USEFULNESS OF C- REACTIVE PROTEIN AND NEWBORN SCALE SEPSIS FOR SCREENING OF NEONATAL SEPSIS AT MUHIMBILI NATIONAL HOSPITAL IN DAR ES SALAAM.

BY

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A dissertation Submitted in (partial) Fulfilment of the Requirements for the Degree of Master of Medicine (Paediatrics and Child Health) of Muhimbili University of Health and Allied Sciences

Muhimbili University of Health and Allied Sciences
October, 2013

CERTIFICATION

The undersigned certify that they have read and hereby recommend for acceptance by Muhimbili University of Health and Allied Sciences a dissertation entitled***Usefulness of C-reactive protein and Newborn scale of sepsis for screening of neonatal sepsis at Muhimbili National Hospital in Dar es Salaam,***in (partial)fulfillment of the requirements for the degree of Master of Medicine (Paediatrics and Child Health) of Muhimbili University of Health and Allied Sciences.

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DECLARATION AND COPYRIGHT

I, **Martha Franklin Mkony**, declare that this **dissertation** is my own original work and that it has not been presented and will not be presented to any other university for a similar or any other degree award.

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ACKNOWELDGEMENT

It has indeed been a difficult and long journey towards completion of my training and this dissertation. But the support of the following, just to mention a few, has greatly contributed towards this piece of work.

My supervisors, Dr. A. Massawe and Prof. M.I. Matee for their guidance and patience as they devoted their time in the preparation from proposal development to the report, I truly appreciate your mentorship.

The head of department MUHAS – Dr. R. Kisenge, head of department MNH – Dr H. Mwamtemi, Head of firm IV – neonatal ward Dr. E. Majaliwa, Head Microbiology (CPL) Dr. KasubiMabulafor their dedicated support and assistance to make this work possible.

The wonderful laboratory team from both MNH and MOI for their devotion and ensuring quality processing of the samples, not only helped with results but also timely delivery of results to the neonates whose parents had agreed to take part into the study.

Dr. Mucho Mizinduko of Boston University, Department of biostatistics for his advice in data analysis of my dissertation.

I could not have done it all alone without the staff both MUHAS and MNH and my friends and classmates just to mention a few: Amanda, Furaha, Gudila, Honesta, Irene, Monica, Mwajuma, Regina, Pampil and Daniel Maro for their encouragement and support throughout in the course of my training.

My home partners and parents, Grace and Franklin Mkony as we call each other, who have been pillar of strength. Your trust in me gave the reason to move on.

My special thanks go to MOI for processing all CRP samples at a zero cost.

My sponsor, Belgium Technical Cooperation for covering the entire cost of my training including this dissertation, I will always treasure the opportunity that has been offered towards this ladder of achievement in my carrier.

I remain indebted to the mothers and guardians who allowed their neonates to participate in this study, all the staff in the neonatal ward at Muhimbili National Hospital for their good cooperation during the data collection period. To my colleagues and intern doctors rotating in

the neonatal ward for their tireless assistance during the data collection, and follow up of these lovely neonates.

Dear lord, you have and always will be good to me. Thank you for granting me good health throughout and giving me a steady mind to fulfill my dreams.

DEDICATION

Children always bring a bundle of joy to our families. Some will call them little angles because of the blessing they bring along.

My love for children made me chose to study Paediatrics, and God blessed my choice with arrival of these lovely babies: Jennise Grace, Bethuel-Kwimbere, Annabel Ngyisaria, and the precious twins Patricia and Prisca.

To you I dedicate this work.

ABSTRACT
Background

Significant challenges exist in the diagnosis of neonatal septicaemia due to the non specific nature of clinical presentation as well as problems in laboratory confirmation of suspected cases. In most deprived countries often diagnosis is made on the basis of clinical suspicion and antibiotics are prescribed empirically.

Objective

To determine prevalence of neonatal sepsis, spectrum of etiological agents and their antibiotic susceptibility pattern and evaluate the efficacy of Rubarth's newborn of sepsis and C- reactive protein in the diagnosis of neonatal sepsis using blood culture as a gold standard.

Methodology:

This was a hospital based prospective cross sectional study conducted at the neonatal ward of the Muhimbili National Hospital in Dar es Salaam city from March 2012 to April 2013. Participants were neonates who had clinical features suggestive of neonatal sepsis by WHO criteria.Babies were physically examined and investigations which included; a bloodfor culture and sensitivity, full blood picture andtwo serial measurements of C – reactive protein (CRP), taken 12 hours apart were collected. Rubarth's newborn scale of sepsis which is based on combining physical findings and FBP results, was used for scoring sepsis. The efficacy of Rubarth's newborn scale of sepsis and serial CRP was assesses by calculating sensitivity, specificity, negative and positive predictive values as well as likelihood ratios (LHR). Blood culture was used as a gold standard and if the confidence did not include 1 and p value of < 0.05 was considered statistically significant.

Results:

A total of 208 neonateswere recruited out of whom 40 (19.2%) blood culture had a positive blood culture. The isolated organisms were *Klebsiella species (35%), Coagulase Negative*

Staphylococus (30%), Staphylococcus aureus (10%), Escherichiacoli (22.5%), and *Pseudomonas species (2.5%)*. The overall resistance to the WHO recommended first line antibiotics was for cloxacillin 100% , ampicillin 96.4% and gentamicin 39% while for second line drug ceftriaxone was 41%. Resistance to vancomycin and amikacin was 53.6% and 13.9% respectively. Clinical features that were significantly associated with neonatal sepsis were fever (67.3%), fast breathing (79.8%),and low muscle tone (38.9%) and this was statistically significant with$p < 0.001$.The first CRPhadsensitivity of 87.5% and specificity of 70.8% , the likelihood ratio for positive test was 3, while LHR for negative tests 0.18 both with a p value of <0.001. Combined CRP had sensitivity of 97.4% and specificity of 53.7%. Rubarth'sneonatal score of sepsis had sensitivity of 65% and specificity of 79.7% serial CRP had sensitivity of97.4%. Combining CRP and neonatal scale of sepsis reduced sensitivity to 94.71%as compared to when CRP was used alone.

Conclusion: Serial CRP has a high sensitivity of 97.4% to diagnose neonatal sepsis. The etiological agents to neonatal sepsiswereidentified to be *Klebsiellaspp, CoNS, S. aureus,E. coli*, and *Pseudomonas spp*. These agents were found to be sensitive to amikacin and resistant to the currently prescribed first line antibiotics and moderate resistant to the second line drugs whose use can be guided by sensitivity results.

Recommendation: In the management of suspected neonatal sepsis, serial CRP done twelve hours apart in combination with Rubarth's Neonatal scale of sepsis can be used for screening of neonatal sepsis. Once the results for the screening tests are available a blood sample for culture can be taken for those neonates with a positive test. There is also a room for follow up studies on usefulness of CRP in combination with RNSOS in monitoring for response to treatment. Because of high resistance observed, there is a need to have follow up studies to assess the efficacy of the current first line antibiotics used in the management of neonatal sepsis.

