BACTERIAL INFECTIONS IN NEONATES IN THE KENYATTA NATIONAL HOSPITAL NURSERY, May-July 1981, a prospective Study

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This thesis is my original work and has not been presented for a degree in any other University.

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SUMMARY

The pattern of neonatal bacterial infections in the Kenyatta National Hospital (KNH) nursery was analysed over a three month period with a view of finding out the causative organisms and their antibiotic sensitivity pattern. Any suspected infected infant was subjected to a batch of bacterialogical investigations which included blood, urine, cerebrospinal fluid, rectal and umblical swab cultures. Other body surface swabs were taken as necessary. Predisposing factors were looked for.

Klebsiella and Escherichia Coli were the commonest organisms incriminated in the aetiology of neonatal infections in this study, accounting for 38% of all isolates. Staphylococcus aureus and Staphylococcus albus accounted for 27%. Aminoglycosides gave the best sensitivities against all gram negative organisms tested, with gentamycin being superior to Kanamycin. Lincomycin, chloramphenicol and minocycline gave the best sensitivities against gram positive organisms.

INTRODUCTION

Infections are an important cause of morbidity and mortality during the neonatal period when they may fulminate and cause death within hours. The newborn infant's increased susceptibility to infection can partly be explained by the immaturity of his immune system. The premature with his associated low levels of immunoglobulins, complement, polymorphonuclear phagocytic activity and lysozymes shows an increased susceptibility to infection (1). The male infant has been noted to show a two-fold higher incidence of sepsis, meningitis and pneumonia than the female (2, 3). This has been coupled with the observation that lgM levels are lower in the male than female infant suggesting a sex-linked factor in immune response (3). Heavy exposure of the newborn infant to pathogens is a major predisposing factor in neonatal sepsis. This may occur through the maternal blood stream, from an infected uterine wall following rupture of membranes or from passage through the birth canal. Postnatally, the neonate meets an invironment full of bacteria, thus increasing chances of heavy colonisation and possible infection of the skin, umblicus and alimentary tract. Bacteria which are nonpathogenic in the older people can be pathogenic to the newborn infant. While colonisation does not necessarily mean infection with

the particular organism, a definite diagnosis can be assumed from positive cultures of blood, urine and cerebrospinal fluid.

Early diagnosis of infection in neonates can be difficult as many infections show no symptoms at birth. When symptoms occur they may be so subtle and may mimic a host of other conditions common during this period, such as idiopathic respiratory distress syndrome, jaundice, haemorrhagic disease of the newborn, nonspecific skin rashes and hypothermia. Simple and early routine laboratory investigations such as white blood cell counts may give inconsistent results and leucopenia, leucocytosis or normal white blood cell counts may accompany severe infections in neonates (4). Xanthou et al however, (5, 6) maintain that there are definite white blood cell changes in severely infected newborn infants.

Glasgow et al have noted that as many as 2% of all foetuses are infected in utero and up to 10% of infants are infected during delivery or during the first month of life (3). The same authors have also pointed out that inflammatory changes are evident in up to 25% of newborn autopsies. Faced with the urgency to treat infection in the newborn, workers in this field will therefore tend to

put any seemingly infected infant on some broad spectrum antibiotic in order to play it safe, at least while still awaiting more definitive laboratory data. Patterns of bacterial infections and antibiotic sensitivities vary not only from place to place but also from time to time. Lack of information on neonatal infections in the Kenyatta National Hospital nursery stimulated the author to carry out this study.

AIMS AND OBJECTIVES

(a) To find out the pattern of bacterial infections in neonates in the KNH nursery at least over the period of study and provide a basis for future comparative work, and

(b) to provide data on antibiotic sensitivity pattern in order to facilitate the choice of antibiotics prior to laboratory confirmation.

MATERIALS AND METHODS

This study was carried out in the Kenyatta National Hospital (KNH) nursery attached to the KNH Obstetric Unit. The Unit acts as a referral centre for high risk deliveries from around the Nairobi area as well as a small percentage of low risk deliveries from the same area.

The KNH nursery (at the time of study and has since moved to new premises) consisted of three rooms A, B and C separated by solid walls. Room A admitted preterm infants born within the obstetric unit and requiring incubator care as well as sick term infants requiring intensive care. Room B admitted term infants with minor problems for observation and any infants graduating from room A and C. Room C admitted babies born before arrival to the Unit, either from home, the gynaecological ward or from the satellite maternity units within the vicinity of KNH. Any baby less than 24 hours old, term or preterm could be admitted to nursery C. Transfer of infants from nursery C to either of the other two although occurred, was limited to minimum. Due to shortage of space it was not uncommon for more than one infant to share a cot or an incubator. The staff between the three rooms interchanged on day to day basis. As part of a teaching set up, both qualified medical and

nursing staff together with their student counterparts manned the three rooms in rotation. No special isolation procedures were in practice. Mothers were allowed in the rooms only during feeding times as breast milk feeding was encouraged as much as possible either by suckling or tube-feeding of expressed breast milk where necessary. Complementary formula feeds were used in some few cases.

