ANTIBIOTIC TREATMENT IN PRETERM BABIES BORN BEFORE ARRIVAL (BBA) AT KENYATTA NATIONAL HOSPITAL.

A DISSERTATION PRESENTED IN PART FULFILLMENT FOR THE DEGREE OF MASTER OF MEDICINE (PAEDIATRICS) AT THE UNIVERSITY OF NAIROBI.

DECLARATION

I certify that this dissertation is my own original work and has not been presented for a degree in any other University.

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ACKNOWLEDGEMENTS

DEDICATION

To my Husband and our beloved Children.

TITLE

ANTIBIOTIC TREATMENT IN PRETERM BABIES BORN BEFORE ARRIVAL (BBA) AT KENYATTA NATIONAL HOSPITAL.

Research Question

Is there benefit in treating all Preterm BBAs at KNH-NBU as potentially infected?

LIST OF ABBREVIATIONS AND EXPLANATIONS

BBA - Born Before Arrival (Born outside Kenyatta National Hospital)

LBW- Low Birth Weight

KNH- Kenyatta National Hospital

NBU- New Born Unit

KDHS- Kenya Demographic Health Survey

DIC- Disseminated Intravascular Coagulation

CXR- Chest X-Ray

ANC- Antenatal Clinic

S.E.S.- Socio Economic Status

NRBC- Nucleated Red Blood Cell

SEPSIS- Septicaemia

TBAs – Traditional Birth Attendants

PROM – Prolonged Rupture of Membranes (>12hrs.)

PBF – Peripheral Blood Film

VLBW – Very Low Birth Weight Babies

GBS – Group B beta haemolytic streptococci

SPSS - Statistical Package for the Social Sciences

RDS – Respiratory Distress Syndrome

Gms - Grams

TABLE OF CONTENTS

SUMMARY

Neonatal Septicaemia has been a subject of periodic reviews in many parts of the world. An incidence of 1/1000 to 3/1000 live births has been reported in developed countries, compared to 4/1000 to 9/1000 reported in Africa [1,2,3,4]. Preponderance of higher sepsis rate in BBAs has been found in some studies [10,11,12], but other studies have not shown BBAs to be at a higher risk of infection [18,19]. Since in the absence of predisposing factors to sepsis it is unusual for an infant to develop early onset sepsis after an uneventful pregnancy and delivery, it was the aim of this study to determine if there was benefit in treating all Preterm BBAs as potentially infected at admission in the absence of such factors. The diagnosis of septicaemia was based on clinical grounds together with a positive blood culture and suggestive haematologic parameters. Infants who developed jaundice, fever respiratory difficulties, irritability, lethargy and diarrhoea were investigated. Blood cultures were obtained from a peripheral vein after aseptic preparation to the skin to minimize contamination by skin flora. The infants were evaluated radiologically when this was indicated. The initial treatment for the Cases and any baby in the Control group who showed signs of sepsis included a combination of crystalline penicillin and gentamicin in two divided doses. The antibiotics were altered accordingly depending on the organisms and their pattern of antibiotic sensitivity when this became available.

The present study showed an overall prevalence of infection of 37% in all preterms entered into the study, 33% in BBAs who were treated with routine antibiotics, 40% in BBAs who were not started on antibiotics at admission and 37 % in babies who were born in the KNH Labour Ward. In all the three groups, gram-negative organisms were the highest isolates with Klebsiella being the leading isolate. The only gram–positive isolate was coagulase negative staphylococcus, which showed high resistance to penicillin (100%), with moderate sensitivity to erythromycin (70%). The gram-negative organisms showed good sensitivity (80-100%) to gentamicin and other aminoglycosides and cephalosporins.

In conclusion, there was no significant difference in sepsis rate, bacterial isolates and sensitivity to antibiotics in the three groups and therefore routine antibiotics should be discouraged in all preterm BBAs and treatment instituted for only those with suspected sepsis considering perinatal, natal and other risk factors for sepsis. An aminoglycoside and a cephalosporin should be the drugs of choice in a neonate with suspected sepsis while awaiting culture and sensitivity results.

1.0 INTRODUCTION AND LITERATURE REVIEW

1.1 Introduction

Despite the development of more sophisticated diagnosis and management of neonatal sepsis in recent years, bacterial infection remains a major cause of neonatal morbidity and mortality. It is estimated that the incidence of neonatal sepsis varies from less than 1/1000 to 8/1000 live births and it is influenced markedly by the quality of the intrauterine life, host factors and environmental factors and therefore it is even higher in preterm infants.

In the pre-antibiotic era, mortality from neonatal sepsis exceeded 90%. This has fallen to a range of 10% to 50% since the advent of antibiotics. (1,2,3,4)

Early onset disease is defined as infection that occurs within the first 7 days of life. It usually presents as a fulminant multisystemic illness. It is associated with high mortality varying in some series from 15% to 60% and such infants usually have a history of one or more significant obstetric complications. Among these are premature delivery, low birth

weight, premature rupture of membranes, chorioamnionitis, maternal peripartum abnormal vaginal flora (e.g. streptococci carrier, sexually transmitted diseases), obstetric manipulations e.g. vaginal examinations in the presence of ruptured membranes and foetal hypoxia. It is unusual for an infant to develop early onset sepsis after an uneventful pregnancy and delivery. Initial empiric therapy should be aimed at those at high risk. In the choice of antibiotics, one should take into consideration the organisms associated with early onset sepsis and their antibiotic sensitivity.

At Kenyatta National Hospital New Born Unit (KNH-NBU), it is the practice to start all BBAs on antibiotics at the time of admission with the assumption that they are most probably infected during their birth outside hospital. This study was undertaken with the aim of proving whether these babies are actually infected and whether the type of antibiotics used (crystalline penicillin and gentamicin) should still be the drugs of choice.

1.2   Literature Review.

All over the world, neonatal Sepsis continues to be a common problem contributing significantly to high morbidity and mortality. All the neonates, especially the premature ones, are uniquely susceptible to

severe and overwhelming infections due to their immature immune systems. Antibiotics are therefore extensively used in most cases in their treatment.

A neonatal sepsis incidence of 1-3/1000 live births has been reported in developed countries compared to 4-9/1000 reported in Africa [1, 2,3,4] *with a mortality rate of 20% – 30%, and case fatalities of 15%-30%* [5].

At KNH, BBAs are routinely treated with antibiotics (crystalline penicillin and gentamicin) without waiting for proof or evidence of infection.

Babies Born Before Arrival are mainly a problem of developing countries. Studies done have shown that only 44% of the women in Kenya deliver in hospitals and 55% of the women deliver at home [6, 7, 8]. In another study, it was shown that 60% of rural women and 25% of urban women deliver their babies at home [9].

Studies done in various parts of the world have shown BBAs to be at higher risk of morbidity and mortality as compared to babies born in hospitals [10, 11,12].

Spillane, in his study on BBAs at Coombe Women's Hospital, found a BBA prevalence rate of 6.4% [14]. *Boopalan* found a BBA prevalence of 0.44% and a perinatal mortality of 58.4/1000 live babies in BBAs compared with 10.1/1000 for all hospital born babies [13]. The commonest morbidities in the two studies were LBW, hypothermia, hypoglycemia and infections. However, they found that the high perinatal mortality was related to immaturity and LBW rather than the baby being a BBA.

In their study on infections, *Rajals et al* found that out of 190 babies admitted at the Khaulo Hospital over the study period, 160 hospital born babies and 30 BBAs satisfied the criteria for infection. The mortality rate in the hospital born babies was 14% compared with that of 27% of BBAs [15]. *Azubuike* stressed the importance of male sex, prematurity and delivery outside hospital as significant factors in neonatal sepsis and mortality [16].