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ACRONYMS

BMC	**Bugando Medical Centre**
CRP	**C –Reactive Protein**
CoNS	***Coagulase negative staphylococcus***
DST	**Drug Sensitivity pattern**
EOS	**Early Onset Sepsis**
E.coli	**Escherichia coli**
FBP	**Full Blood Picture**
HSS	**Haematological Scoring System**
LOS	**Late Onset Sepsis**
MOI	**MuhimbiliOrthopaedic Institute**
MNH	**Muhimbili National Hospital**
MUHAS	**Muhimbili University of Health and Allied Science**
RNSOS	**Rubath's newborn scale of sepsis**
S.aureus	***Staphylococcusaureus***
WBC	**White blood cells**
WHO	**World Health Organisation**

CHAPTER ONE

1.0 INTRODUCTION

1.1. Background and Literature Review

Neonatal sepsis is a clinical syndrome characterized by signs and symptoms of infection with or without accompanying bacteremia in the first month of life. It is among the major problem in the newborn period associated with high morbidity and mortality. It is estimated that approximately 4 million neonates die every year in low-income countries due to various reasons, including sepsis [1-3]

It encompasses various systemicinfections of the newborn such as septicemia, meningitis, pneumonia, arthritis, osteomyelitis, and urinary tract infections. Superficial infections like conjunctivitis and oral thrush are not usually included under neonatal sepsis.[1]
Basing on the nature, time of onset and common pathogen isolated, neonatal sepsis can be classified as early and late onset sub types.

Early onset sepsis (EOS), which occurs within the first 72 hours of life, usually presents with respiratory distress and pneumonia. In severe cases, the neonate may be symptomatic at birth. In EOS, the source of infection is generally the maternal genital tract.[4]Some maternal and/or perinatal conditions have been associated with an increased risk of EOS and understanding these potential risk factors would help in early diagnosis of sepsis. The main risk factors for early form of neonatal sepsis outlined below;

1. Low birth weight (<2500 grams) or prematurity
2. Febrile illness in the mother with evidence of bacterial infection within 2 weeks prior to delivery.
3. Foul smelling and/or meconium stained liquor.

4. Rupture of membranes >24 hours.
5. Single unclean or > 3 sterile vaginal examination(s) during labor
6. Prolonged labor (sum of 1st and 2nd stage of labor > 24 hours)
7. Perinatal asphyxia (Apgar score <4 at 1 minute)

Infants with two risk factors are usually considered as suspected cases and are due for investigation and management Presence of foul smelling liquor or three of the above mentioned risk factors warrant initiation of empiric antibiotic treatment as they have a high risk of neonatal sepsis.[2]

The late onset sepsis (LOS) usually presents after 72 hours of age and can either be nosocomial (hospital-acquired) or community-acquired infections. These neonates are mainly diagnosed to have septicemia, pneumonia or meningitis.

Neonatal sepsis remains a major diagnostic problem in neonatal medicine, with the definitive diagnosis involving cultures of blood or other normally sterile body fluids. Abnormal hematological counts, acute-phase reactants, and inflammatory cytokines have low sensitivity and specificity, especially at the onset of illness. Previous studies have shown that combinations of different test parameters does improve diagnostic test performance.[5]

Although various haematological indices have been utilised to screen for sepsis, most of them are neither highly sensitive nor specific and are commonly affected by perinatal factors like maternal hypertension, asphyxia and haemolytic disease. Clinicians have been prescribing antibiotics to newborn babies who report to be having fever to empirically treat presumed sepsis even when there are no any localising signs for infection for the fear of mortality and complication that are associated with septicaemia.[6]

Obstetric practises have been modified significantly in order to reduce the risk of vertical transmission by adopting procedures such as cleaning of the perineum with antiseptics.

[7]Other measures include reducing vagina examination and antibiotic coverage in women with leaking liquor or with prolonged rupture of membrane.[7, 8]

1.2. Causative organisms

The common bacterial isolates for early neonatal sepsis include *Klebsiellapneumoniae*, *Staphylococcus aureus*and *Escherichia coli*.*S aureus* remains a very important neonatal pathogen in developing countries, responsible for 8—22% of bloodstream isolates in different regions. *S.aureus* has historically plagued nurseries with numerous reported outbreaks. The main source of spread of infection is the hands of health-care providers.[9-12]

The spectrum of pathogens in south Asia and Africa is quite different from that observed in neonates in developed regions where G*roup B streptococci*, *Escherichia coli*, and *coagulase-negative staphylococci* are the predominant pathogens. The prevalence rate of confirmed sepsis was significantly lower among in-born babies compared with out-born babies.[13]

1.3. Recommended treatment

The WHO report of 2005 on antimicrobial treatment of neonatal sepsis recommended use of ampicillin and gentamicin as first line treatment for both early and late onset of sepsis and or ceftriaxone in the neonates with meningitis[1]. The empirical use of antibiotics in neonates involves using broad-spectrum drugs to be continued for a total of 10 days, after a clinical response has occurred. This was determined by the antimicrobial sensitivity pattern of the etiological agents whose composition is dependent on infant's age, and is influenced by organisms within the neonatal unit (hospital-acquired infection).[1]

Recent studies have shown a change on the sensitivity pattern to the recommended regime. Studies done in sub Saharan Africa showed that there is considerable *in vitro* resistance to the first-line antibiotics in current use.

In Nigeria,Ougulensi et al had shown that, of the suspected cases, only 16.6% of neonates had a positive blood culture, where by the overall sensitivity to Ofloxacin was 95.1%. The overall sensitivity of the organisms to cefuroxime and gentamicin was low (56.4% and 56.4%, respectively). It was remarkable that the sensitivity of all the isolates to gentamicin was less than 60%. Indeed, *Klebsiella* had the lowest sensitivity to both cefuroxime and gentamicin. Thus, it might be necessary to consider substituting another aminoglycoside agent for gentamicin. Amikacin, with spectrum of activity similar to that of gentamicin, may be suitable for this purpose .There was also a moderate sensitivity of the isolated organisms to the second- and third-generation.[9, 11, 13-16]

A study done in Kenya, in 2003 revealed that blood isolates were resistant to ampicillin and gentamicin but showed good *in-vitro* sensitivities to amikacin, cefuroxime and the third generation cephalosporins (ceftriaxone, ceftazidime and cefotaxime). Another study in Mulago Hospital in the year 2000 atKampala,Uganda reported resistance of organisms to ampicillin (except *Group B Streptococcus*) and most of the organisms were sensitive to gentamicin and reported that third generation cephalosporins; ceftriaxone and ceftazidime showed high sensitivity against Gram-negative organisms like *E. coli*, *Salmonella spp*. and *Proteus spp*. These drugs however showed low sensitivity for *Group B Streptococci* (*GBS)* and *S. aureus.*[4, 12, 17]

Studies that were done in Tanzania also showed an increase in resistance being isolated. Previous studies that were conducted in 1999 at MNH by Urassa et al had shown that the first line antibiotics i.e. ampicillin and gentamicin were sensitive to isolated organism, however recent studies done at MNH between 2004 and 2012 and at Bugando Medical Centre in Mwanza in 2009 showed that the resistance is increasing where by 49% of gram negatives isolates were resistant to third generation cephalosporins and 28% of Staphylococcus aureus were found to be Methicillin resistant Staphylococcus aureus (MRSA)[3, 10, 11]

This implies the need for newer and more expensive drugs for treatment for neonatal sepsis calls for regional specific studies to determine drugs that can be used for management of septicaemia.

1.4. Investigations

The diagnosis of neonatal sepsis has continued to remain a challenge because of minimal signs at presentation which are also similar to a non-infectious process. The situation is even more so when routine standard test are not available due to limited resources especially in developing countries. Other available tests are non specific and hence clinicians opt to empirical treatment.

