari yangu nimejitolea kutoa idhini kwa niaba ya mtoto wangu kushiriki katika utafiti huu.Nimeshaelezwa sheria na kanuni zote zinazohuzika na utafiti huu na zitajumlisha kutolewa damu ili kuchunguza viini vyote vile vinazo weza kuwepo na kuthibitisha kwa maabara kama viini hivi vinaweza kutibiwa na madawa yaliyo pendekezwa na shirika la afya ulimwenguni (WHO).Nemeelezwa ya kwamba yale yote yanayonihusu yatafichwa na yatabaki kuwa siri.Matokeo ya utafiti huu yatajumulishwa na yale ya maabara na yote yatachapichwa kwa ajili ya usayansi lakini majina yangu hayataorodheshwa katika nakala hizo.

Jina la mtoto----------

Sahihi ya mzazi kwa niaba ya mtoto----------

Tarehe----------

Sahihi ya anayeuliza maswali.----------

Tarehe----------

Appendix II:

DATA COLLECTION FORM

SOCIO DEMOGRAPHIC CHARACTERISTICS

Serial Number_____

Date_____

Sex: M ( ) F ( )

PRESENTING ILLNESS

1. Diarrhea
   - Present (……acute <14 days/…….chronic >14 days/……..blood stained)
   - absent
2. Vomiting
   - Present(….vomits everything/….not everything)
   - absent
3. cough
   - present(….acute<14 days/…chronic>14 days)
   - absent

4. Difficulty in breathing
   - Present
   - Absent
5. Ability to drink/breast feed
   - Able
   - Not able
6. Level of consciousness
   - Alert
   - Not alert
7. Convulsions
   - Present
   - Absent
8. FEVER
   - Present (record temperature……..)
   - Absent

9. Others (specify……..)

PAST MEDICAL HISTORY

Has your child recently admitted to hospital?

- Yes (specify When/ Where……/Why…….)
- No

Has your child been diagnosed with a chronic illness?

- Yes (specify disease……../When diagnosed……..)
- No

IS your child currently on any antibiotic medication?

- Yes (specify name……)
- No

Has the child been on any antibiotics in the last one week?

- Yes (specify name……?
- No

Is your child currently on Septrin prophylaxis? Yes ( ) No ( )

Has your child fallen sick in the last three months? Yes ( ) No ( )

Is your child always taken to hospital when they fall ill Yes ( ) No ( )

What is the nutritional status of your child? Healthy ( ) Not healthy ( )

ANTHROPOMETRY

Maternal:

Height……..Weight……left MUAC……..

Child:

Weight (kg)……Height/ Length (cm)…… Left mid up[per arm circumference (cm)……..

Weight for Height Z (WHZ) score on admission……

Weight for age Z score on admission……

Height for Age Z score on admission……

PHYSICAL EXAMINATION

GENERAL EXAMINATION

1. Visible severe wasting
   - Present
   - Absent
2. Bilateral pitting edema of lower limbs
   - Present
   - Absent
3. Pallor
   - Present
   - Absent
4. Fever/hypothermia(temperature……..degree centigrade)
5. Jaundice
   - Present
   - Absent
6. Generalized Lymphadenopathy
   - Present
   - Absent
7. Digital clubbing
   - Present
   - Absent
8. Oral thrush
   - Present
   - Absent
9. Dysmorphic
   - Present
   - Absent
10. 0bvious gross malformations
    - Present
    - Absent
11. Other finding
    (specify)……
    ……)

CENTRAL NERVOUS SYSTEM

1. Head circumference……centimeters
2. Level of consciousness
   - Alert

- Respond to Voice
- Respond to Pain
- Unresponsive

3. Papillary signs
   - Normal
   - Abnormal
4. Neck stiffness
   - Present
   - Absent
5. Kerning's signs
   - Positive
   - Negative
6. Posture
   - Normal
   - Abnormal
7. Muscle tone
   - Normal
   - Abnormal (specify……hypertonic/……hypotonic)
8. Muscle power
   - Normal
   - Reduced
9. Deep tendon reflexes
   - Normal
   - Abnormal(…..brisk/…..depressed
10. Abnormal movement
    - Present
    - Absent
11. Neural tube defects
    - Present
    - Absent