During the period 4th May to 31st July 1981, all neonates admitted to the nursery from the labour ward, post-natal wards or born before arrival to the unit and suspected to be infected were admitted into the study. Selection for possible infection was based on any one or a combination of the following clinical criteria:- lethargy, fever or hypothermia, unusual jaundice, diarrhoea and/or vomiting, weight loss or static weight and hepatosplenomegaly not associated with obvious heart failure (7). Since livers and occasionally spleens may be palpable in some normal neonates, for the purpose of this study, hepatomegaly of more than 2 centimetres was considered significant (8). An attempt was made whenever possible to subject each infant to a batch of bacterialogical investigations which included culture of blood, urine, rectal and umblical swabs and cerebrospinal fluid. Other body surface swabs were taken where indicated.

Small volume 5(millilitre) transport media were used for blood cultures requiring only one millilitre of blood per specimen bottle. In order to cover as many of the strict anaerobes as possible, sodium thioglycollate broth was used for blood culture transport medium although it was appreciated that some species of strict aerobes like Pseudomonas might be missed (Wamola, personal communication). At least two blood culture specimens were obtained per infant usually within a span of ten minutes. All samples were obtained from a superficial vein either on the dorsum of the hand or the flexor surface of the elbow. Skin cleansing in all specimen collection was done using 5% chlorhexidine solution in water.

Only direct suprapubic bladder aspiration specimen of urine were obtained for the study. These were collected using the method described by Drummond (9). The procedure was only carried out once and if met with failure was abandoned for the particular infant. Lumbar puncture was done using a disposable scalp vein needle gauge 25 and the skin cleansed as for the other procedures.

All specimens were taken before antibiotic treatment was started or at the latest within 12 hours of starting treatment, a time limit that was arbitrarily chosen

for the present study. This led to the exclusion from the study of five "sick"[1] neonates who had been on treatment for more than 12 hours by the time they were reviewed by the investigator. At the end of intravenous fluid therapy through an umblical venous catheter, specimens of catheter tips from infants in the study and any other asymptomatic infants outside the study cases were collected for bacterial culture studies. All specimens were collected and delivered by the investigator within one hour of collection. They were processed in the microbiology department of the hospital under supervision of a particular laboratory technician and one of the supervisors for the investigator. Bacterial sensitivities were tested using the disc diffusion method with at least eight antimicrobial drugs incorporated in the commercially prepared mastering discs. For gram positive organisms the commercial discs used incorporated benzyl penicillin 1 unit, minocycline 30mcg, erythromycin 15mcg, cotrimoxazole 25mcg, methicillin 5mcg, chloramphenicol 30mcg, ampicillin 10mcg and lincomycin 2mcg. For gram negative organisms, the following antibiotic incorporated discs were used; ampicillin 25mcg, minocycline 30mcg, cotrimoxazole 25mcg, streptomycin 10mcg, kanamycin 30mcg, gentamycin 10mcg, sulphafurazole 200mcg

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Footnote[1]: infants who fulfilled the clinical criteria for entry into the study.

and chloramphenicol 30mcg. Pyopen (carbenicillin) 100mcg, polymixin B 300mcg and gentamycin 10mcg were tested against all cultures of Pseudomonas isolated.

An attempt was also made to have white blood cell counts done on infants in the study as well as on control normal infants matched for gestation, sex, birth weight and age. These were performed on Coulter electronics counter Model S using free flowing heel prick blood specimens. One hundred white blood cell differential counts were done on Wright stained thin blood smears. These were evaluated by a haematology laboratory technician in the department of Paediatrics and the investigator, each having had to go through all the slides in turns and averaging the results. Due to unforeseen technical problems with the Coulter counter it was not possible to perform the haemotological study on all infants selected for the bacterialogical study and an even smaller number of controls was done.

To try and assess some of the perinatal factors predisposing to neonatal infection, throat and nasal swabs were taken from 30 members of the nursery staff. It was hoped that all the nursery staff would be investigated but some refused to co-operate. Specimens were collected in the mornings soon after reporting on duty and were carried out only once for each

individual. Surface swabs from resuscitation equipment in the labour ward and incubators in the nursery and swabs of solutions used for storing various tubings used for resuscitation or feeding in the nursery were also taken. (Disposable paper handkerchiefs were used for drying hands throughout the period of study and these were not swabbed). Mothers' vaginal swabs and urine cultures were taken where indicated by possible pueperal sepsis.

Where autopsies were done, the results were recorded.

RESULTS

During the period under study, there were 951 live births in the Obstetric unit and 87 admissions of infants born before arrival to the unit, giving a total of 1,038 registered live births. Of these, 366 (35%) were admitted to the nursery for observation. The total number of babies entered in the study was 89 (24% of nursery admissions). Twenty nine of these were born before arrival to the unit. The frequency of presenting symptoms in the study group is as shown in table I.

Table I. Frequency of presenting clinical features (n=89)

Clinical finding	Number of Infants	Percentage
Lethargy	72	80.1
Jaundice	53	59.5
Repiratory distress	24	26.9
Alteration in temperature	22	24.7
Poor feeding/poor digestion[1]	22	24.7
Weight loss/static weight	21	23.6
Diarrhoea and/or vomiting	14	15.7
Apnoeic spells	11	12.4
Obvious cord sepsis	10	11.2
Discharging eyes	8	8.9
Skin rash/petichiae	8	8.9
Hepatosplenomegaly	6	6.8
Twitching	4	4.5
Sclerema	4	4.5
Abdominal distension[2]	2	2

Footnote [1]: Large gastric aspirate three hours after previous feed.