For the diagnosis of neonatal sepsis, ideally a series of tests should be done. This includes investigations such as cultures from blood, swabs from orifices, urine and cerebral spinal fluids, FBP, inflammatory makers such as CRP, and imaging especially in cases of pneumonia. For neonates with signs of local infection a swab is normally done for culture and sensitivity.

1.5. Blood cultures

Blood culture is the gold standard in the diagnosis of suspected sepsis. A small blood volume of as low as 0.2 to 0.5mls have been shown to be enough for isolation of bacteriological agents.[18] However, increased blood volume (1 to 2mls) is required for detection of low bacteraemia especially where there is history of prior use of antibiotics.

1.6. Inflammatory markers

The use of inflammatory markers, which rises in inflammatory condition including infection such as C – reactive protein and procalcitonin when available can be used as screening tool which may suggest an ongoing bacterial or viral infection.[5, 19-23]

C – Reactive protein

CRP is an acute phase protein, which is raised in inflammatory disorders and tissue injury. It is the most extensively acute phase reactant studied so far. Its levels may increase from 100 to 1000 folds in response to bacterial infections. The levels usually begin to rise 6 to 8 hours after the infection, with a half-life of 19 hours.

Because of this delay serial CRP, two to three samples taken 12 to 24 hours apart has been shown to be more useful than a single measured CRP in the diagnostic evaluation of neonates with suspected infection.The sensitivity of the test is up to 93% and has higher sensitivity than total neutrophils counts and immature to total neutrophils ratio. Other studies have also proven to be more sensitive than a Leucocytes measured from a full blood picture. The advantage of CRP include its very low serum levels in normal infants, and its rapid rise within 6 to 8 hours after onset of sepsis and a large incremental increase after the onset of infection thus can be a very useful diagnostic tool of sepsis.[24-28]

A study done in Blank children hospital in Iowa USAin and Thailand in 2002 by Nuntnarumit et al showed that quantitative serial CRP levels, obtained 24 hours after the onset of signs and symptoms of infection, with serial measurements 12 to 24 hours apart, offer the most sensitive and reliable information to guide on the duration of antibiotics e.[26, 29]

At least 2 CRP levels, obtained 24 hours apart, with levels < or = 10 mg/L, are needed to identify infants unlikely to be infected. The use of CRP to exclude infection may allow clinicians to discontinue antibiotics at 48 hours in select infants, limiting extended unnecessary antibiotic exposure.[5, 29]

When CRP is done serially from 2 or 3 times has been shown to have increased sensitivity ranging from 78.9 to 98% and specificity from 84% to 97% of detecting cases suspected to have sepsis and therefore can be used as adjuvant tool to guide a physician on when to stop antibiotics for children who had received empirical treatment. The higher sensitivity is

observed with use of quantitative than qualitative assessment of CRP.[30]Therefore neonates who were admitted with suspicion of neonatal sepsis and started on empirical treatment with antibiotics following the negative results of CRP, the clinicians can stop the antibiotics thus can minimize antibiotic exposure and shorten hospital stays. The diagnostic accuracy of serial measurements of serum CRP levels, this can also be used for monitoring the severity of sepsis and improvement after initiation of treatment.[27, 29, 31-34]

1.7. Haematological scoring system

This is another test that can be used for screening for sepsis and is readily available in most of the settings. It is usually a combination of various parameters from full blood picture. In FBP, total leukocyte count, neutrophils and platelets are predictors of ongoing infection are the parameters are used.[5, 28], The extreme values usually indicate an ongoing infection process.[35]

Total leucocyte count is of little clinical use in the diagnosis of neonatal infection, because of the wide variation in values and the overlap between normal and abnormal values. Neutropenia has been found to occur more commonly in association with sepsis, compared with neutrophilia, probably because of increased adherence to altered endothelial cells and utilization at the site of infection. Neutropenia alone as a sign of sepsis can be misleading, as it can also occur in asphyxia neonatorum and in certain inborn errors of metabolism. Therefore, it must not be used in isolation as a predictor for the presence or absence of sepsis. Recent studies have shown that neonates with sepsis develop thrombocytopenia, possibly because of disseminated intravascular coagulation and the damaging effects of endotoxin on platelets. Combining the parameter of the FBP is the form of a Haematological Scoring System(HSS) that has been recommended and can serve as a screening tools.[36]

1.8. Neonatal scale of sepsis

This is among haematological scoring tool that are used for screening for neonatal sepsis. This tool was developed by Rubarth in 2005 in San-franscisco – USA, to assist the nurses in the

triage of a sick neonate. The scale takes into consideration the clinical presentation of the neonate, and integrates it with FBP and blood pH results.

The tool has two parts. The first part includes the physical examination findings namely skin colour, capillary refill time, muscle tone, response to pain, respiratory distress, respiratory rate, temperature and apnea. The second part has blood investigations results for pH, and components of FBP. The total score from both parameters is 55. The higher the score the more likely the presence of sepsis. A minimum cut off value for a total score of 10 was validated and found to have sensitivity of 93% has been agreed to be used for assessment of suspected neonatal sepsis (see Annex 1). A child with a score of more than 10 is likely to have sepsis and should receive the recommended treatment. [34]

1.9. Problem statement

Adequate and timely diagnosis of neonatal sepsis remains an important challenge to the clinician especially in developing countries.[2] Blood culture which is the gold standard fordefinitive diagnosis takes at least 48 hours up to 6 days as reported by Musoke et al in Kenya[17] by which time the infection may have progressed with important consequences on the morbidity and mortality of the neonatal.[2, 17]

Inflammatory markers such as CRP has not been widely utilised in our setting. Unlike blood culture, CRP level is not affected by prior antibiotic therapy, so may be particularly useful in Sub-Saharan Africa where a significant number of neonates may have been given antibiotics before presentation at the hospital.

Rubarth's neonatal scale of sepsis which uses a combination of haematological scoring from FBP results, pH results and clinical presentation of the patient is another way of rapidly identifying a sick neonate. This tool,which is feasible in resource deprived countries, can be of greater value if combined with simple laboratory parameters such as with CRP.

Both CRP and neonatal scale of sepsis have not been utilized in routine settings, partly because their diagnostic potential has not been evaluated.

Moreover, the empiric treatment of cases is faced by change of the sensitivity pattern of the isolated organisms implicated in neonatal sepsis while the recommended treatment has remained the same.This has been shown by a study conducted by Urassa et al (1999) at MNH where 97.3% of isolated organisms were sensitive to the prescribed antibiotics. Later in 2005 Bloomberg et al had shown at MNH resistance was upto50%. Kayangeet al in 2010 had shown that of about 49% of gram negatives isolates were resistant to third generation cephalosporins and 28% of *S.aureus* were found to be Methicillin resistant *Staphylococcus aureus* (MRSA).[3, 11, 16]The high level of resistance has also been reported in Iran by Marzban et al[37]which showed resistance of 87% to the WHO recommended treatment while in

Viswanathan et al in 2012[38]showed 100% resistance of Gram negative bacilli to ampicillin and gentamicincausing a shift to vancomycin and amikacin.

With these challenges faced, there is a clear need to improve our diagnostic protocol and reduce a request of un- necessary cultures. Also there is a need to review a trend of sensitivity pattern of blood culture results of the aetiological agents so that we can offer appropriate treatment.[9]

1.10. Rationale

Rapid diagnosis and early treatment is a key to serving life. These tools can provide us with timely results and provide a clinician with scientific proof on the choice of the management to be offered in suspected neonatal sepsis.