In Kenya, *Meme* found a neonatal mortality of 53.3/1000 live births at KNH and a tenfold increase in neonatal mortality in home delivered babies as compared to hospital delivered babies [17]. *Kasirye,* in his study on Neonatal morbidity and mortality at KNH-NBU, did not find a

significant difference in mortality between BBAs and hospital delivered babies. He attributed this low mortality in BBAs to the possibility that many infants cannot reach major hospitals and die before being attended. With increasing number of TBA's who have undergone training, and many local private and public health centers, many of these infants are now able to reach hospitals [18]. *Malenga*, looking at bacterial infections in neonates at KNH-NBU, found positive cultures in 41.4% in BBAs and 40% in hospital born babies. As there was no significant difference between the two groups, she concluded that most infants acquired the infection in the nursery. These infections accounted for 20% mortality in all neonates admitted. In her study, sex, gestational age and place of birth did not affect the rate of positive cultures [19]. *Yuko*, at the same institution, found an incidence of sepsis of 12% in preterm babies admitted with RDS. Her study excluded BBAs [20]. *Omondi* in his study of characteristics of mothers presenting with BBAs at KNH, found a clinically significant risk of sepsis in home delivered babies compared to hospital born babies. In his study, BBAs formed 7.3% of all admissions to NBU and had a case fatality of 35% compared to 9.6% for hospital born babies. Attendance of ANC was found to be an important factor in a baby being born before arrival [38]. Lack of ANC attendance contributed to high morbidity in some studies [9,12,14, 38].

With many studies pointing towards higher morbidity rates in BBAs and the absence of a clear cut aseptic technique used at the time of delivery, together with the kind of environment to which BBAs are born, there has been a tendency to treat all these infants for presumed sepsis with broad spectrum antibiotics – crystalline penicillin and gentamicin. This persistent high antibiotic use in the neonatal unit poses the danger of selective proliferation of virulent resistant strains of bacteria. An additional problem is emergence of other microorganisms that have cross-resistance patterns to similar drugs [21]. This practice not only exposes the premature infant to drug toxicity e.g. ototoxicity from gentamicin, but also escalates the cost of managing such infants which is a real financial burden especially to developing countries.

From the literature review, it appears that majority of BBAs are not at higher risk of infection compared to the hospital born, in absence of risk factors for sepsis [13, 14,19]. Their pattern of morbidity is due to their being premature and LBW like the hospital born rather than being BBAs [13, 14, 19]. Direct figures to support this impression are, however, lacking [18].

While early diagnosis of neonatal sepsis requires a high index of suspicion on the part of the clinician, optimal antibiotic therapy requires current knowledge of the causative organisms and the antibiotic sensitivity patterns [21].

This study aimed at finding out the prevalence of septicaemia in BBAs and whether routine antibiotic use is of any distinctive benefit to these babies. It also aimed at finding out the causative organisms and their antibiotic sensitivity, a finding that may lead to improvement of antibiotic therapy utilization.

1.3 Study Justification

Rational use of Antimicrobial therapy depends on answers to the following questions:

1. Who should be screened for sepsis?
2. What are the most useful tools in diagnosis?
3. When should treatment be started?
4. What are the guidelines for choice of antibiotic?
5. How long should the therapy last?

These questions are raised with the aim of trying to make sure that only those requiring therapy get it. This would help in minimizing the development of antimicrobial resistance as well as reducing the cost of treatment without compromising neonatal outcome.

The study carried out considered the above questions since:

1. BBAs admitted to NBU-KNH are treated as potentially infected resulting in increased use of routine antibiotics (crystalline penicillin and gentamicin).
2. There are conflicting studies on the risks of infections in BBAs.
3. There are conflicting reports on the prevalence of sepsis in BBAs.
4. There is need to establish if routine treatment is necessary especially if baby is well.
5. Indiscriminate antibiotic use leads to emergence of resistance and therefore the need to investigate before starting on treatment.

1.4   Research Question

Is there benefit in treating all Preterm BBAs at KNH-NBU as potentially infected?

MAIN OBJECTIVE

TO FIND OUT WHETHER IT IS BENEFICIAL TO TREAT ALL PRETERM BBAs AS POTENTIALLY INFECTED.

1.5   Specific Objectives.

1. To determine the prevalence of bacterial infection among Preterm BBAs.

2. To determine the type of bacteria infecting Preterm BBAs at KNH-NBU.

3. To establish whether it is beneficial to treat all Preterm BBAs as potentially infected.

2.0 METHODOLOGY

2.1 Study Design

Experimental/Intervention Study.

2.2 Study Population

❖ *Source of Population* – All admissions to NBU-KNH

❖ *Case Definition*: Preterm BBAs admitted to the NBU-KNH, during the study period, who had no additional risks of infection.

❖ *Control I Definition:* Preterm BBAs who were admitted to NBU and were birth weight and gestational age matched to cases and had no additional risk factors of infection.

❖ *Control II Definition*: Pre-term babies delivered in KNH Labour Ward who were admitted to NBU and were Birth Weight and gestational age matched to cases and had no additional risk factors of infection.

2.3 Study Area

The study area was the New Born Unit at the Kenyatta National Hospital (NBU-KNH), which admits the following babies: -

All babies with birth weight <2000gms or >4000gms, respiratory distress, asphyxia, jaundice, suspected or confirmed sepsis, gross congenital anomalies and babies of those mothers with high risk pregnancies e.g. Those who are diabetic, hypertensive or Rhesus negative.

2.4 Sampling

The sampling was sequential for all those who satisfied the definition of Cases, Control I and Control II. Each Case was compared to the next BBA (Control I) and baby born at KNH Labour ward (Control II), who were birth weight and gestational age matched to the Cases.

2.5 Sample Size

The sample size was 86

2.6 Sample Size Formula

$$N = n_1 + n_2 = \frac{4(Z_\alpha + Z_\beta)^2 \pi(1-\pi)}{(\pi_1 - \pi_2)^2}$$

Where

$$\pi = \frac{(\pi_1 + \pi_2)}{2}$$

$\pi_1 = P_{IN}$ (In Born Babies)
$\pi_2 = P_{OUT}$ (Out Born Babies)

For

$Z_\alpha = 1.65$ for $\alpha = 0.05$
$Z_\beta = 1.28$ for $\beta = 0.10$
$\pi_1 = 0.12$
$\pi_2 = 0.4$

Then

$$N = \frac{4(1.65+1.28)^2 * 0.26 * 0.73}{(-0.28)^2}$$

$$= 85.6$$
$$\approx 86$$

2.7 Inclusion Criteria

All pre-term babies admitted to NBU during the study period who satisfied the definition of case and/or control.

2.8 Exclusion Criteria

Any pre-term baby admitted to NBU who had additional risk factors of infection, which included those babies with signs of birth asphyxia, those born to mothers with prolonged rupture of membranes, those born to mothers with history of foul smelling amniotic fluid (chorioamnionitis), those who were referred and had obvious signs of sepsis, those babies whose mothers were on antibiotic treatment or history of maternal fever and those whose mothers did not give consent for participation in the study.

2.9 Diagnosis of Sepsis

For purposes of the study, the following criteria were used in identification of such neonates. Signs in the new born baby using Gotoff criteria (*see Appendix I*); laboratory investigations based on blood culture and full blood count; together with positive clinical features, with positive blood cultures were considered diagnostic of infection. Other diagnostic criteria were positive clinical signs (2 or more) according to *Gotoff criteria* and any two or more of the following laboratory features (*Rodwel* criteria using the white cell indices and morphology whereby a score of one is given for each of the parameters): - abnormal total leucocyte counts (WBC of $>30\times10^9$ /L on day 1 and $> 20\times10^9$ /L on subsequent days or

Leucopenia of <5x10^9 /L); abnormal total neutrophil counts; elevated immature polymorphonuclear cell counts; 1:T Ratio of >0.2 (Immature: Total Leucocytes); left shift and toxic granulation on peripheral blood film and platelet counts <150,000/ mm^3 (A score of 3 or greater identifies infants with sepsis with a sensitivity of 96%).

The white cell series were characterized as described by *Reich* and *Deykin* and Reference Values of *Monroe et al* were used. Corrected white blood count was calculated using the formula

$$\frac{100 \text{ x } \textbf{WBC}}{100 + \textbf{NRBC}} = \textbf{Corrected WBC,}$$

where NRBC is Nucleated RBC.

And where indicated as shown by suggestive clinical presentation of the baby, lumbar puncture for babies with suspected features of meningitis, CXR where the baby had features of pneumonia and stool culture in cases of diarrhoea.