[2]: Cases of intestinal obstruction were not included.

The signs and symptoms were varied and nonspecific. Lethargy and jaundice each accounted for more than 50% of the presenting features in the study infants. Attempts to match the signs with any particular infection were unsuccessful.

Table II shows some of the predisposing factors and problems that were looked into. There were more female (63%) than male infants in the study group with a proportionately larger number (61%) of positive cultures other than umblical swabs. Such characteristics as sex, gestational age, place of delivery did not seem to significantly affect the rate of positive cultures of blood, urine or cerebrospinal fluid in the groups compared, (X^2 test, $P > 0.05$). This could partly be due to the small numbers involved.

Table II Predisposing factors

Factor examined	
Male	
Female	
Preterm	
Full term	
Born at KNH maternity	
Born before arrival	
Membranes ruptured over 24 hours	
Membranes ruptured less than 24 hours	
Maternal pueperal sepsis	
SVD	
C/S	
Vacuum extraction	
Breech extraction	

*P > 0.05, not significant, X^2 test.

examined in study infants (n = 89)

Number of infants	Number with positive blood, urine, CSF or rectal swab cultures	Percentage with positive cultures
33	14	42.4)*
56	22	39.3)
60	25	41.7)*
29	11	37.9)
60	24	40.0)*
29	12	41.4)
21	9	42.9)*
68	27	39.7)
12	6	50.0%
61	27	44.3)*
21	8	38.1)
3	0	0.0)
4	1	25.0)

Table III shows the results of the various bacterialogical investigations undertaken. Of the 89 study infants, 81 (91%) had at least one positive culture. The highest yield of positive cultures was that of umblical swabs (84.2%). However, 43 (48%) of the infants had positive cultures other than umblical swabs or body surface swabs only. A definite diagnosis of bacterial infection could be assumed in these 48% since, as pointed out earlier, positive umblical swab alone could simply mean bacterial colonisation of the cord stump. That umblical colonisation could lead to infection is, however, evident in eleven of the cases where the organisms isolated from the umblical swabs were similar to those found in the blood (ten), urine (two) and cerebrospinal fluid (one). [The numbers here add up to more than eleven because of co-existence of positive blood cultures with positive CSF and urine cultures in two infants). Three of the ten positive blood cultures associated with cord sepsis occured in infants whose umblical veins were catheterised for exchange blood transfusion during the first week of life.

Table III: Total number of specimens from study infants (n = 89)

Type of Specimen	Total	Number Positive	Percentage Positive
Blood	199	35	17.6
CSF	49	1	2.0
Urine	40	3	7.5
Rectal swabs	62	6	9.7
Umblical swabs	57	48	84.2
Umblical catheter tips			
- symptomatic	27	24	88.9 *
- asymptomatic	20	13	65.0
Other surface swabs	22	13	59.1
Blood Kahn Test	10	2	20.0
Total	436	143	32.7

* X^2 test, $P < 0.05$, significant.

Table IV: Blood cultures and percentages

Total number taken = 199

Positive cultures = 35 (17.6%)

Organism	Total	Percentage
Klebsiella	12	34.3
Staphylococcus albus	7	20.0
Escherichia Coli	4	11.4
Staphylococcus aureus	4	11.4
Other	8	22.9

Blood cultures were taken as positive if at least any two specimens from the same infant grew similar organisms or the infant improved on appropriate therapy or did not improve on antibiotic which sensitivity results suggested resistance. In four of the seven cases of Staphylococcus albus positive cases there were associated positive umblical swab or umblical catheter tip cultures. Klebsiella was the commonest organism here accounting for 34.3% of positive cases.

Table V: Umblical swab cultures

Total number = 57

Positive cultures = 48 (84.2%) mixed organisms.

Organism	Total	Percentage
Staphylococcus aureus	18	22.5
Klebsiella	13	16.3
Escherichia Coli	12	15.0
Streptococcus faecalis	10	12.5
Proteus	8	10.0
Staphylococcus albus	7	8.7
Pseudomonas	2	2.5
Other	10	12.5
Total	80	100.0

Table VI: Rectal swabs

Total number = 62

Positive cultures = 6 (9.7%)

All were enteropathogenic E Coli of different subtypes, suggesting no epidemic infection during the period under study.

E Coli Serotype	Number	Percentage
0142 K 86 (B)*	2	33.3
0119 K 69 B 14	2	33.3
026 K 60 B 6	1	16.7
0128 K 67 B 12	1	16.7
Total	6	100.0

Table VIIa: Umblical catheter tip cultures from study infants

Total number = 27

Positive cultures = 24 (88.9%)

Multiple organisms isolated in some cases)

Organism	Total	Percentage
E Coli	10	26.3
Klebsiella	9	23.7
Proteus	6	15.8
Staphylococcus albus	4	10.5
Streptococcus faecalis	2	5.3
Staphylococcus aureus	1	2.6
Other	6	15.8
Total	38	100.0

Table VIIb: Umblical catheter tip cultures from asymptomatic infants[1]

Total number = 20

Positive cultures = 13 (65.0%)

Multiple organisms isolated in some cases).