RESPIRATORY SYSTEMS

1. Chest deformity
   - Present
   - Absent
2. Respiratory rate…….breaths per minute
3. Respiratory distress
   - Present
   - Absent
4. Percussion note
   - Normal
   - Abnormal(……..hyper-resonant/….dull/,,,,stony…stony dull
5. Breath sounds
   - Normal
   - Abnormal(…..bronchial…../decreased)

6. Added sounds
    - Present(……..rhonchi/……crepitation/……pleural rub)
    - Absent

CARDIOVASCULAR SYSTEMS

1. Temperature of extremities
    - Warm
    - Cold
2. Capillary refill time
    - <3 seconds
    - >3 seconds
3. Peripheral pulses
    - Normal
    - Abnormal(absent/weak/ irregular/bounding/collapsing
4. Heart rate……beat per minute
5. Visible neck pulsations
    - Present
    - Absent
6. Central cyanosis
    - Present
    - Absent
7. Precordium
    - Normal
    - Prominent/hyperactive
8. Heart sounds
    - Normal
    - Abnormal- specify-loud p2,palpable p2
9. Pathological heart murmurs
    - Present
    - Absent

ABDOMINAL EXAMINATION

1. Fullness
    - Normal
    - Distended
2. Movement with respiration
    - Present
    - Absent
3. Rigidity/guarding
    - Present

- Absent

4. Tenderness
   - Present
   - Absent
5. Splenomegaly
   - Present….cm
   - Absent
6. Hpatomegaly
   - Present……..cm
   - Absent

7. Abnormal masses
   - Present
   - Absent
8. Fresh surgical incision wounds
   - Present
   - Absent

MUSCULOSKELETAL EXAMINATION

1. Any gross abnormality of the spine (kyphosis,scoliosis)
   - Present
   - Absent
2. Any bone deformities/lesions
   - Present
   - Absent
3. Joint swelling
   - Present
   - Absent

SKIN

1. Severe skin disease
   - Present
   - Absent
2. Burns
   - Present
   - Absent

APPENDIX 111

THE SCREENING FORM

Presence of the clinical feature of severe malnutrition:

- Bilateral pitting pedal Edema : yes ( ) no ( )
- Visible severe wasting: yes ( ) no ( )

Take the following anthropometric measurement.

- Age in years_____
- Height in cms:_____
- Weight in kgs_____
- Length in cms _____
- Weight for height z scores _____

Is your child currently on any antibiotics: yes ( ) no ( )

Has the child been on any antibiotics in the last one week: yes ( ) no ( )

Is your child currently on Septrin prophylaxis? Yes ( ) no ( )

Has your child been recently admitted in hospital yes ( ) no ( )

Take detailed clinical history, physical exam and draw blood from the following.

Take 3mls of venous blood aseptically from any child meeting the criteria for severe malnutrition and exclusion criteria as defined below.

- Severe malnutrition weight for height Z score <-3 SD of median WHO standard z scores for boys and girls.
- Presence of visible severe wasting
- Presence of nutritional edema.

Exclude:

- Those not meeting above definition.
- Those currently on antibiotics
- Those on follow up after discharge from ward
- Antibiotics in last one week.
- Length less than 49 cm

Aseptic technique to observe during phlebotomy:

- Wash hands with soap and water for minimum 3 min
- Clean skin of patient with 70% alcohol swab and povidone iodine
- Wear sterile gloves
- Draw 3mls of venous blood using 10cc syringe and 23G needle

Swab culture bottle with povidone iodine, Change needle and inject blood into culture bottles.

Put all samples with serial numbers and dates into cold box and send to lab within two hours.

Appendix IV

Lab result recording form

Serial number/hospital number_____ (Must correspond with serial number on the sample send to lab)

Age_____

Sex_____

WRITE THE NAME OF BACTERIAL ISOLATE USING THE INTERNATIONAL NOMENCLACTURE

Name of bacterial isolate	**Chloramphenical**		**Ampicilin**		**Gentamycin**		**Cotrimoxazole**		**Amoxicillin**	