3.0 DATA COLLECTION

This study was conducted from 7th August to 31st December 1999 and 15th August through 15th October 2000.

3.1 Method of Data Collection

At admission, all babies were weighed and a detailed antenatal and natal history taken. Gestational age assessment was done using Dubowitz Score [23] and for infants whose mothers could remember, it was calculated from the 1st day of the last menstrual period.

The details of history and personal details were taken and entered into the Proforma I (Appendix I).

The neonate was examined and an informed consent taken from the mother before the investigations were done.

The babies who satisfied the definition of case were then entered into the study.

A sample of blood was obtained from the neonate from a peripheral vein under aseptic technique. A total of 1 to 2mls of blood was taken and divided into 0.5 to 1ml for a blood culture and 0.5 to 1ml put into a micro container for a full blood count, a drop of blood was put on a clean blood slide for immature: Total (I/T) ratio of the Neutrophils.

At admission, the babies who satisfied the definition of Cases were started on antibiotics (crystalline penicillin and gentamicin) and the other group (Control I) was not started on treatment at admission. The two groups were matched for gestational age (± two weeks) and for birth weight (within ± 200gms of the stated weight). All babies entered into the study were followed up for seven days and signs of sepsis documented. Any baby in the untreated group who showed signs of sepsis later was started on antibiotic cover promptly. A repeat of laboratory tests was done on the 3rd day and any subsequent day of life whenever sepsis was suspected. Matched hospital born babies (Control II) were enrolled into the study and after informed consent had been obtained from the mothers, they were subjected to the same investigations and follow up. The results obtained were entered into each subject's record and the investigator informed the caretakers of any significant results for appropriate intervention. Positive clinical features, with positive blood cultures were considered diagnostic of infection.

Other diagnostic criteria were positive clinical signs (2 or more) according to *Gotoff criteria* [5] and any two or more of the laboratory features shown by *Rodwel* criteria using the white cell indices and morphology whereby a score of one is given for each of the parameters [24].

For purposes of this study, immature polymorphonuclear cells included band cells, metamyelocytes and promyelocytes.

3.2 Ethical Considerations

Permission was sought from the Ethical Committee, KNH and granted as per the attached letter of approval.

3.3 Statistics

The data obtained was entered into the computer. This was then analyzed using SPSS. Frequency distribution of the data, statistical tests of significance were carried out using χ^2 (chi-squared), McNemar's statistical test and z-test. The level of significance was $p<0.05$

4.0 RESULTS

4.1 Descriptive Statistics of Subjects.

A total of 90 subjects were entered into the study i.e. 30 subjects in each group of Cases, Control I and Control II. Cases were BBA Preterm babies who were started on antibiotic therapy at admission. Control I were BBA Preterm babies, who were not started on antibiotic treatment at admission and Control II were those born at KNH Labour Ward.

The Controls were birth weight and gestational age matched to Cases.

4.1.1 Distribution of Subjects according to Birth Weight at Admission.

Table 1 below shows the distribution of subjects according to birth weight at admission.

Table 1: Birth Weight of Subjects at Admission

Weight in Gms.	Cases Number	%	Control I Number	%	Control II Number	%	Totals Number	%
1000-1250	5	16	3	10	5	17	13	14
1251-1500	13	42	12	40	6	20	31	34
1501-1750	7	23	6	20	10	33	23	26
1751-2000	5	19	9	30	9	30	23	26
Total	30	100	30	100	30	100	91	100
Mean Wt. Gms.	1404		1450		1440		1431	

The range of birth weights was 1000g to 2000g. The mean birth weight was 1430g for all the subjects whereas it was 1404g for Cases, 1450g for

Control I and 1440g for Control II. There was no significant difference in the birth weights for all the 3 groups. The z-values for the significance test were 0.0946 and 0.116 at P values 0.05, 0.02 and 0.01. (p>0.05)

4.1.2 Distribution of Subjects according to Sex

Chart 1: Distribution of Subjects according to Sex
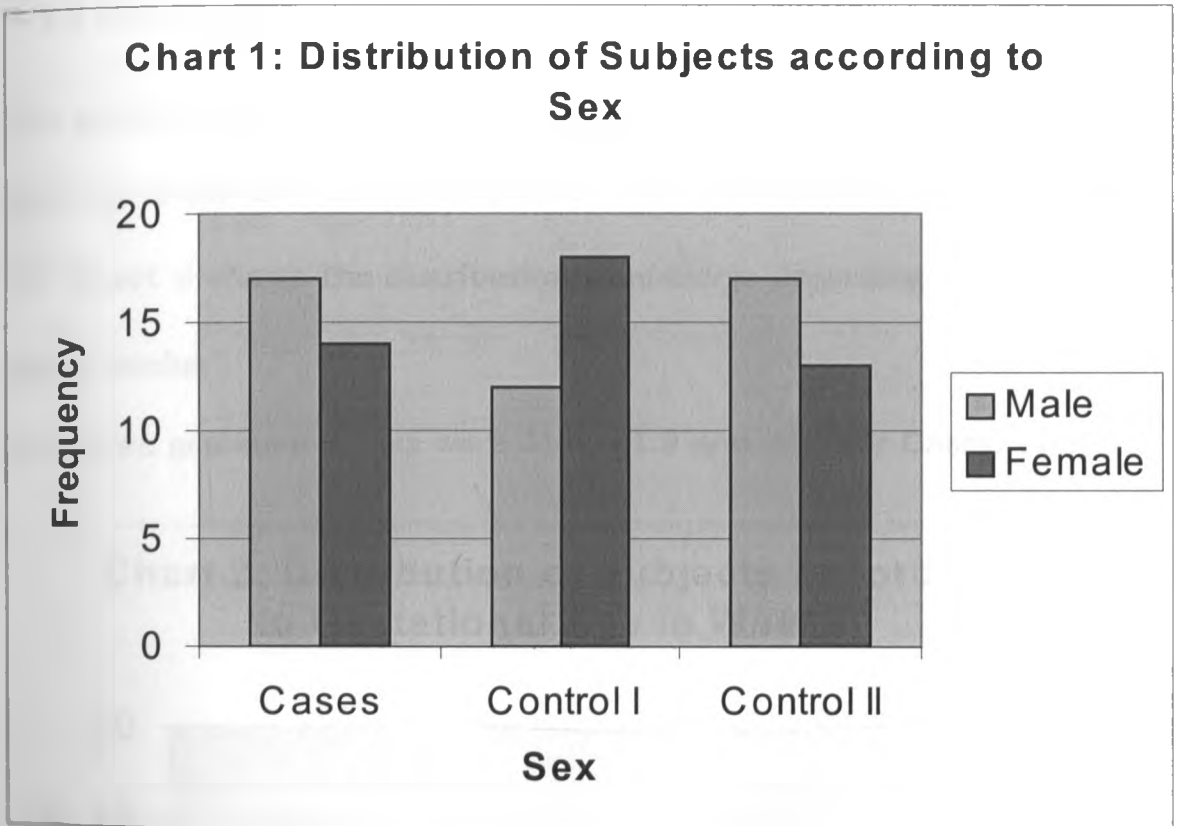
Chart 1 shows the distribution of subjects according to sex.

The male: female ratios were 1.2:1, 1:1.5 and 1.3:1 for Cases, Control I

and Control II respectively

There was no significant difference in the distribution of Subjects when

sex ratios were compared.

4.1.3 Distribution of Subjects according to Gestational Age in Weeks

The gestational ages of the subjects were determined by considering the

first day of the last menstrual period of the mother or by *Dubowitz* score

[23]. Chart 2 shows the distribution of subjects according to gestational

age in weeks.