Organism	Total	Percentage
E Coli	5	27.8
Streptococcus faecalis	4	22.2
Klebsiella	4	22.2
Staphylococcus albus	3	16.7
Staphylococcus aureus	2	11.1
Total	18	100.0

Footnote[1]: infants in this group were all asymptomatic at the time the catheter tips were sent for culture.

There was a significant difference in the rate of positive cultures for catheter tips from symptomatic and asymptomatic infants (X^2 test, $P < 0.05$), suggesting a contributory role of umblical catheterisation in the aetiology of neonatal infections. The pattern of organisms in the two groups was similar. In the asymptomatic infants, bacterialogical results were received in all but four after they had been discharged from the nursery. Since it is customary not to readmit infants to the nursery once discharged home, these were lost to follow up. However, the four who had since developed symptoms while they were still in the nursery because of low birth weight, and their specimens grew *E Coli (three) and Staphylococcus aureus* (one), were subsequently entered into the study. It is possible that contamination of the catheter tips during withdrawal could have accounted for positive cultures in some cases. However, in three of the study cases other than those originally asymptomatic, blood cultures yielded similar pathogens to those obtained from catheter tip cultures.

Table VIII: Other body surface swabs (abscess, skin, eye and nasal swabs)

Total number = 22

Positive cultures = 13 (59.1%)

Organism	Total	Percentage
Staphylococcus aureus	4	25.0
Klebsiella	3	18.8
Pseudomonas	2(both from eyes)	12.5
Staphylococcus albus	2	12.5
Gonococcus	2	12.5
Other	3	18.8
Total	16	100.1

Of the fourty urine specimens three were positive, two grew Klebsiella and one Citrobacter. Bacterial were reported seen but no growth was obtained in five cases. Few red blood cells were reported in some cases but these were most probably traumatic rather than a result of infection.

Fourty nine specimens of cerebrospinal fluid were obtained. Only one grew Escherichia Coli with similar antibiotic sensitivity pattern to the same organism isolated from the blood and umblical swab cultures of the same infant who eventually died. Most of the samples were reported blood stained and since it was not possible to study the haemograms at the same time due to the breakdown of the Coulter electronics counter,

it was not possible to make any meaningful comparative white blood cell counts between the blood and cerebrospinal fluid. Countercurrent - immunoelectrophoretic (CIE) studies were not carried out due to lack of antisera.

Environmental Cultures

Thirty nursery staff had their nasal and throat swabs cultured. Four (13%) were nasal and throat carriers of coagulase positive staphylococcus aureus. Seventy three percent were nasal carriers of Staphylococcus albus and 60% were throat carriers of Streptococcus Viridans. Beta - haemolytic streptococcus was isolated from throat swab of one of the nurses. It was not possible to carry out Lancefield group tests on the organism. The role of these carrier states in the nursery will, however, remain conjectural. Of the surface swabs from incubators, cots and sinks as well as antiseptic solutions used for storing various tubings in the labour ward and nursery, Streptococcus faecalis was isolated from the photobox used for treating hyperbilirubinaemia in nursery B. Pseudomonas was isolated from hibitane solution on the resustation bench in the labour ward and one of the bowls containing the same solution in nursery C. It is to be noted here that two of the fatal Pseudomonas infections isolated from the umblical cord and eye swabs were from babies in nursery C who shared an incubator. Culture of penicillin eye drops used in this nursery yielded no

growth as did several specimens of hibitane solution obtained straight from the main pharmacy, suggesting possible contamination of the antiseptic solution on the wards.

Evidence of maternal infection was apparent in twelve cases. Six of their infants had positive cultures other than umblical swabs but correlation between maternal and neonatal organisms was only evident in three cases. One baby with Klebsiella septicaemia had a mother who grew Klebsiella from a high vaginal swab and two infants with clinical features of congenital syphylis were confirmed serologically together with their mothers. Maternal infection was inferred in two cases who grew gonococcus from eye swabs.

Table IX shows combined frequencies of the various bacteria isolated from the study infants.

Table IX combined frequencies of bacterial isolates from study infants (n = 179)

Organism	Frequency	Percentage
Klebsiella	39	21.9
E Coli	28	15.6
Staph. aureus	27	15.1
Staph. albus	20	11.4
Proteus	14	7.8
Strept. faecalis	14	7.8
Pseudomonas	7	3.9
Strept. viridans	3	1.8
Other	26	14.7
Total	179	100.0

Klebsiella and E. Coli head the list of important gram negative organisms incriminated in the aetiology of neonatal infections in this study, accounting for 38% of all isolates. Klebsiella accounted for 34% of positive blood cultures, 67% of urine cultures, 16% of umblical swabs and 24% of umblical catheter tips. E. Coli accounted for 11% of blood cultures, 15% of umblical swabs, 27% of catheter tip cultures and for the only positive cerebrospinal fluid culture. Other gram negative organisms isolated included Proteus, Pseudomanas, Enterobacter, Acinebacter, Citrobacter, Alkaligenes faecalis species and gonococcus. Of the gram positive organisms, Staph. aureus and Staph. albus together accounted for 27% of all isolates, with the former more commonly isolated from umblical swabs (23%) and body surface swabs (25%) including the eyes. Other organisms in this group were Stept. faecalis, Strept viridans, Micrococcus, Corynebacteria and syphilis.