The rapid tests are not meant to replace blood culture but as adjuvant tests while waiting for blood culture results. The test can also be potentially useful in resource deprived settings. The cost for processing CRP is cheaper as it cost only a third compared to the cost to process a blood culture and also results are obtained sooner than that of culture which facilitate in the management of the neonate suspected to have sepsis.

Both CRP and the scale of sepsis do not require higher level of technical expertise which is of value in a limited resource setting. When used in combination the sensitivity of the test is even higher thus providing a strong evidence to the clinicians regarding the choice of treatment[27].Both tools can form part of diagnostic protocol for suspected neonatal sepsis.

In this study, blood culture was used as a gold standard to validate the tools and also provided an update on the sensitivity pattern of the isolated organism.

2.0. Research questions

1. What is the prevalence of neonatal sepsis at MNH?
2. What are the etiological agents of neonatal sepsis at MNH?
3. What is the current sensitivity pattern of isolated organisms for neonatal sepsis at MNH?
4. What is the usefulness of Rubarth's newborn scale of sepsis?
5. What is the usefulness of CRP in the diagnosis of neonatal sepsis?

5.0. Objectives

3.1. Broad Objective

To determine prevalence of neonatal sepsis, spectrum of etiological agents and their antibiotic susceptibility pattern and evaluate the efficacy of Rubarth's newborn scale of sepsis and C-reactive protein in the diagnosis of neonatal sepsis.

3.2. Specific Objectives

Primary objectives

3.2.1 To determine the sensitivity, specificity, negative and positive predictive of Rubarth's newborn scale of sepsis in diagnosing neonatal sepsis at MNH.

3.2.2 To determine sensitivity, specificity, negative and positive predictive values of serial CRP in diagnosing neonatal sepsis at MNH.

Secondary Objectives

3.2.3 To determine the proportion of neonatal sepsis at MNH.

3.2.4 To determine the antimicrobial sensitivity pattern of the bacterial isolated from neonates with sepsis against the commonly prescribed antibiotics at MNH.

CHAPTER TWO

4.0. METHODS AND MATERIALS

4.1. Study design:

This was a hospital based, prospective descriptive study.

4.2. Study area:

The study was conducted at Neonatal ward of the Muhimbili National Hospital, which receives neonates delivered at MNH labor ward and neonates, referred from other hospitals within Dar es Salaam and some from upcountry. The ward has a capacity of over 130 beds, admitting approximately 25 babies per day, with a total annual admission estimated at 7500. The hospital is also has a modern laboratory facility and skilled personnel capable of performing most of the tests for diagnosis of neonatal sepsis

4.3. Study duration.

The study was conducted from March 2012 to April 2013

4.4. Study population.

Study populations were neonates who were admitted at Neonatal ward at MNH during the time of the study.

5.5. Recruitment of study participants

Parents or guardians of the eligible study participants were given a detailed explanation of the study and invited to participate into the study after they have given written informed consent (Refer Appendix II/III). Neonates who met the inclusion criteria were included until a sample size of 208 neonates was reached.

Five nurses were trained as research assistants.

5.6. Inclusion Criteria

A neonate who met clinical criteria by WHO case definition for septicemia [39] was and parent/guardian consented to the study was included. The clinical definition included any one of the following features

- History of difficulty feeding.
- History of convulsions
- Movement only when stimulated
- Respiratory rate $\geq$ 60 breaths per minute
- Severe chest indrawing.
- Axillary temperature $\geq 37.5^0$C
- Axillary temperature $\leq 35.5^0$C
- Bulging anterior fontanelle ,
- Signs of infection on the skin with pus spots and umbilicus pus spots

5.7.Exclusion Criteria

- Very sick children in decompensate state and requiring resuscitation
- Neonates with severe congenital malformation such as anencephaly

5.8. Sample Size Estimation

The sample size was determined by Epi info version 6.0 using the prevalence of blood stream infection of 13.9% a figure that was found by Bloomberg et al in the same hospital [14]
The maximum likely error (E) =5%

The sample size was calculated by the following formulae

$N= Z^2 P (100- P)/ E^2$

Where Z = Critical value 1.96 corresponding to 5% significance level

N = Estimated sample size

E = Margin of error (5%)

P = Prevalence of proven bacteraemia is 13.9% as shown by Bloomberg et al [14]

Therefore, $N = (1.96)^2 \times 13.9(100-13.9) / (5\%)^2 = 183.9$

The minimum sample size calculated was 184**.** To account for a design effect 10% the eventual sample size was 208.

Questionnaire piloting

Two week prior to commencement of data collection a pilot was done to test the practicability of the questionnaire and the questionnaire was modified. The results from the pilots were not included for analysis.

5.9. Data collection

Demographic and clinical information

A standardized structured questionnaire was used to collect demographic and clinical information which, included details of a thorough physical examination. Weight was measured using SECA beam balance (CMS weighing equipment, London, United Kingdom) to the nearest 100gm.

Blood culture

Aseptic techniques were observed. Blood was collected form peripheral vein access.Approximately two millilitres of blood was inoculated into the paediatric blood culture bottles (BacT/ALERT PF Organon-Teknika Corp., Durham, N.C.). Blood culture bottles were incubated at 37^0C for 24 hours after which the aliquots were sub- cultured on solid agar plates; MacConkey, blood and chocolate agars for up to 96 hours before being regarded as no growth.

Antimicrobial susceptibility testing

Antimicrobial sensitivity testing was performed for antimicrobials which included first and second line antibiotics for treating neonatal sepsis at MNH; first line antibiotics are ampicillin, cloxacillin and gentamicin and second line is ceftriaxone. Also testing for alternative drugs which were amikacin and vancomicin was done. The drug concentrations were; ampicillin 10 µg, cloxacillin 30 µg, gentamicin 10 µg, ceftriaxone 30 µg,amikacin30 µg and vancomycin30µg. Sensitivity was performed by Kirby Bauer diffusion method using Mueller Hinton agar with incubation of 24hours at 37^0C. Sensitivity was determined by according to clinical laboratory standard institute standards. Results were recorded as resistance,intermediate and sensitive. During data analysis intermediate were categorized as resistant.

5.10. Full blood picture

For determination of full blood picture, 0.5mls of blood was collected in vacutainers containing EDTA (Ethylenediaminetetra-acetic acid) and analysed by CELLDYNE 3700 (Abbott diagnostic divisions, United States of America). Calibration of the machine was done every morning before processing.The normal ranges as per RNSOS were; 5000 and30, 000/ml for WBC, 4700 and 9400 for neutrophils, 5000 and 5000/ml for lymphocytes and 150,000 and 450,000/ml for platelets. The extreme value on either side was suggestive of ongoing neonatal sepsis.

5.11. Rubarth‘s newborn scale of sepsis

All neonates who met case definition were assessed byRubarth’s newborn scale of sepsis. The tool has two parts. The first part includes the physical examination of the patient and the second part involves the FBPresults which were compiled soon after the results. The first part has laboratory findings with 5 items; the total score for this category is 20, while the second part has clinical features assessing 8 parameters with total score of 35. The total score from both parameters is 55. The higher the score the more likely the presence of sepsis. A cut off point of a combined total score of more than 10 has a sensitivity of 93% has been agreed to be used for assessment of suspected neonatal sepsis (see appendix I).