The mean gestational ages were 31.1, 31.9 and 31.1 for Cases, Control I

Chart 2: Distribution of Subjects according to Gestational Age in Weeks

Legend:
- <=28
- 29-32
- 33-36

X-axis (Gestational Age (Weeks)): Cases, Control I, Control II
Y-axis (Frequency): 0, 5, 10, 15, 20
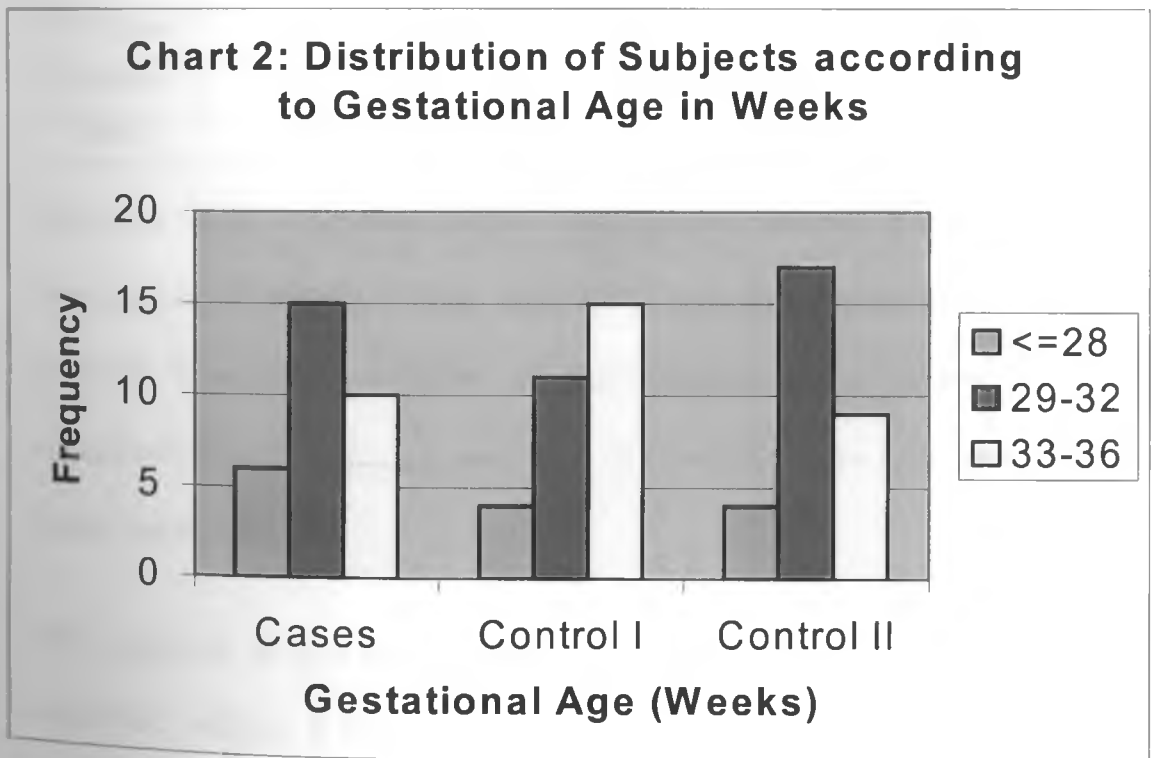
and Control II respectively.

There was no significant difference between the gestational ages when z-tests were applied for all gestational age groups (P>0.05).

4.1.4 Age Distribution at Admission

Table 3 below shows the distribution of subjects according to age at admission.

Table 3: Distribution of Subjects according to Age at Admission (Hours)

Age (Hrs)	Cases		Control I		Control II		Totals	
	Number	%	Number	%	Number	%	Number	%
<1	0	0	0	0	8	26	8	8
1-4 hrs	4	12	6	20	17	56	27	29
5-10 hrs	10	32	11	36	5	16	26	28
11-14 hrs	12	38	7	23	0	0	19	20
15-20 hrs	5	16	6	20	0	0	11	12
Total	31	100	30	100	30	100	91	100

From the table, only the infants born at KNH Labour Ward i.e. Control II were admitted within 1 hour after birth and this represented 27% of the Control II subjects.   100% of the hospital born babies (control II) compared to 47% of cases and 50% of Control I were admitted within 10 hours after birth.

The majority of the BBAs (70% of Cases and 60% of Control I) were admitted within 5-15 hours.   None of the hospital born babies was

admitted beyond 10 hours after birth. The mean age at the time of admission was 6.1 hours for Cases, 4.9 hours for Control I and 2.9 hours for Control II (Data not tabulated).

Using Z test of significance, values of 0.0719 and -0.1967 were computed at critical values of 2.447, 3.1430 and 3.707 for P values at 0.05, 0.02 and 0.01. There was no significant difference in age at admission between all the subjects.

4.1.5 Distribution of Subjects according to ANC Attendance.

Chart 3 shows the distribution of subjects according to ANC attendance. From Chart 3, 40% of mothers for Cases and 37% for Control I attended ANC compared to 47% of mothers who delivered in hospital. Sixty-six

Chart 3: Distribution of Subjects according to ANC Attendance
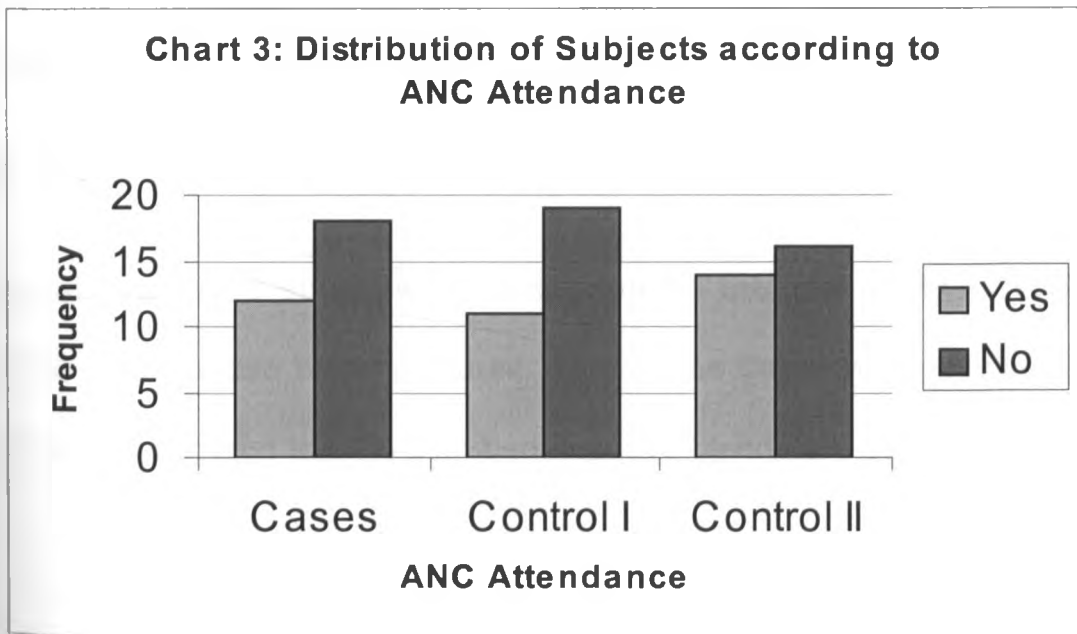
(66%) of the mothers who did not attend ANC had babies whose birth weight was <1500g (Data not tabulated). There was no significant difference of ANC attendance between all the subjects (P>0.1).

4.2 Sepsis Rates in the Subjects

4.2.1 Distribution of Subjects according to Positive Blood Cultures

Table 4 shows the distribution of subjects according to positive blood cultures. The prevalence of Sepsis was 33% for Cases, 40 % for Control I and 37% for Control II.

Table 4: Blood Culture - Positive Results

	Cases	Control I	Control II
	No. (%)	No. (%)	No. (%)
Septic	10 (33)	12 (40)	11 (37)
Not septic	20 (67)	18 (60)	19 (63)
Total	30 (100)	30 (100)	30 (100)

χ^2 =0.288 (p>0.1)

Overall, out of 90 subjects who were entered into the study 33 of them (37%) had positive blood cultures. 33% of the Cases had positive blood cultures compared to 67% who had negative blood cultures.

Of the Control I subjects, 12 out of 30 (40%) had positive blood cultures compared to 18 (60%) who had negative blood cultures.

Out of the 30 Control II subjects, 11 (37%) had positive blood cultures compared to 19 (63%) who had negative blood cultures.