Antibiotic Sensitivities

Tables Xa and Xb show the results of the in vitro antibiotic sensitivity tests for the major gram negative and gram positive organisms respectively. For the gram negative organisms, kanamycin and gentamycin gave the highest sensitivities with gentamycin being the better of the two against all the organisms tested in this group. This could be partly due to the fact that kanamycin has been used in the unit longer than gentamycin. Sensitivity of Klebsiella to gentamycin of only 72% (51% to Kanamycin) and that of

E. Coli of 86% (79% to kanamycin) are cause for alarm and call for constant monitoring of the situation. Pseudomonas which was tested against gentamycin, carbenicillin and polymixin B showed 100% sensitivity to the latter two antibiotics which were never used in the nursery and 80% sensitivity to gentamycin. Cotrimoxazole and chloramphenicol gave the next best sensitivities while ampicillin gave very poor results against all gram negative organisms tested.

For the gram positive organisms, the highest sensitivity was shown to minocycline and chloramphenicol, the two antibiotics that are normally contraindicated at this age and are therefore not used much in this setting as well, Table Xb. Lincomycin gave the next best sensitivities with Staph. aureus showing 78% sensitivity and Staph. albus 60%. Benzyl penicillin was particularly ineffective against four of the six organisms tested thus, Staph. aureus (4%) Staph. albus (10%), Strept. faecalis (0%) and Micrococcus (33%). Strept. viridans which was isolated in three instances was the only organism which showed 100% sensitivity to benzyl penicillin and most other drugs against which it was tested. Sensitivity tests for gram positive organisms against aminoglycosides kanamycin and gentamycin were not performed.

Therapy and Results

Antibiotics were prescribed for the infants after specimens had been taken in all but 13 cases where these were collected within 12 hours of starting treatment. Of

Table X,a Gram negative organisms: Percentage in vitro sensitivities to antibiotics

Organisms	Number Tested	Antibiotics									
		Amp.	Mino	Cotr	Strept	Kana	Genta	Sulph	Chlora	Pyo	Poly
Klebsiella	39	0	31	65	10	51	72	20	23	-	-
E. Coli	28	11	29	86	15	79	86	21	57	-	-
Proteus	15	47	0	47	33	80	100	40	40	-	-
Pseudomonas	5	-	-	-	-	-	80	-	-	100	100
Citrobacter	7	0	43	57	29	86	86	57	57	-	-
Enterobacter	5	20	80	100	0	60	60	20	40	-	-
Acinebacter	4	50	25	50	25	100	100	50	75	-	-
Alkaligenes	1	0	0	0	0	0	100	0	0	-	-

Key to antibiotics

Amp	- Ampicillin	25mcg	Genta	- Gentamycin	10mcg
Mino	- Minocycline	30mcg	Sulph	- Sulphafurazole	200mcg
Cotr	- Cotrimoxazole	25mcg	Chlora	- Chloramphenicol	30mcg
Strept	- Streptomycin	10mcg	Pyo	- Pyopen (Carbenicillin)	100mcg
Kana	- Kanamycin	30mcg	Poly	- Polymixin B	300mcg

Table Xb Gram positive organisms: percentage in vitro sensitivities to antibiotics*

Organisms	Number Tested	Antibiotics							
		Pen G	Mino	Erythro	Meth	Cotr	Chlora	Amp	Linco
Staph. aureus	27	4	100	59	52	89	89	4	78
Staph. albus	20	10	90	60	20	30	35	40	60
Strept faecalis	14	0	79	71	0	0	86	86	7
Strept. viridans	3	100	100	100	67	33	100	100	100
Corynebacterium	3	67	100	100	100	100	100	100	100
Micrococcus	3	33	33	0	67	33	33	67	0

Key to antibiotics

Pen G - Benzyl Penicillin I Unit

Mino - Minocycline 30mcg

Erythro - Erythromycin 15mcg

Cotr - Cotrimoxazole 25mcg

Meth - Methicillin 5mcg

Chlora- Chloramphenicol 30mcg

Amp - Ampicillin 10mcg

Linco - Lincomycin 2mcg

*Kanamycin and gentamycin were not used to test sensitivities of gram positive organisms.

the latter, six gave positive bacterial cultures nevertheless.