5.12. CRP

For determination of CRP two serial measurements were done at an interval of 12 hours. Blood sampleswere centrifuged for separation of the serum within 60 minutes of blood collection. The serum sample was then mixed with a standard reagent for one minute and analysed by COBRA 400/400 plus system (Roche Diagnostic limited, Switzerland). A value of more than 10mg/l was considered positive and be likely associated with sepsis. Samples that were not analysed within 24 hours of collection were stored at $\leq 20^{o}$C. Calibration of the machine using a standard sample was done every morning before processing of the samples. Sensitivity specificity, positive predictive values, negative predictive values and likelihood ratio were determined using blood culture as a gold standard

5.13. Ethical considerations

The aims and benefits of the study were explained to the parents/guardians. Parents/guardians of eligible neonates were asked to provide written permission for their babies to participate in the study. Participants' information which was filled in the questionnaires was kept confidential with no any identifying information. Standard management was given to all neonates regardless of their participation to the study. The results obtained were used in the management of the neonates

5.14. Ethical clearance and permission to conduct the study:

Ethical clearance to carry out this study was sought fromthe higher degree research and publication committee of the Muhimbili University of Health and Allied Sciences (MUHAS). Permission to conduct the study at Muhimbili National Hospital was obtained from the Directors of Clinical Services of the hospital.

5.15. Data analysis

Questionnaires were edited for consistency and quality check. Data was then entered in the statistical package for social science (SPSS) version 18 for statistical analysis.

The usefulness of the CRP and Rubarth's newborn scale of sepsis in the diagnosis of neonatal sepsis was assessed by calculating sensitivity and specificity, positive and negative predictive value and likelihood ratio(LHR)using blood culture results as a gold standard. Median and frequency tables were used to summarize the data.

Relationship whose p value was less than 0.05 was regarded as statistically significant.

CHAPTER THREE

6. RESULTS

6.0. Baseline characteristics

Out of the 208 neonates, maleswere 108 (51.9%), with male female ratio of 1.1:1. The median age of the study participants was 5.6 days, with age range of 1and 28 days. Slightly more than half (52.9%) of the infants aged less than 4 days, and majority of them (81.7%) had body weight of ≥ 2.5Kg.The clinical features that were commonly encountered were fever 67.3%, low muscle tone 38.9% and fast breathing 79.8% as shown on **table 1** below.

Table 1: Baseline demographic characteristics of the neonates enrolled in the study

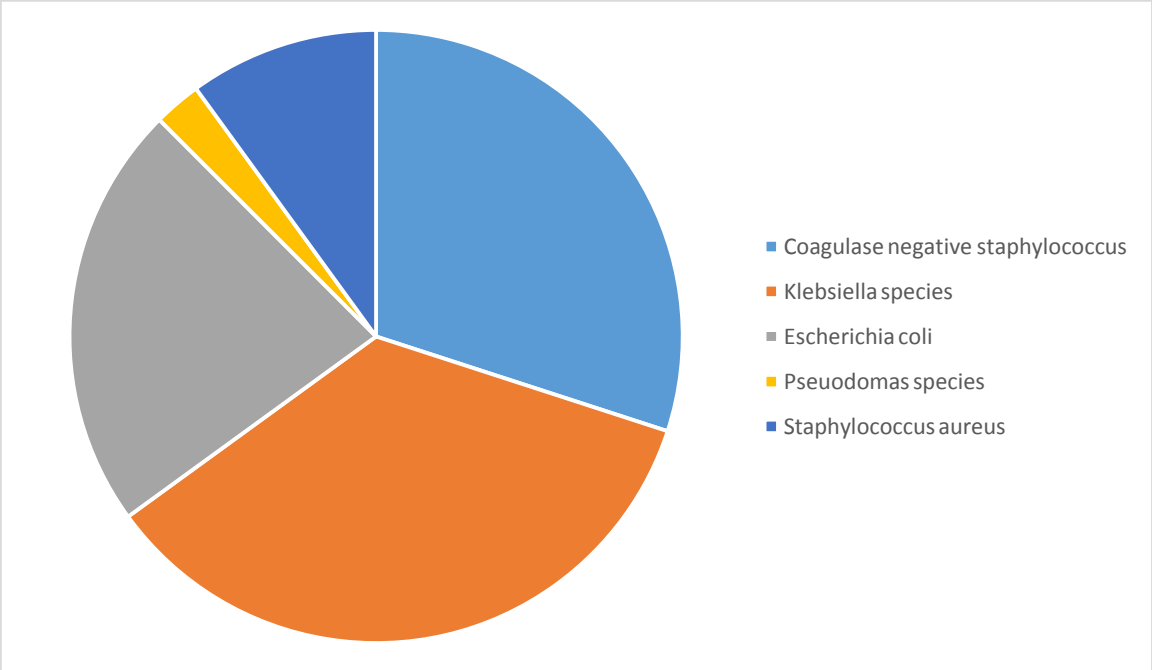
	N = 208	**FREQUENCY %**
AGE GROUP		
0 – 3	109	52.9
4 – 28	99	47.6
SEX		
MALE	108	51.9
FEMALE	98	48.1
BODY WEIGHT		
<1000	2	0.96
1 – 1.4	10	4.81
1.5 – 2.5	26	12.5
>2.5	170	81.7
CLINICAL FEATURES		
FEVER	147	67.3
LOW MUSCLE TONE	81	38.9

FAST BREATHING	166	79.8

6.2. Isolated bacterial pathogens

Of the 208 participants, positive blood culture was found in 40(19.2%) blood samples. The organisms isolated were *Klebsiellaspp (35%), E.coli*(22.5%),*CoNS* (30%), *S.aureas (10%),* and *Pseudomonas aeroginosa (2.5%)*. *Klebsiellaspp*was found to be a predominant organism in both early and late onset sepsis.

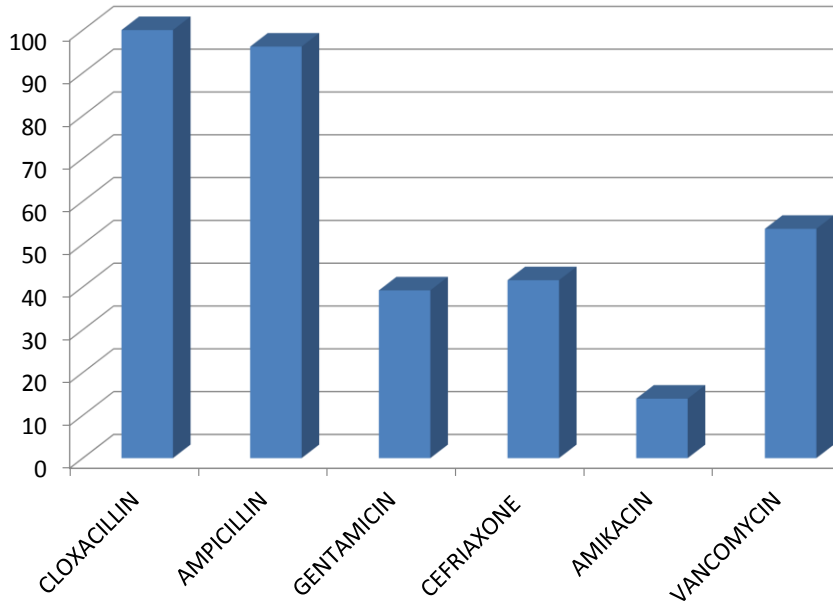
Figure 1: Distribution of the isolated bacterial pathogens



6.3. Antimicrobial sensitivity pattern of the isolated organism.

The overall resistance of isolated organisms to the recommended first line antibiotics for ampicillin was 96.4%, 100% to cloxacillin while gentamicin had moderate resistance of 39%. For recommended second line ceftriaxone it was 41%. Resistance to vancomycin and amikacin was found to be 53.2% and 12.9%, respectively. **(Figure 2)**

Figure 2: Overall percentage resistance of isolated organisms to the recommended drugs



6.4. Clinical features presentation in association with blood culture results

Of the clinical features that were investigated only high temperature, low muscle tone were significantly associated with neonatal sepsis while breathing rate was not. Although slightly more females were found with neonatal sepsis this was not statistically significant as seen on Table 2 below.