Overall χ^2 **(chi-squared)** was 0.288, which shows no significant difference (P>0.1). When cases were compared to Control I, χ^2=0.287 (P>0.1), there was no significant difference. Similarly, Cases vs. Control II, χ^2=0.073 (not significant) and Cases vs. Combined Controls χ^2=0.215 (P>0.1). Using odds ratio, an odds ratio of 1.2 was obtained for Cases vs. Control I, which showed no significant difference (Taking a significant odds ratio of 1.5).

4.2.2 Distribution of Subjects according to Positive Blood Culture vs. Birth Weight.

Table 5 below shows the distribution of subjects according to positive blood cultures versus birth weight.

From the table, 40 % of cases (7 out of 18) with birth weight less than 1500gms compared to 25% of those who had weights greater than 1500gms, had positive blood cultures. For Control I, 53% of those whose birth weights were less than 1500 grams had positive cultures. For Control II, it was 64% for those whose birth weight was less than 1500 gms compared to 21% of those whose birth weight was more than 1500

gms. Overall, there was no significant difference between cases, Control I and control II, when positive blood cultures were considered vs., birth weight. But in each group of subjects, babies whose birth weight was less than 1500 gms had higher rate of sepsis.

Table 5: Distribution of Subject according to Positive Blood Culture vs. Birth Weight

Weight (gms)	Cases			Control I			Control II		
	Number	Positive	% (P/T*100)	Number	Positive	% (P/T*100)	Number	Positive	% (P/T*100)
1000-1500	18	7	39	15	8	53	11	7	64
1501-2000	12	3	25	15	4	27	19	4	21
Total	30	10	33	30	12	40	30	11	37

*Where P/T is the number of positive blood culture divided by the number of subjects.

From the same table, 7 out of 10 cases who had positive blood cultures had a birth weight <1500g compared to 3 out of 10 cases, $\chi^2=1.25$, (P<0.1). There was a significant difference between the cases when birth weights at admission were considered i.e. the babies whose birth weights were <1500g had more positive blood cultures.

Out of 12 subjects in Control I who had positive cultures, 8 (67%) were of birth weight <1500g compared to 4 (33%) of those whose weights were 1500 - 2000g. For Control II, 5 subjects out of 8 (63%) had positive cultures (in those of weights <1500g) compared to 3 out of 8 (37%)

(Weight>1500g). There was a significant difference when birth weights were considered in each group (p<0.05)

4.3 Sepsis Rate in Relation to Haematological Parameters.

4.3.1 Sepsis Rate using Haematological Indices

Table 6 shows sepsis rate in the subjects when haematological indices were used.

Table 6: Sepsis Rate using Haematological Indices (A Score of 3 or greater)

	Cases		Control I		Control II	
	Number	%	Number	%	Number	%
Septic	16	53	19	67	20	63
Not Septic	14	47	11	33	10	37
Total	30	100	30	100	30	100

p>0.1 (for both Cases vs. Control I and Cases vs. Control II)

Overall, the sepsis rates in all 3 groups of subjects were higher when hematological indices were considered.

Of the 30 Cases, 16 subjects (53%) were septic when haematological (White Cell Indices) were used.

Of the 30 Control I subjects, 19 were septic and of control II 20 (67%) had evidence of sepsis compared to 10 (35%) who didn't have.

Comparing Cases vs. control I χ^2. McNemar = 2 and comparing Cases vs. Control II χ^2 McNemar = 2.61 (No significant difference).

When abnormal leucocyte counts were considered, it was found that most of the subjects in all the 3 groups had leucocyte counts within the normal range for the age. Leucocytosis was seen in 6 of the 90 subjects studied. Leucopenia was uncommon, seen in 3 of the 90 subjects. The subjects who had leucopenia also had positive blood cultures, which showed that leucopenia is a good predictor of sepsis. When abnormal neutrophil counts were considered, it was found that Neutrophilia was the commonest presenting haematological feature. Neutropenia was not seen in any of the subjects. Low platelet count (<150,000) was also seen especially in the subjects who had severe sepsis with overt coagulopathy and died of severe hemorrhage secondary to DIC. (Data not tabulated)

4.3.2 Bacteriology in the First Week

Among the subjects, gram-negative septicaemia was the highest. Klebsiella ranked highest in all the three groups of subjects studied as shown in Table 7 below.

From the table, 3 subjects of the cases had more than 1 bacterium isolated (19%). 3 of the Control I had more than 1 type of bacteria isolated. For Control II, 2 subjects had more than one bacterium isolated. Coagulase negative staphylococcus was the only gram positive

bacteria isolated and this accounted for 19% of all isolates for the Cases, 7% of all isolates for Control I and 17% of all isolates for Control II. In 3 of the Cases where the coagulase negative staphylococcus was isolated, its clinical significance was questioned since it occurred as a 2nd isolate. In one Case, it was the only bacterial isolate, and was therefore considered significant.

Table 7: Bacteriology of the 1st Week

Bacteria	Cases	%	Control1	%	Control II	%
CNS	3	19	1	6.7	2	17
Klebsiella	8	50	10	66.7	6	50
Citrobacter	2	12.5	2	13	2	17
Enterococcus	1	6.25	1	6.7	1	8.3
Acinetobacter	1	6.25	1	6.7	1	8.3
Enterobacter	1	6.25	0	0	0	0
Total	16	100	15	100	12	100

CNS= Coagulase Negative Staphylococcus.

The commonest bacteria isolated were Gram negative, which accounted for 81% of all isolates in the Cases, 93% for Control I and 83% for Control II. There was no significant difference when Cases, Control I and Control II were compared using bacterial isolates. The types of bacteria isolated were similar in the 3 groups. The commonest bacterial isolate was Klebsiella in all the 3 groups of subjects studied. This accounted for 50% of all isolates in Cases, 67% of isolates in Control I and 50% in

Control II subjects. There was no statistical difference when the subjects were compared in the three groups (P>0.1). Of the 2 Cases who had positive blood cultures on Day 1, one had enterococcus and the other had coagulase negative staphylococcus. For the Control I group, the only subject who had positive blood culture on Day one had citrobacter species.

4.3.3 Sensitivity Pattern of Isolated Bacteria to Commonly used antibiotics

Table 8 shows sensitivity pattern of isolated bacteria to commonly used antibiotics.

Table 8: Percentage Antibiotic Sensitivity Pattern

DRUG / BACTERIA	GENTAMICIN	AMIKACIN	CEFTAZIDIME	CEFTRIAXONE	PENICILLIN
STAPH (COAGULASE NEGATIVE)	30	NT	NT	NT	0
ACINETOBACTER	80	100	90	100	NT
CITROBACTER	51	69	NT	NT	NT
ENTEROCOCCUS	0	0	20	10	0
KLEBSIELLA	80	75	75	80	25
ENTENOBACTER	100	100	100	100	NT

NT= Not Tested

With the exception of Acinetobacter, there was good sensitivity by all gram-negative organisms. Coagulase negative staphylococcus showed very high resistance to crystalline penicillin (100%) and good sensitivity

to erythromycin (70%). The Enterococcus species isolated, was resistant to virtually all drugs used commonly in the NBU. The poor sensitivity of the enterococcus species could suggest that this bacteria was hospital acquired.

5.0   DISCUSSION

Neonatal septicaemia is an important cause of morbidity and mortality among hospital patients in the tropics [2, 17, 32]. It is a life threatening neonatal emergency and any delay in diagnosis and treatment may have devastating consequences.

The study carried out looked at BBAs who are mainly a problem of developing countries where most women (60%) have been found to deliver their babies at home [6, 7, 8]. The incidence of BBA has been variously reported all over the world and it ranges from 0.9-15% [39]. The commonest morbidity reported in various studies includes LBW, hypothermia, hypoglycemia and infections [10,11,12]. With the assumption that BBAs are potentially infected, there has been use of routine antibiotic treatment of these babies at the KNH-NBU.