The choice of antibiotics to a large extent depended upon the availability of drugs. Combinations of benzyl penicillin (50,000 units/Kg 12 hourly) or ampicillin (62.5mg/Kg/12 hourly) with kanamycin (up to 20mg/Kg/24 hours) or gentamycin (5mg/Kg/24 hours) or oral ampiclox neonatal drops (0.6ml 8 to 12 hourly) were used. Following laboratory reports treatment was revised in 7 cases with two (30%) deaths, one from E. Coli septicemia with meningitis and the other from Klebsiella septicaemia. In 14 cases where laboratory data had confirmed bacterial resistance to the antibiotics used but treatment had continued unchanged because of delay in getting the results, 9 (64%) of the infants died. Klebsiella (7cases) and Pseudomonas (2 cases) had been isolated from blood, catheter tips, eye and umblical swabs, and these infants had been treated with a combination of benzyl penicillin and kanamycin. This emphasizes the relatively low sensitivity of Klebsiella to kanamycin as well as the importance of this organism in the aetiology of neonatal infections in the KNH. The two infants who succumbed to Pseudomonas infection were both born outside the hospital and shared an incubator in nursery C where Pseudomonas was isolated from a bowl of antiseptic solution used for storing tubings for feeding and resustation, suggesting a possible hospital acquired infection. Treatment continued unchanged due to appropriate sensitivities in 66 cases with 18 (27%)

deaths. Clinical improvement followed in one case where antibiotics had been changed on clinical grounds despite the laboratory report showing sensitive Klebsiella organism to the original gentamycin used. Amikacin was used in this case. Table XI shows the results here. Significantly higher death rate occured in the group where treatment was not revised and the organisms showed resistance to the antibiotics used.

There were 31 deaths out of the total of 89 study infants. All except two had at least one positive bacterial culture and 12 had only positive umblical swabs. Other factors like prematurity could have played a role in many of these deaths. Of the two that had negative bacterial cultures, one was a 2,200 gramme infant whose umblical swab grew Candida albicans and the other was a 1,040 gramme second twin delivered three hours after the first macerated stilborn.

Of the thirteen that had post-mortem examination done, evidence of meningitis was found in four (30%). In one of these a diagnosis of E. Coli meningitis had been made antemortem following lumbar puncture in an infant who was lethargic, jaundiced, had diarrhoea and splenomegaly. With the other three, lumbar puncture was unsuccessful but clinical features included lethargy, apnoeic spells, irritability and jaundice. These are common but nonspecific

Table XI Therapy and Results

Management	Total number	Deaths	Percentage deaths
a) Treatment revised following laboratory report showing bacterial resistance	7	2	28.6
b) Treatment not revised despite laboratory report showing bacterial resistance	14	9	64.3
c) Treatment not revised on basis of laboratory report showing bacterial sensitivity	66	18	27.3

X^2 test, $P < 0.05$ significant for group (a) against (b) and for group (c) against (b)

symptoms suggesting that lumbar puncture should form part of the routine investigations for a sick neonate. Umblical swab was the only positive specimen and grew E. Coli in one of these other three infa ts. In the remaining two, blood and cathetar tip grew Pseudomonas and E. Coli. Although skin surface swabs grew Klebsiella, Staph. albus and Strept. viridans, subarachnoid and intraventricular haemorrhage were associated with death in another four of the cases examined post-mortem. Pneumonia with alveolar haemorrhage was found in five cases in whom the diagnosis had not been suspected clinically but blood culture had yield E. Coli in one and Klebsiella in the other two cases.

Haematological results

As pointed out earlier, it was not possible to carry out haematological study on all infants in the study due to some technical fault with the Coulter electronics counter. However, comparative results for some six infected infants and six matched controls at age of one day are shown in table XII. Although some differences exist in the means for total white cell counts, mature neutrophils, monocytes and lymphocyte counts, these are not significant, (t test, $P > 0.05$). Further studies are, however, required to evaluate this.

Table XII Haematological values X 10^9/L (white blood cell counts and differentials).

Age in days	Total WBC	Polys	Lymph	Mono	Myelo	Stabs	Cesin	Nucleated RBC. per 100 WBC
1	5.0	1.5	3.0	0.3	-	0.2	-	-
	12.0	5.2	5.8	0.8	0.2	-	-	-
(6 cases)	16.9	10.1	5.2	1.6	-	-	-	7
a) infected	18.5	14.9	2.9	0.7	-	-	-	-
infants	20.2	9.9	5.5	1.8	0.4	2.6	-	22
	21.6	15.8	5.4	0.4	-	-	-	4
*mean	15.7	9.6	4.6	0.9	0.3	1.5	-	11
1	11.4	6.8	4.3	0.1	-	0.1	0.1	-
	12.2	4.7	6.8	0.6	-	0.1	-	14
(6 cases)	13.2	4.8	6.6	1.6	-	0.1	0.1	-
b) control	14.2	9.2	4.3	0.7	-	-	-	4
infants	19.9	15.5	4.0	0.4	-	-	-	-
	19.9	8.0	11.3	0.6	-	-	-	-
*mean	15.1	8.2	6.2	0.6	-	0.1	0.1	9

*t test, $P > 0.05$, not significant.

DISCUSSION

Of the registered 1,038 live births in the Obstetric Unit during the period of the study there were 85 neonatal deaths, a neonatal death rate of 81.9 per thousand live births. Of the 89 infants entered in the study, 31 died. Eighteen of these deaths had positive bacterial cultures other than of umblical swabs only. Proven bacterial infections therefore accounted for 20% of all the neonatal deaths during this period. Over a period of six months partially overlapping with the present study, autopsy examination of 500 stilbirths and deaths during the first day of life drawn from several hospitals in Nairobi (Lucas, unpublished report) showed 18 cases (3.6%) of congenital syphilis, 16 cases (3.2%) of extrapulmonary infection and 14 cases (28%) of pulmonary infection (cause of infection not established). The other major killers in Lucas's study were traumatic intra-cranial haemorrhage, intrapartum asphyxia and congenital malformations. There is no doubt therefore that in Nairobi, infection is an important contributor towards perinatal mortality.