Table 2: Association between blood culture results with age group, body weight and clinical presentation

	BLOOD CULTUREN = 208(%)		P value
	GROWTH	**NO GROWTH**	
SEX			
Male	18(45)	90	
Female	22(55)	78	P = 0.33
AGE GROUP			
0 – 3 DAYS	11(27.5)	98	
4-28 DAYS	29(72.5)	70	P <0.01
BODY WEIGHT			
<2.5	9(22.5)	29	
>2.5	31(77.5)	139	P = 0.44
CLINICAL FEATURES			
TEMPERATURE			
Normal	3(7.5)	53	
High	37(92.5)	103	
Low	0	12	P <0.01
MUSCLE TONE			
Normal	13(32.5)	111	
Low tone	25(62.5)	56	
Flaccid	2(5)	1	P < 0.01
Breathing rate			

Normal	4(10)	36	
Fast breathing	37(90)	131	P = 0.29

6.5. Rubarth's newborn scale of sepsis

The association between blood culture results and neonatal sepsis scores are shown in Table 3 below. From the total score it was found the tool could identify 26 out of 40 neonates with positive blood cultures, and 134 patients among 168 who had no growth on blood culture were and also were detected negative by the test as shown on **table 3** below

Table 3: Association between blood culture results and total score for neonatal scale of sepsis

	BLOOD CULTURE	
TOTAL SCORE	GROWTH	NO GROWTH
≥10(positive)	26	34
<10 (negative)	14	134
TOTAL	40	168

When the results were analysed it was found that the sensitivity of the Rubarth's neonatal SOS was 65%, specificity was 79.7%. The likelihood ratio (LHR) of the positivewas 3.24 and LHR negative testwas 0.43. BothLHR were statistically significant with a p value <0.01. This means that of scale can correctly identify cases with sepsis and those without sepsis.

Full blood picture results

Looking at the parameters of FBP as a component of Rubarth's newborn scale of sepsis, thrombocytopenia, leukopenia and neutropenia werestatistically significant associated with positive blood culture with p<0.01 as shown on **table 4** below:

Table 4: Association between blood culture results and platelets, leucocytes and neutrophils

	BLOOD CULTURE		**$\chi 2$ p value**
Platelets	**GROWTH**	**NO GROWTH**	
positive< 100,000	21	19	p<0.01
Negative >100,000	19	149	
Leucocyte			
positive< 5000	26	12	
Negative 5000 – 30,000	14	156	p<0.01
Neutrophils			
positive<2000	19	18	
Negative >2000	21	150	p<0.01

6.6. C reactive protein

The results showed that CRP was positive in 35 out of 40 samples among those witha positive blood culture and negative in 119 out of 168 samples with negative blood culture as shown on **table** 5 below

Table 5: Association between blood culture results and CRP_1 results

	BLOOD CULTURE	
CRP_1	GROWTH	NO GROWTH
≥ 5 (POSITIVE)	35	49
<5 (NEGATIVE)	5	119
TOTAL	40	168

Key: CRP_1 means the first CRP collected.

On testing the efficacy of the test, it was found that sensitivity was 87.5%, while specificity was 70.8%. The positive predictive value was 41.7% while negative predictive value was 95.9%. Likelihood ratio for positive test was 3 while for negative test was 0.18 and both were statistically significant with a p value <0.01. The statistical significance of the test implies its ability to correctly identify suspected cases of neonatal sepsis.

A second sample for CRP (CRP_2) was subjected to all babies except for four who died before a sample was taken. It was found that test could identify 30 out of 38 with a positive blood culture and 125 of 166 with a no growth in blood culture as shown on **table 6** below

Table 6: Association between blood culture results and CRP_2results

	BLOOD CULTURE	
CRP_2	GROWTH	NO GROWTH
≥ 5 (POSITIVE)	30	41
<5 (NEGATIVE)	8	125
TOTAL	38	166

Key: CRP_2 Means the second sample of CRP collected.

The analysis of the results showed that sensitivity was 78.9%, specificity was 75.8%. Thepositive predictive value was 42.3% while negative predictive value was 93.9%.Both LHR were statistically significant with $p<0.01$.

Effect of serial CRP

When the two CRP tests were combined i.e. CRP_1 and CRP_2 the sensitivity of the test increased to 97.4% while overall specificity was decreased to 53.7%. This means that the likelihood of diagnosing suspected cases increases when the tests are done serially.

6.8. Combined serial CRP and total score for neonatal score of sepsis.

The results serial CRP and total neonatal scale of sepsis were combined and then compared with blood culture and it was found that the two tests combined had sensitivity of94.7% while specificity was found to be at 55.1%.

CHAPTER FOUR

7. DISCUSSION.

The proportion of neonatal sepsis in this study was found to be 19.2% among those who met WHO criteria for serious bacterial infection This finding is higher than that of Bloomberg et al [16] who had a prevalence of 13.9% and slightly lower than that of Mhada et al [10] who had a prevalence of 24% in the same setting. Collectively all the three studies shows the high burden of neonatal sepsis at MNH. In a setting were blood culture can not be done, all the enrolled study participants would have been treated empirically with antibiotics indicating the need of improving our diagnostic methods so that suspected cases can be quickly identified and offered the right treatment.

7.1. Utility of C reactive protein

From this study it was found that CRP had high sensitivity (CRP_1 – 87.5%and CRP_2 78.9%) while specificity was moderate (78.9% and 75.8%).These values are similar to other studies done in Kenya by Kumar et al in 2010 [40], Ogunlesi et al in 2010 in Nigeria [13] , west el al[30]and Bomela et al in[32] south Africa where the range was between 75 – to 100%.Sensitivity of CRP in this study was on the higher range because of quantitative measurement of CRP which is reported to be superior to qualitative measurement.[40].

The combined CRP had a much higher sensitivity of 97.4% and specificity of 53.65%. The means more subjects will be detected when subjected to a serial test hence improving chances of identifying a sick neonate. The usefulness of serial test not only increases sensitivity but can also be used to monitor progress of treatment as shown by other in the region[20, 27, 32, 36]however this was not tested but can be used determined its usefulness in our setting in future studies.

The cost of CRP at MNH compared to that of blood culture at the time of data collection was found to be a third of a cost to process blood culture. Also the results are obtained within 6hrs from the time the samples are sent to the laboratory. This has an implication on the care of sick neonates as those who are unlikely to require hospitalization will be spared from empirical treatment. Therefore more room will be available for sick neonates reducing overcrowding hence improving care which not only spare use of empirical treatment but also allow space for other sick neonates and reduce family anxiety cost to both family and the hospital.