In this study, a total of 90 subjects were recruited and divided into three groups i.e. Group 1: BBAs who had antibiotics started at admission, as is the practice in this institution (Cases). Group 2: BBAs who were not started on treatment at admission (Control I) and Group 3: hospital born babies (Control II). The subjects were matched for gestational age and

birth weight. The birth weights ranged from 1000g to 2000g. The male to female ratios were 1.2:1, 1to 1.5 and 1.3 to 1 for the Cases, Control I and Control II respectively. The subjects were quite comparable with regard to sex distribution (Chart1) and gestational age (Chart 2).

When age at admission was considered (Table 3), it was found that BBAs (70% of Cases and 60% of Control I) were admitted within 5 to 15 hours compared to the hospital born babies, of whom the majority (100%) were admitted before 10 hours of age. This may be explained by the fact that there were difficulties with transport for the BBAs. Bureaucratic delays at admission could have been another contributing factor since admissions of BBAs is done through casualty. This was in agreement with Omondi who, in his study at the same institution, observed that lack of transport was the major contributing factor to babies born before arrival - contributing to 48% of all BBAs [38]. Bester in his study, found similar results, that is, 47% of BBAs to be due to lack of transport [12].

Accessibility to hospital especially at night is poor in most Nairobi city estates. Such delays in a baby being admitted can directly influence their outcome since it could contribute to hypoglycemia and hypothermia, which are common morbidities in LBW and preterm babies. These factors could predispose babies to septicaemia or they could have

also influenced the results whereby such babies could have been excluded from the study since signs of neonatal septicaemia are very non-specific in the early stages and may not be clinically distinguishable from those caused by other neonatal problems e.g. hypothermia and hypoglycemia [5]. Despite the delay in admission for BBAs, the prevalence of sepsis was the same in all the study subjects.

The other factor contributing to delay to come to hospital could be cultural influence. In most African societies, the man is the master and head of the family. The seemingly inferior status of the African women results in their limited part in decision-making processes even when it involves child bearing. For example the decision, to transfer a desperately ill pregnant woman to a hospital is always made by the man and in his absence others maybe unwilling to make the decision leading to delays to come to hospital for early intervention. On the other hand, the assumption that delivery is a natural process coupled with traditional dislike of operational deliveries could make most mothers wish to deliver at home for fear of such operations [6, 7, 8].

Antenatal clinic attendance is important for a good maternal and foetal outcome [9, 12, 38, 39]. In the present study, there was no significant difference between mothers who delivered outside KNH (BBAs) and those

who delivered in the KNH Labour ward, (Chart 3). This was not in agreement with other workers who found that the women who delivered at home were more likely not to have attended ANC [9, 12, 14, 38]. Possible explanation for this included, low S.E.S., unemployment, single mothers and primigravida. A teenage mother, single mother or primigravida is likely to be shy about her most likely unwanted pregnancy and usually tries to conceal their pregnancy. The same factors have also been found to contribute to BBA [3, 12, 38, 39]. ANC attendance did not influence the sepsis rate in all the subjects studied, i.e. there was no significant difference when ANC attendance was considered in relation to positive blood cultures.

The present study showed that most women (66%), who did not attend ANC had babies whose birth weights were less than 1500g (VLBW). Late start of ANC attendance could explain this result which is in agreement with *Mati et al* who observed that most mothers attend clinic once or twice and a number of them from this study were found to have started clinic attendance in 2nd and 3rd trimesters [39].

A septicaemic rate of 33% was found in BBAs in the present study, based on positive blood culture results (Table 4). This compared well with 37% of hospital born babies. There was no statistical difference in sepsis rate

when BBAs were compared with hospital born babies (p>0.1). There was no difference between BBAs who were started on antibiotics and those who were not. These results are in agreement with *Kasirye* and *Malenga* [18,19]. This, however, was not in agreement with other workers who found home delivered babies to be at an increased risk of infection compared to hospital born babies [10,11,12,15,16]. In the present study, the subjects were matched for gestational age and birth weight. These factors have been found to influence the rate of sepsis in newborn babies. For example the lower the birth weight the higher the sepsis rate. The study is in agreement with other workers who similarly found that infection was higher in babies whose birth weight was less than 1500 gms compared to those whose birth weights were more than 1500 gms [22,25,26]. On considering other maternal factors such as low SES, inadequate antenatal care, as well as other baby factors such as LBW, hypothermia, hypoglycemia, higher infection rates were found in babies who weighed less than 1500 gms at birth. The present study, however, only considered LBW as the only risk factor for sepsis and has shown that place of birth does not predispose babies to increased risk of infection. The other predisposing factors leading to increased risk of early onset sepsis shown by *Alausa et al and Omondi* were lacking in this study, which excluded infants who had such risk factors [4,38]. The

similar sepsis rate between BBAs and hospital born babies could have been due to exclusion of the other risk factors as compared to other studies whose sepsis rate in BBAs was higher [10,11,12,15,16]. These workers included all babies in their studies, and this could have included a substantial number of those babies with increased risk to infection for example birth asphyxia, PROM, maternal fever which are the main indications for admissions for babies to NBU. BBAs are likely to suffer serious consequences when such factors are considered as compared to hospital born babies where intervention could be earlier, for example, delivery through caesarian section or starting the mother on antibiotics before delivery, as is the case with maternal infection.

This study also showed a higher sepsis rate after 48 hours of stay in the nursery. It was observed that most positive blood cultures were obtained on the third and subsequent days after admission. Only 3% of the infection of the study group occurred on day one of admission. This could imply that the infections could have most likely been acquired within the nursery and not influenced by place of birth. This result agrees with other workers, who implicated nosocomial infections in their studies [19,29,30].

Nosocomial infections are seen mostly in patients who undergo invasive procedures e.g. vascular catheterization. As more infants survive through the first days of hospitalization, the incidence of hospital-acquired infections rises. The use of antibiotics in some of the infants in the present study for suspected septicaemia may have promoted multiple antibiotic resistant gram-negative septicaemia. This is in agreement with other published data [2,3].

When sex was considered, there was no significant difference in sepsis despite the fact that the subjects were not matched for sex. This was not in agreement with other workers, who showed male sex to have higher preponderance to developing sepsis than female sex [3,16,28]. *Washburn* and his colleagues have postulated a sex linked factor that relates to the females' possession of two X chromosomes where they implicated a protective gene located on the X chromosome, which is involved in the synthesis of immunogobulins. A female with a double dose of genes possesses a greater resistance to infection [28].

When bacteriology was considered (Table 7), the commonest isolates seen were gram-negative bacteria (81%). These have been associated with severe neonatal infections. Klebsiella was the highest isolate, accounting for 50% of isolates in the Cases, 67% in Control I and 50% in Control II subjects. There was no statistical difference when the subjects were

compared in the 3 groups (P>0.1). This result was in agreement with other workers who also found Klebsiella among the commonest organisms causing neonatal sepsis [29,35,36,37]. The bacterial isolates are seen more in nosocomial infections.

In contrast to the reports from the nurseries in North America and Western Europe, group B beta hemolytic streptococci (GBS) and L. Monocytogenes were not significant pathogens among infected preterm babies at KNH. In this part of the world and elsewhere in the tropics, majority of early onset septicaemia is caused by gram-negative bacteria rather than GBS. The difference in the incidence of GBS may reflect a genetic factor or differences in sexual practices [2, 3, 30]. The isolation of gram-negative organism may be due to lack of proper hygiene in nurseries in the developing countries [42].

Coagulase negative staphylococcus was the most single gram-positive organism responsible for septicaemia in this study (Table 7). Since S. epidermidis (coagulase-negative staphylococcus) is present on the skin, isolation of this organism from cultures of blood may represent skin contamination. However, invasion of blood may occur as seen in this study where aseptic technique was observed. The apparent increase in septicaemia due to coagulase negative staphylococcus has been

associated with increased survival of very small premature infants with immature immune systems. These infants have increased risk to septicaemia by coagulase negative staphylococcus due to the invasive procedures that they undergo for maintenance and monitoring, which includes long-term vascular access devices. Coagulase negative staphylococci are the predominant causes of vascular- catheter related infections [45].