Gram negative organisms Klebsiella and E Coli accounted for 38% of all bacterial isolates in this study while gram positive organisms Staph. aureus and Staph. albus accounted for 27%. The isolation rates of

Staph. albus of 11.4% of all isolates and 20% of blood culture isolates in this study are lower than the 32.8% annual rate for the same organism found by Wamola and Mirza in their five year retrospective study of bacteriology of septicaemias in adults and children at KNH, 1976-80 (10). They thought this high figure was due to contamination of the culture specimens by normal skin flora. Their average annual positive isolation rate from blood cultures during this five year period was 20.8% as compared to 17.6% of blood cultures in this study. The preponderance of gram negative organisms in this study is in keeping with the general observation that primary infection with gram negative coliform bacteria is particularly high during the first few weeks of life (1,2). The real reasons for this are not fully known but it is thought that during this period serum IgM levels which are often specific in the protection against infection with gram negative organisms in the older persons are low, as the infant is unable to passively acquire these through the placenta. Studies have shown that although the human infant is capable of synthesizing immunoglobulins of the IgG and IgM classes as early as twenty weeks of gestation mainly in the spleen, this capacity at birth is only a tenth of that of the adult (2).

Emergence of group B Beta-haemolytic Streptococcus as

an important cause of neonatal sepsis has been reported by several authors (11, 12). In some centres, more than half the cases have been due to this organism. In this study, no single case of this organism was isolated either from study infants or from the mothers treated for pueperal sepsis. It was not possible to group, the Beta-haemolytic Streptococcus isolated from a throat swab of one of the nurses. Again the real reasons for the changing patterns of aetiological organisms in neonatal sepsis remain obscure. Host factors that could alter the relationship of normal vaginal flora, such as prolonged use of contraceptive pill have been suggested by Wilson et al (11). These authors emphasize that the trend is a puzzling one since this organism is highly sensitive to most commonly used antibiotics including penicillin G. Reduced use of such antibiotics by mothers during preganancy or changes in resistance patterns of these bacteria cannot per se explain this observation. It is only through constant monitoring that the local situation in the KHN can be evaluated.

Correlation between aetiological organisms and perinatal risk factors was not strongly established in this study (table II). Only umblical venous catheterisation was noted to be associated with an increased risk of sepsis with E Coli, Staphylococcus and Klebsiella. Gluck et al (2) in their series noted an association between Klebsiella sepsis and surgical

procedures. Similar findings to those by Gluck et al were noted by Bergqvist et al (13) who also concluded that complications during pregnancy and delivery were mostly associated with group B Beta-haemolytic Streptococcus infection while invasive procedures like umblical catheterisation was associated with staphylococcal infection.

Two deaths in this study were attributed to hospital acquired resistant strain of Pseudomonas. The two infants, both born at home shared an incubator in Nursery C. Pseudomonas was also isolated in course of an environmental survey from a bowl of hibitane in this particular nursery. Nosocomial Klebsiella infection especially with multidrug resistant strains has been associated with antibiotic therapy (14, 15). These authors argue that gastrointestinal acquisition and carriage of Klebsiella leads to infection elsewhere and contamination of the environment like sink drains, floors, table tops and inhalation equipment. Water containing devices have in some centres contributed to epidemics with organisms which thrive in moist areas such as Pseudomonas, Klebsiella and Flavobacter (16), as was possibly the case with these two infants in this study.

There is great similarity between organisms isolated from the umblical swabs - Staphylococcus, Klebsiella and

E Coli and those associated with sepsis in this study. Gluck et al (2) point out that the cord and skin are the main source of infection in the newborn. They maintain from their earlier study (17) that there is no association between organisms that the personnel handling the infants harbour and those infecting the infants. Air borne infection is less important than cross infection between the infants through the personnel handling them. They advocate use of prophylactic antiseptic cord and skin care. In their study, use of hexachlorophene antiseptic cream was associated with reduced Staphylococcus aureus infection in their nurseries as well as in the families of treated infants in the community. At the same time they did not feel that the increase in gram negative infections was related to this practice.

An epidemic of gastrointestinal infection was not noted over the period of this study although one of the enteropathogenic E Coli subtype 0119 isolated from two infants was associated with a nursery epidemic of diarrhoeal disease in Mulago Hospital, Kampala (18). Of interest is that one of the two infants presented with lethargy, jaundice and bloody diarrhoea. The latter symptom was specifically noted by Masembe (18) in her Kampala study in association with E Coli 0119 and 086 gastroenteritis. Use of breast milk could be a possible explanation for abating epidemic infection in the KNH nursery over this period while in Mulago formula feeds

were used more liberally. The protective role of human milk against infection with E Coli, Salmonella and Shigella in the newborn is well known (19, 20). Studies have been reported where epidemics of E.Coli gut infection which did not respond to antibiotic therapy were brought under control by use of breast milk (20). It is the general impression too of the nursery staff at KNH that diarrhoeal disease in the nursery tends to fluctuate with the availability of breast milk which in turn depends on whether the mothers' hostel in the hospital is in operation or not (personal communication).