7.2.Rubarth's newborn scale of sepsis

This tool combined hematological score and the physical findings. The study found its sensitivity and sensitivity was moderate compared to when it was validated by Rubarth. The different findings in this study when the tool was applied is because some of the parameters could not be assessed because of limited resources[38]

However when looking at itemized parameters of the tool, from full blood pictures results, neutropenia, leukopenia and thrombocytopenia were all found to be highly associated with sepsis indicating its usefulness in the diagnosis of sepsis. Similar findings have been shown by Manucha et al in India[36]who found that absolute neutropenia and thrombocytopenia was highly associated with neonatal sepsis. The low performance of the tool in our setting can be because of one of the parameter could not be assessed because of lack of lab reagent.

7.3. Effect of Combined CRP and Rubarth's neonatal scale of sepsis.

Combining CRP and the total NOS in our study had a higher sensitivity (97.4%) thaneither of the test when performed alone. At MNH where the study was conducted FBP is almost always available unlike blood culture. Hence for screening for neonatal sepsis, an additional test; CRP have added value for identifying neonates likely with sepsis, and therefore blood culture can be reserved for neonates who have a positive test. This can therefore be useful when especially in resource poor setting where blood cultures are not routinely done. The

effect of combining the two test increases the sensitivity similar to Garland et al [27] and Hengst et al [29]. Contrary to our study Manucha et al in India[36] concluded there was no advantage of combing hematological test with CRP in the management of neonatal sepsis. The difference in the findings of the two studies can be because of different type of hematological scoring tool used, our tool had combination of blood investigation results together with physical findings which can explain a high sensitivity while Manucha et al had used scored using only hematological parameters.

7.4. Aetiological agents

The common etiological identified by blood culture were *Klebsiellaspp, CoNS, E.coli,S.aureus and Pseudomas spp*. These organisms are similar to other places especially in developing countries for causes of neonatal sepsis.This study unlike others that have been done at MNH, reported CoNS to be a second common isolate for neonatal sepsis. Although this has been considered as potential contaminant in adult population, but in NICU it can be a potential etiology requiring treatment.[4, 41]Similar findings have been shown Mugalu et al in 2006 who demonstrated CoNS was also responsible for neonatal sepsis.[4]

Similar to other studies in sub Saharan Africa, GBS is not a common organism and also implicated in early onset of sepsis compared to late onset which was also found to be predominant in the current study. This study did not find any neonate with GBS.

7.5. Sensitivity of the isolates

The study has also shown the bacterial isolates had a high resistance to ampicillin and gentamicin in the range of 94 to 100% while resistance to gentamicin and ceftriaxone was moderate of 41%.Studies which were conducted between 1999 and 2012 at MNH and Bugando in Tanzania[3, 10, 11, 15]have shown the gradual increase on the resistance not only with the recommended first line antibiotics but also to the alternative antibiotics

vancomicinand amikacin where resistance was observed to be was 53% and 13.9% respectively. The following table shows a change in resistance pattern

Table 7: Trends of resistance to antibiotics used in management of neonatal sepsis

Drug	Blomberg et al ,2005	Mhada et al 2012	Current study
Ampicillin	95%	88.2%	96.4%
Cloxacillin	12.5%	85.2%	100%
Gentamicin	34%	58.8%	39%
Ceftriaxone	Not done	16.2%	41%
Cefuroxime	24.6%	20.6%	
Amikacin	Not done	1.5%	12.9%
Vancomycin	Not done	Not done	53.2%

The change in sensitivity which is remarkable to the fist line antibiotics which imply a need to reconsider change of our treatment protocol as the drugs appears not be effective for treatment of neonatal sepsis. This also has cost implication as the alternative may be expensive. Amikacin from this study is observed to be performing better compared to a recent study by Mhada et al in 2012[(10)] in the same setting, its resistance is also raising indicating the need to limit its use empirically to avoid further emergency of resistance.

This change in sensitivity is also observed in other parts of the world, for example in Pakistan resistance is as high as 100% to almost all the WHO recommended first line regime for treatment of neonatal sepsis that they have recommended use of Amikacin and Vancomycin as their first line[(38)].

7.6. Study limitations

- Anaerobic organisms and other etiological causes of sepsis were not studied due to limited resources.
- Other causes of raised CRP were not investigated.
- Blood pH and neutrophils (I/T) ratio was not determined because of lack of availability of laboratory identification test.

CHAPTER FIVE

8.1. Conclusions

This study found that CRP when used alone, serially or in combination with Rubarth's neonatal scale of sepsis has a high sensitivity to screen for suspected neonatal sepsis.The etiological agents to neonatal sepsis were identified to be *Klebsiellaspp, CoNS, S. aureus,E. coli*, and *Pseudomonas spp* which were 100% resistant to cloxacillin and observed moderate resistance to the second line drugs. Least resistance was observed with amikacin.

8.2. Recommendations:

In the management of suspected neonatal sepsis,serialCRP done twelve hours apart in combination with Rubarth's Neonatal scale of sepsis can be used for screening of neonatal sepsis. Once the results for the screening tests are available a blood sample for culture can be taken for those with a positive test. There is also a room for follow up studies on usefulness of CRP in combination with RNSOS in monitoring for response to treatment.

There is a need to have follow up studies to assess the efficacy of the current first line antibiotics used in the management of neonatal sepsis because of a high resistance observed.

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10.1. Appendix I: Newborn scale of sepsis (SOS) Rubarth ©2005
Name_____ Date of Exam _____ Age at Exam _____(days)

PARAMETERS	VALUES	PATIENT SCORE
LABORATORY RESULTS		
White Blood Cell Count	<5,000 = **5** , > 30,000 = **2**, 5,000-30,000 = **0**	
Immature: Total Neutrophil Ratio	> 0.3 = **5**, 0.2- 0.3 = **3**, < 0.2 = **0**)	
Platelet Count	< 100,000 = **3**, _ 100,000 = **0**)	
Absolute Neutrophil Count	<1000 = **5**, 1000-2000 = **3**, > 2000 = **0**	
Blood Acidity	pH < 7.25 = **2**, pH 7.25-7.34 = **1**, pH normal 7.35-7.45 = **0**	
CLINICAL INDICATORS:		
Skin Color	Ashen/Grey = **5**, Dusky = **3**, Mottled = **2**, Acrocyanosis = **1**, Pink = **0**	
Perfusion (Cap. Refill)	sec = **5**, Moderate 6-7 sec = **3**, Fair 4-5 sec = **1**, Good < 4 sec = **0**) Poor > 7	

Muscle Tone	Flaccid = **5**, Low tone = **3**, Good tone = **0**	
Responsiveness to Pain	No response = **5**, Some response (withdrawal) = **2**, Active Crying = **0**	
Respiratory Distress	Present with grunting = **5**, Present no grunting = **3**, None = **0**	
Respiratory Rate	100 = **5**, RR 60-99 = **3**, RR < 60 = **0**	
Temperature	Low temp < 36.5º C = **3**, High temp > 37.5º C = **2**, Normal 36.5 – 37.4º C.= **0**	
Apnea	Present = **2**, Absent = **0**	
TOTAL SCORE		