Cross-infectivity was observed in 11% of the subjects studied. In one subject the 2nd bacterial isolate was coagulase negative staphylococcus whose clinical significance was questionable. The other isolates were gram-negative. In the absence of establishing of a barrier between infected neonates and those who do not habour the organisms, coupled probably with lack of proper hygiene and limited space, cross-infectivity was shown. Cross-contamination with subsequent cross-infectivity from one patient to another accounts for 10-20% of gram-negative bacillary infections [41,42]. This was in agreement with the present study where it accounted for 11% of bacterial isolates in the subjects. Most resistant organisms arise from the patients' endogenous flora rather than from the outside sources. Sophisticated genotyping of multiple hospital isolates confirms that marked majority of the gram-negative organisms colonizing or infecting hospitalized patients are distinct from one another, even

among patients occupying the same unit at the same time [41,42]. This was not proved in the study.

Sharing of incubators by these infants and a lot of movement from incubator to another at times without putting into consideration the type of bacteria each infant had, could have contributed to cross-infectivity. This is seen mainly in an effort to isolate the babies who had proven sepsis in order to minimize spread of infections to uninfected babies, which more often than not is done late because of the delays in results reaching the ward. Lack of enough space is another possible contributing factor to ineffective isolation. Lack of hygiene and absence of establishment of a barrier between infected infants and those who did not habour the organisms is another contributing factor.

The use of antiseptics e.g. hexachlorophene has been shown to decrease staphylococcal colonization e.g. in hand washing practices. The chemical however is ineffective against gram-negative enteric bacilli [2, 3, 30]. Repeated hand-washing reduces the colonizing bacteria. This could have been the case in this study, which showed preponderance of gram-negative bacteria compared to gram-positive bacteria.

In most studies done, there have been no controversies as to the choice of antimicrobial agents used in the treatment of suspected sepsis. Selection of antibiotics should be based on postnatal age at onset of the disease, patient specific factors including invasive procedures, previous antibiotic therapy and prevalence of the bacterial species most likely to cause infection. In most centres, penicillin combined with an aminoglycoside like gentamicin has been recommended. From this study, the gram-negative organisms, which were the highest isolates, showed high sensitivity to gentamicin and 3rd generation cephalosporins.

In the Western world, penicillin combined with an amino glycoside are useful antimicrobials for empiric treatment of GBS and L. Monocytogenes [42]. This is not in agreement with the present study and elsewhere in the tropics where the commonest bacteria isolated are the gram-negative organisms. A 3rd generation cephalosporin and an aminoglycoside are drugs of choice recommended, for the treatment of Klebsiella and Enterobacter septicaemia from this study.

The treatment of citrobacter, which was among the gram-negative isolates in the present series, is more controversial. This organism showed a sensitivity of 50% to gentamicin and 70% to amikacin.

Sensitivity to 3rd generation cephalosporins was not done for this particular bacteria in the present study. Citrobacter, Enterobacter, Serratia, Proteus and Pseudomonas species have been shown by other workers to be causative organisms of sepsis in this institution [19, 20]. These organisms have been shown to carry a chromosomally encoded inducible B-lactamase. Normally, this enzyme is under repressor control and many isolates appear sensitive to the commonly used antibiotics. Exposure to the Beta-lactam antibiotics however results in induction of expression of the enzyme, which persists as long as the inducer is present. When mutation occurs in B-lactamase repressor gene, production of beta-lactamase is permanently induced and the organism becomes resistant to the Beta-lactam antibiotics. In this case even the organisms that were initially susceptible to a beta lactam antibiotic may become highly resistant during therapy [40,41,42]. This could have been the case, in the present study where the empiric therapy for suspected septicaemia included initial use of penicillin (Beta-lactam antibiotic). Infections due to gram-negative bacilli should therefore be treated with a combination of a 3rd generation cephalosporin and an aminoglycoside (e.g. gentamicin).

Enterococcus species in the present study showed resistance to virtually all antibiotics commonly used in the NBU in this institution. In general,

Enterococci have been shown to have high resistance to many antibiotics including cephalosporins, penicillinase resistant penicillins and aminoglycosides. Previously, Enterococci were treated with cell wall active agents e.g. penicillin, vancomycin, and cephalosporins combined with aminoglycosides. This was on the basis that cell wall active antibiotics were shown to facilitate bacterial uptake of the aminoglycosides. In recent years, high-level resistance to these antibiotics has been prevalent among these bacteria. Management of infection caused by multiple drug resistant Enterococci therefore is still a dilemma [43,44]. From the present study, it also remains a dilemma due to high level of resistance shown.

All coagulase negative staphylococci isolated in the study subjects were resistant to penicillin (100%) (Table 8). Data from other studies at the same institution and elsewhere in the tropics show similar results [2,3,19,20]. Coagulase negative staphylococcus, though a normal skin flora, has been associated with blood stream invasion leading to septicaemia. It is associated commonly with intravascular catheters and other invasive procedures [45]. Most hospital acquired staphylococcus are resistant to penicillins and cephalosporins. In most centres, penicillinase resistant penicillin e.g. oxacillin and methicillin are preferred and in case of resistance to such antibiotics vancomycin is the

drug of choice [46]. In the present study, sensitivity was looked at in relation to penicillin and gentamicin in particular. It was observed however that there was moderate sensitivity of 70% to erythromycin (data not tabulated). The use of oral antibiotics is however of questionable efficacy in the treatment of septicaemia, especially in preterm babies whose absorption of substances from the gut may be poor. The absorption is particularly poor in an infant who has septicaemia in whom even enteral feeding is problematic. From the present study, antibiotic therapy for staphylococcal septicaemia still remains unanswered. However, since staphylococcal septicaemia was not as common as gram-negative septicaemia, 3rd generation cephalosporins and aminoglycosides are still drugs of choice for empiric therapy of neonatal sepsis at KNH.

Erythromycin, although of questionable efficacy, may be tried where staphylococcal sepsis is suspected. Alternatively, other drugs like penicillinase resistant penicillins and vancomycin may be considered.

From the results obtained, there was no significant difference in sepsis rate, type of bacteria causing septicaemia and sensitivity to antibiotics between Cases, (BBAs who were treated with antibiotics at admission)

Control I, (BBAs who were not started on treatment until they showed features of infection) and Control II (Hospital Born babies).

6.0 CONCLUSION

1. A sepsis rate of 37% was found in this study among Preterm babies admitted to KNH-NBU.

2. Sepsis rate in BBAs who were started on antibiotics was 33%.

3. Sepsis rate in BBAs who were not started on antibiotics at admission was 40% and for babies born at KNH Labour Ward was 37%.

4. There was no significant difference in prevalence of infection between BBAs and babies born at KNH Labour Ward.

5. There was no significance difference in sepsis rate in BBAs who were started on antibiotics at admission (Cases) and those who were not started on antibiotics (Control I).

6. There was a higher sepsis rate in babies with birth weights less than 1500 gms compared to babies whose birth weight was more 1500 gms.

7. The most common bacteria isolated was gram-negative in all the three groups with Klebsiella being the highest isolates.

8. The only gram-positive bacteria isolated was coagulase negative staphylococcus, which showed high resistance to penicillin (100%).

9. The gram-negative bacteria isolated showed good sensitivity to gentamicin and other aminoglycosides and cephalosporins.

7.0 RECOMMENDATIONS

Blind therapy for all BBAs at KNH-NBU should be discouraged and treatment instituted for only those with suspected sepsis considering perinatal, natal and other risk factors for sepsis.

For a neonate who is suspected to have sepsis, cephalosporins (3rd generation) and an aminoglycoside (gentamicin) should be drugs of choice while awaiting culture and sensitivity results.