The antibiotic sensitivities of the various organisms isolated provide some guidelines on the choice of antibiotic drugs when faced with possible sepsis in the newborn in the KNH. The aminoglycosides kanamycin and gentamycin gave the best sensitivities against all gram negative organisms tested. Gentamycin with sensitivities of 72%, 86% and 80% respectively against Klebsiella, E Coli and Pseudomonas was better than kanamycin and would be the drug of choice in the absence of laboratory data. Ampicillin was particularly ineffective against most of the gram negative organisms tested. Minocycline, chloramphenicol and lincomycin gave the best sensitivities against gram positive organisms. Chloramphenicol was the best against Strept. faecalis against which lincomycin gave very poor results. Penicillin G was the least efficacious against all the gram positive organisms

except for Strept. viridans while ampicillin gave only slightly better results against this group of organisms. The sensitivity results are comparable to those found by Wamola and Mirza in their five year retrospective study (1976-1980) in the same laboratory (10), although the actual percentage sensitivities for both groups of organisms are slightly lower in this study, a trend that is not entirely unexpected. Use of chloramphenicol in dosages of 100mg/kg/24 hours has invariably been associated with toxicity in the newborn (21). On the other hand, complete absence of toxicity has been reported with doses of 25mg/kg/24 hours by these authors. In view of these sensitivity results, its use would be recommended in the KNH nursery, and indeed survival of one infant with Staphylococcus aureus septicaemia complicated by multiple subcuteneous abscesses was attributed to the use of chloramphenicol, at dosages of 25mg/kg/24 hours.

It has not been possible to establish the role of white blood cell counts in the investigation of infections in the newborn in this study due to some unforeseeable technical problems. Of the studies done on six of the one day old infected neonates and six matched controls, the means for total white cell counts, mature neutrophils and moncytes were higher and the mean lymphocyte counts were lower in the infected group than in the controls,

but the differences were not significant. Although white blood cell counts have been regarded as nonspecific in neonatal infections (3, 4), Xanthou (5, 22) concludes that during the neonatal period, quantitative and qualitative changes in white cell counts in the healthy full-term and premature infants follow a remarkably constant pattern. Such alterations as an increase in immature forms of polymorphonuclear cells with toxic granulation and a drop in lymphocyte counts always accompany severe infection. Neutropenia in infected infants frequently means neutrophil storage pool depletion in the bone marrow and therefore compromised host resistance (23). However, peripheral blood neutrophils may be an unreliable predictor of depletion of this pool without further evaluation of the bone marrow. Neutropenia may accompany normal neutrophil storage pool if there is margination of circulating neutrophils to post capillary venules after endotoxin challenge.

CONCLUSION AND RECOMMENDATIONS

Proven bacterial infections accounted for 20% of neonatal deaths in the unit over the period of study. Gram negative organisms were more commonly associated with neonatal infections than gram positive organisms. Diagnosis of neonatal infections was difficult due to the similarity of symptoms with many other conditions prevalent during this period. Isolation of a particular organism from a given specimen therefore often posed the question of aetiological significance especially when multiple organisms were isolated. Based on the nonspecific symptoms as criteria for entry into the study, however, 40% of the study infants were assumed infected following isolation of bacteria from blood, urine, cerebrospinal fluid and rectal swabs. Another 8% had positive catheter tip cultures only and were therefore possibly infected. Fourty two percent of the study infants had positive umblical swab cultures only and 10% had negative cultures. In eleven cases (12%) similar organisms were isolated from umblical swab cultures as were isolated from blood, urine and cerebrospinal fluid cultures.

Antibiotics were administered to all study infants. Although it was appreciated that many infants who did not

probably have infection were treated, this can be justified on the basis that a neonate is an immunologically compromised host. A high rate of umblical cord stump bacterial colonisation and possible dissemination of the organisms into the blood stream is a further justification for use of antibiotics in the symptomatic infants. Antibiotic sensitivities for all bacterial isolates including umblical swab cultures were therefore considered for the purpose of this study. The recommendations are:-

a) Gentamycin is to be used in the management of possible neonatal sepsis prior to availability of laboratory data in the KNH nursery.

b) Meticulous measures should be taken to combat infection in the late catheterisation of umblical vein for procedures like exchange blood transfusion. Due to heavy colonisation of the cord stump with both gram negative and gram positive organisms prophylactic antibiotics are recommended in such cases. Gentamycin plus lincomycin or chloramphenicol, the latter in dosages of 25gm/kg/24 hours (21) would cover most important organisms.

c) Storage of resustation or feeding instruments in antiseptic solutions which might themselves promote

growth of pathogenic organisms is not recommended. Where costs dictate this practice, care should be taken to change the solution daily.

d) When investigating sepsis in the newborn, a thorough work up should include lumbar puncture since symptoms at this age are not organ specific.

e) Since place of delivery does not appear to significantly affect the rate of infection, isolation of infants should be based on presence of infection rather than place of delivery.

f) Regular monitoring of aetiological organisms and their antibiotic sensitivities should be carried out to evaluate the nature of the changing pattern of neonatal infections in the KNH especially if antibiotics are to be administered prior to laboratory results.

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