10.2. Appendix II: Questionnaire

Identification

1. Patient study code ……

2. Hospital Registration Number ……

3. Patient Name ……

4. Date of Birth ...../……. /….....

5. Sex: 1. M 2. F

6. Address: Residence …… District……

7. Date of Admission: ……. /……. /…….

8. Time of Admission: …….

9. Place of Delivery …… 1. Home 2. Hospital 3. Other

10. Mode of delivery … 1. SVD 2. LSCS 3. Assisted B/Del 4. Assisted Forceps Del 5. Assisted vacuum Del

11. Source of Information: 1. Parent 2. Guardian

12. Results

	Scores of Sepsis	**CRP level**	**FBP results**
Day 1	✓	✓	✓
Day 2		✓	

13. BLOOD CULTURE RESULTS 1. POSITIVE 2. NO GROWTH

14. Gram stain 1. Gram negative 2 Gram positive

ORGANISM	AMPICILLIN	CLOXACILLIN	GENTAMYCIN	CEFRIAXONE	Vancomycin	AMIKACIN
S.aures						
E.coli						
Klebsiellasp p						

Proteus spp						
S.epidermidis						
S.pneoniae						
Pneudomanasspp						
Other						

10.3. AppendixIII: Consent

10.3.1.English

Consent to participate in the study to determine the bacterial pathogens, anti-microbial susceptibility pattern and outcome of neonatal bacterial septicaemia among neonates admitted in neonatal unit at Muhimbili National Hospital (MNH).

My name is Dr.Martha Franklin Mkony. I'm a Resident in Paediatrics and Child Health MUHAS. I'm doing a research study in order to determine the efficacy of CRP and Neonatal scale of sepsis in the diagnosis of neonatal sepsis. I would like to ask your permission that your child participates in this study.

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

Study aims

This study will determine the usefullness of C-reactive protein and Newborn scale of sepsis for screening of neonatal sepsis. Also common causative bacterial pathogens and their anti-microbial susceptibility pattern of neonatal bacterial septicaemia among neonates admitted in neonatal ward will be determined.

How to participate in the Study

Your baby will be examined fully for sign and symptoms of neonatal bacterial septicaemia.

If you agree your child to join the study, you will be required to answer some questions, also, physical examination will be done to your child by the investigator; this includes routine physical examination [body weight, OFC]. Axillary temperature by using a mercury thermometer will be taken.

A small amount of blood will be taken using a sterile needle from your child's vein after you have agreed to participate in the study; this blood will be tested for presence of bacteria and other test that will enable us to reach to a diagnosis.

Participation in this study is completely voluntary. Even if you will not participate in this study your child will continue to receive the same service from this centre just like other children.

Confidentiality

Your child's name and other particulars will not be made public in any way and so your participation will be anonymous. Only the chief investigator, assistant's and dedicated laboratory staff will handle the specimens and information obtained.

Benefits

Parents/ guardians whose children will participate in this study will benefit by knowing the problem of their children and the importance of early management to these children.

Risks

The procedures that will be done in this study are common procedure for patients in hospitals and are very safe. We don't expect your child to have experience any problems as a result of this study.

Now I am ready to answer any question you wish to ask concerning the study.

For further questions or problems contact the following persons:

The Principal Investigator:

Dr. Martha Franklin Mkony

Department of Paediatrics & Child Health

Tel: +255 658 – 064338. E-mail: mmkony@gmail.com

Prof. M. Abood

Chairman of the College Research and Publication Committee,

P. O. Box 65001,

Dar es Salam. Tel: 2150302-6

I……..have read or been told the content of this form and Understand. My questions have been answered. I agree/disagree my child to take part in this study.

SIGNATURE OF PARENT/GUARDIAN. I AGREE/DISAGREE TO PARTICIPATE

10.3.2.Swahili

Consent -Swahili

Fomu ya ridhaa ya ushiriki katika utafiti wa kuhakiki vipimo vya CRP na tathmini ya viashiria vya uwepo wa magonjwa ya uchafu/vijidudu kwenye damu kwa watoto wenye umri chini ya mwezi mmoja kwenye wodi ya watoto wa change Hospitali ya Taifa Muhimbili.

Jina langu ni Dr. Martha Franklin Mkony. Mwanafunzi wa Udaktari-bingwa katika Idara ya Magonjwa na Afya ya Mtoto. Ningependa kufanya utafiti ulio tajwa hapo juu kama sehemu ya kukamilisha masomo yangu. Ninaomba ridhaa yako ili mtoto wako ashiriki katika utafiti huu. Awaliyayote, nitakupa maelezo kuhusu utafiti ninaotaka kufanya na halafu nitajibu maswali yote utakayo kuwanayo juu ya utafiti huu.

Madhumuni ya utafiti

Kama nilivyoeleza awali utafiti huu una dhumuni la kutaka kubaini vipimo vitakavyotumika kugundua kwa haraka uwepo wa magonjwa ya uchafu/vijidudu kwenye damu kwa watoto wenye umri chini ya mwezi mmoja

Jinsi ya kushiriki kwenye utafiti

Mtoto wako atafanyiwa uchunguzi wa kina ili kubaini dalili zozote za magonjwa ya uchafu/vijidudu kwenye damu ili kusaidia kubaini vipimo vinavyoeweza kusaidia ugunduzi wa uwepo wa vimelea hivyo kwenye damu kwa haraka.

Utakapo kubali kushiriki kuna maswali yameandaliwa utahitajika kuyajibu. Mtoto atafanyiwa uchunguzi wakina, uzito, urefu na joto la mtoto vitapimwa.

Pia, kiwango kidogo cha damu kitachukuliwa kutoka kwenye mshipa wa damu wa mtoto wako, kwa kutumia sindano safi na salama, utakapo kubali mwanao ashiriki katika utafiti huu. Damu hiyo itapimwa kuangalia kama kuna bakteria kufua na vipimo tajwa.

Ushiriki katika utafiti huu ni wa hiari kabisa. Hata kama hutapenda kushiriki katika utafiti huu mtoto wako ataendelea kupata huduma zilezile kama wanavyopata watoto wengine.

Usiri

Jina la mtoto wako na taarifa nyingine kuhusu mtoto wako hazitaonyeshwa kwa mtu yoyote, na kwa maana hiyo ushiriki wako hautajulikana na mtu. Ni Mtafiti Mkuu na wafanyakazi waaminifu wa maabara pekee ndio watakao shughulikia damu na taarifa zingine za mtoto wako.

Faida

Wazazi/ Walezi ambao watoto wao watashiriki katika utafiti huu watapata faida ya kujua tatizo gani linawasumbua watoto wao, na umuhimu wa matibabu mapema iwezekanavyo.

Madhara

Taratibu zote zitakazofanyika katika utafiti huu ni za kawaida kwa wagonjwa wa hospitali na ni salama sana. Hatutarajii mtoto wako apate matatizo yoyote kutokana na kushiriki utafiti huu.

Sasa nipo tayari kujibu swali lolote unalopenda kuuliza kuhusiana na utafitihuu.

Ukiwa na tatizo au swali lolote tafadhali wasiliana na wafuatao

Mtafiti Mkuu

Dr. Martha Franklin Mkony

Idara ya Magonjwa ya Watoto na Afya ya Mtoto

Simu: +255 773 – 064 338

Baruapepe: mmkony@gmail.com

Prof M. Abood

Mwenyekiti wa Kamati ya Utafiti

S.L.P 651001, Dar esSalaam.

Simu. 2150302-6

Mimi ……..Nimesoma/ nimesomewa maelezo yote yaliyomo kwenye fomu hii na nimeelewa. Maswali yangu yote ya mejibiwa.

Sahihiyamzazi/mlezi .Nakubali /sikubali Mtoto wangu ashiriki