8.0 APPENDICES

8.1 Appendix I - Signs of Sepsis (Adapted from *Gotoff* and *Behrman* 1970)

General

- Does not look well, off colour poor temperature regulation

CNS

- Apathetic/ irritable/ High pitched cry/ jittery /hypotonic / convulsions/ coma

Respiratory

- Apnoea/tachypnoea

- Cyanosis/grunting

- Intercostal recession

Gastrointestinal/abdominal

- Drinks poorly

- Vomits/increased aspirates

- Diarrhoea/constipation

- Abdominal distension and tenderness

- Hepatomegaly/splenomegaly/enlarged kidneys

- Redness and induration of skin

- Flank levidity

Cardiovascular

- Pallor/cyanosis/cutis memorata

- Decreased capillary refill

- Tarchycardia/bradycardia/arrythimia

- Cold clammy skin

- Hypotension

- Oedema

Skin

- Spots/erythema

- Petechiae/Purpura

- Pustules/Paronychia

- Omphalitis

- Sclerema neonatorum

Hematopoietic

- Jaundice

- Bleeding

- Purpura

Musculoskeletal

- Pseudoparalysis

- Odd limb position and pain on movements

- Swelling

8.2 Appendix II- Normal Haematologic Values.

Values	Gestational Age (Weeks)		Cord Blood	Day1	Day3	Day7	Day14
	28	34	Full Term				
Hb (g/dL)	14.5	15.0	16.8	18.4	17.8	17.0	16.8
HCT (%)	45	47	53	58	55	54	52
Red Cells (mm^3)	4.0	4.4	5.25	5.8	5.6	5.2	5.1
MCV	120	118	107	108	99	98	96
MCHC(%)	31	32	31.7	32.5	33	33	33
Retic (%)	5-10	3-10	3-7	3-7	1-3	0-1	0-1
PLT(1000s/m^3)	150	150	296	192	213	248	252

White Cell and Differential Counts in Premature Infants

Birth Weight	<1500 g			1500-2500 g		
Age in Weeks	1	2	4	1	2	4
Total Count x10^3/mm^3						
Mean	16.8	15.4	12.1	13.0	10.0	8.4
Range	6-32.8	10.4-21.3	8.7-17.2	6.7-14.7	7.0-14.1	5.8-12.4
% of Total Polymorph Segmented	54	45	40	55	43	41
Un-segmented	7	6	5	8	8	6
Eosinophils	2	3	3	2	3	3
Basophils	1	1	1	1	1	1
Monocytes	6	10	10	5	9	11
Lymphocytes	30	35	41	9	36	38

Total Neutrophil Count Reference Range in the First 60 Hours of Life
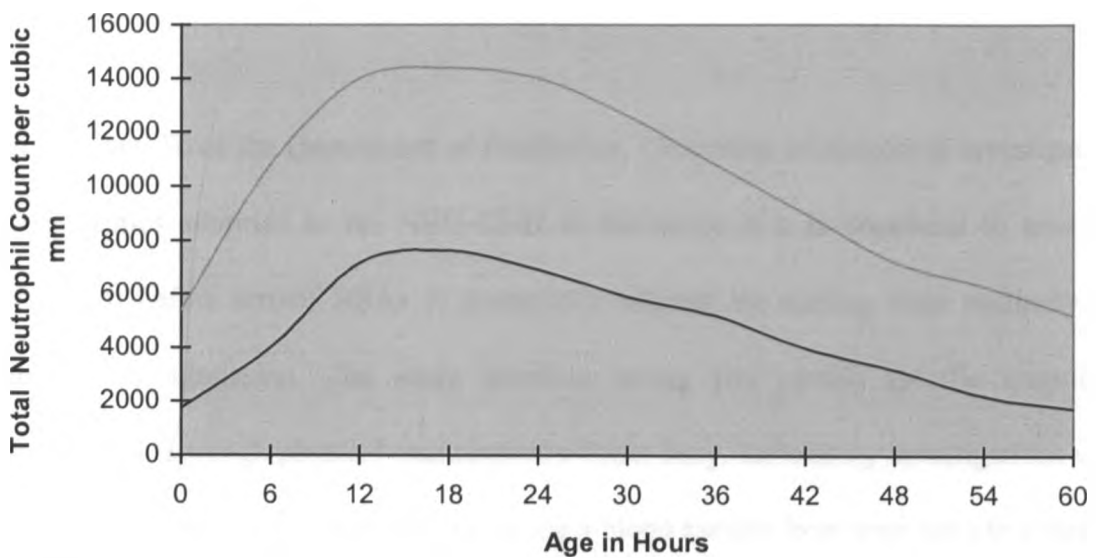
For diagnosis the following laboratory data is used;

1. Band neutrophils >= 0.2

2. Leucopenia < 5000 cells/mm^3

Any 2 or more of the above laboratory features are diagnostic of sepsis in neonates. This gives a sensitivity of 93% and specificity of 88%

8.3 Appendix III - Consent Form

Study No. ....

I, Dr. Lusweti B. of the Department of Paediatrics, University of Nairobi is investigating preterm babies admitted to the NBU-KNH to determine if it is beneficial to treat all babies born before arrival BBAs as potentially infected by starting them routinely on antibiotics at admission. The study involves asking you certain specific questions followed by a thorough physical examination of your baby. Laboratory investigations will then be carried out and this will involve taking a blood sample from your baby to check if there is infection or not. The results of the study will be treated with strict confidence should any problem be detected your baby will be prescribed for the appropriate treatment.

You may quit the study at any stage without any obligation.

I agree that my baby be part of this study.

Name.. Signature (Thumb Print).....................

(Parent)

Witness (Investigator) ....

8.4 Appendix IV - PROFORMA I

Personal Details of Baby

1. Date of Admission ……………………….

2. IP Number ………………………………

3. Name ……………………………………………………………………………...

4. Serial Numbers

      a) CASE …………………………………………..

      b) CONTROL …………………………………..

5. Date of Birth and Exact time or Age at Admission (Hours)

6. Date of Death and Exact time ………………....

7. Sex Male/Female ……………………………………….

8. Place of Birth for BBAs Home:……………………. En route: …………………

   Others Specify……………………………………….

9. Birth Weight (Grammes) ……………………………..

10. Gestational Age by dates ……………………. Or Dubowitz Score ……………..

11. Classification – SGA/AGA/LGA: …………….

12. Diagnosis at admission (Admission criteria)

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13. Outcome

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8.5 Appendix V - PROFORMA II

Maternal Characteristics

1. Age (Date of Birth): ....

2. Residence:

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3. Marital Status 1-Married 2- Single 3- Divorced 4- Separated 5- Widowed ....

4. Occupation of Mother ....

5. Highest Level of Education ....

6. Mother's Parity ....

7. ANC attendance 1- Yes 2- No .... If Yes

- Where ?

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8.6 Appendix VI - PROFORMA III

Clinical Criteria for Diagnosis of Sepsis

Day 1

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Antibiotics Yes/No .... Specify ....

Blood Culture

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Day 3

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Antibiotics Yes/No .... Specify ....

Blood Culture

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Day 7

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Antibiotics Yes/No .... Specify ....

Blood Culture

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8.7 Appendix VII - PROFORMA IV

Laboratory Features

Haematologic Values

Values	Day1	Day3	Day7
Hb (g/dL)			
HCT (%)			
MCV			
Platelets(x10^9/m^3)			
WBC (Total) x10^3			
Polymorphs			
Lymphocytes			
I/T Ratio			
Blood Culture			
Other Investigations			
LP			
CXR			
Urine Culture			
Stool Culture			

KENYATTA NATIONAL HOSPITAL
P.O. Box 20723, Nairobi
Telegrams: "MEDSUP", Nairobi
Email: knh@healthnet.cr.ke

Ref........KNH-ERC/01/963   Date....14 March 2001....

Dr. Bernadine N. Lusweti
Dept. of Paediatrics
Faculty of Medicine
University of Nairobi

Dear Dr. Lusweti,

RE: **RESEARCH PROPOSAL** "ANTIBIOTIC TREATMENT IN BABIES BORN BEFORE
ARRIVAL (BBA) AT KENYATTA NATIONAL HOSPITAL"   (P814/8/1999)

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

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

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

Thank you.

Yours faithfully,

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

c.c. Prof. K.M. Bhatt,
      Chairman, KNH-ERC,
      Dept. of Medicine, UON.

      Deputy Director (CS),
      Kenyatta N. Hospital.

      Supervisors: Prof. R.N. Musoke, Dept. of Paediatrics, UON
                    Dr. F. Were, Dept. of Paediatrics, UON
                    Prof. A. Wasunna, Dept. of Paediatrics, UON

      The Chairman, Dept. of Paediatrics, UON

      The Dean, Faculty of Medicine, UON

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