THE RELATIONSHIP BETWEEN EARLY ONSET NEONATAL SEPTICAEMIA AND MODE OF DELIVERY

BY

DR. OLIVER LULEMBO

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APPROVAL

This dissertation of OLIVER LULEMBO is approved as fulfilling part of the requirements for the award of the Master of Medicine (Paediatrics) Degree by the University of Zambia.

Signed:.....Date: 4th MAY 1988

Signed:.....Date: 4.5.88

Signed:.....Date: 5.5.88

Signed:.....Date: 4/5/88.

D E C L A R A T I O N

I hereby certify that this study is entirely the result of my individual effort. The various sources to which I am indebted have been acknowledged in the bibliography. I also declare that the work presented in This study for the Master of Medicine (Paediatrics) has not been presented either wholly or in part for any other degree and is not currently being submitted for any other degree.

A C K N O W L E D G E M E N T S

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A B S T R A C T

To determine the relationship between early-onset neonatal septicaemia and the mode of delivery among inborn neonates admitted to the neonatal intensive care unit of the University Teaching Hospital, Lusaka, 376 of the 5,112 hospital born babies were studied. The caesarian birth rate was 33 per cent. Early-onset septicaemia was identified in 38 neonates. Mortality was 42 per cent among these infants. Vaginally delivered babies had a significantly higher incidence of early-onset sepsis as well as a higher mortality rate from the disease compared to those infants delivered abdominally. Gram negative enteric bacteria were the most common causative organisms. Low birth weight, prematurity and birth asphyxia increased the risk of developing early'onset neonatal septicaemia among the infants studied irrespective of the mode of delivery. Premature births were significantly more prevalent among vaginal deliveries.

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AIM OF THE STUDY

The aim of this study was to establish the relationship between the route of delivery and subsequent development of early-onset septicaemia in the hospital born neonates admitted to the Neonatal Intensive Care Unit of the University Teaching Hospital, Lusaka, Zambia.

INTRODUCTION

Neonatal Sepsis, or Septicaemia, may be defined as a systemic disease of the newborn associated with "the presence in the blood or other tissues of pathogenic microorganisms or their toxins"; however, the term is used most commonly to mean the presence of a positive blood culture for bacteria (bacteraemia) in association with clinical manifestations of infection (Philip[a], 1985). Disseminated bacterial infections during the first month of life have remained a major cause of infant morbidity and mortality despite the development of broad-spectrum anti-microbial agents and technologic advancements in life support therapy (Mc Cracken[a], 1981).

Silverman et al (1949) have separated neonatal septicaemias into two groups, primary septicaemia and secondary septicaemia associated with major anomalies, focal infections, debilitating illness and surgical procedures. Many authors also think that it is useful to subdivide primary septicaemia into early and late onset for epidemiologic and therapeutic purposes (Gluck et al 1966, Gotoff[a] and Behrman 1970).

The term early onset septicaemia is often used to describe infections occuring during the first five days after delivery; however, in order to implicate intra-uterine (i.e. amniotic fluid) infection, clinical manifestations of infection should occur in the first forty-eight hours (Philip[a], 1985).

Incidence

Klein et al (1976) estimate that as many as 2 per cent of fetuses are infected in utero and up to 10% of infants during delivery or in the first few months of life. Although, figures are influenced by the clinical acumen of the neonatologist and the vigour with which he pursues microbiological investigations, the reported incidence of neonatal sepsis varies from 1 to 5 cases per 1,000 live births (Harrisetal, 1983). Low birth-weight is the most important factor in its genesis, and where rates can be stated with any degree of confidence there is general agreement that they will be 5 to 100 times higher for neonates weighing less than 2,500 grams(Hurley et al, 1981). Sophisticated life support systems in Neonatal Intensive Care Units now allow survival of many babies of Very Low Birth Weight (VLBW), with corresponding risk of serious sepsis intervening as intercurrent or terminal event,

(Placzek et al, 1983).

The mortality rate of neonatal septicaemia prior to 1937 was about 90 per cent (Nyhan et al, 1958). The figure has fallen since the advent of antibiotics and has ranged from 20 to 75 per cent; (Franciosis[a] et al, 1973 and Siegel et al, 1981). Although the mortality rate for early onset bacterial infections has declined (30 to 50 per cent depending on the responsible bacterial pathogen), more than 30 per cent of survivors with central nervous system involvement ultimately develop neurologic handicaps (Mc Cracken[a], 1981). Infection accounts for 10 to 20% of infant mortality. (Davies, 1971). Autopsy data indicate that infections are the primary cause of neonatal deaths in 3.8 per cent of cases and that fatal viral and fungal infections are rare, and that life-threatening disease is overwhelmingly of bacterial origin (Hurley et al, 1981).

Epidemiology and Pathogenesis

Although the incidence of neonatal bacterial disease has remained constant over the past four or five decades, there have been shifts in the predominat responsible pathogens. (Table 1), (Philipa 1985). Group B streptococci and gram-negative enterococci are currently the most common aetiologic agents in North America. (Freedman et al, 1981; Nyhan et al, 1958;

TABLE 1: PREDOMINANT BACTERIA IN NEONATAL SEPSIS AND MENINGITIS IN NORTH AMERICA.(PHILIP[a], 1985)

DECADE	PREDOMINANT BACTERIA	OTHER IMPORTANT PATHOGENS
1930's	Group A Streptococci	Escherichia Coli
		Staphylococcus aureus
1940's	Escherichia Coli	Streptococci
1950's	Staphylococcus aureus	Escherichia Coli
		Pseudomonas aureginosa
1960	Escherichia Coli	Pseudomonas aureginosa Klebsiella-Enterobacter
1970	Group B Streptococci	Escherichia Coli
		Listeria Monocytogenes

Silverman et al, 1949; and McCracken[c] et al, 1966). The causative agents vary among different institutions.

Exposure of the infant to micro-organisms can occur(1) before delivery, as a result of infected amniotic fluid or, less frequently following maternal bacteraemia (2) during deliver, when contact with organisms in the vagina or the perineum may occur, and (3) after delivery, as a result of exposure to organisms in the infants' environment. (Naeye et al, 1978 and Yoder et al, 1983). Some organisms are therefore more likely to be associated with early onset sepsis (Table 2) and others with late onset sepsis (Freedman et al, 1981).

The early onset disease occurs in babies who are usually premature and of low birthweight and who have been born to women who have undergone abnormal pregnancies and deliveries. Premature and prolonged rupture of the membranes (longer than 24 hours) with premature labour, obstetric complaints leading to operative or instrumental delivery, maternal or fetal distress, haemorrhage, maternal anaemia or intercurrent illness and peripartum fever are all factors prejudicial to the birth of an infected baby. (Davies, 1971.

The late onset disease is infrequently associated with maternal obstetrical complications and the microbes responsible are usually those that are being disseminated in the infants' environments, reflecting epidemiologically

TABLE 2: BACTERIA POTENTIALLY PATHOGENIC FOR THE NEWBORN IN THE MATERNAL VAGINAL VAULT. (FREEDMAN ET AL, 1981)

BACTERIA
Staphylococcus albus
Fecal Streptococci
Anaerobic and Microaerophilic Streptococci
E. Coli
B-hemolytic Streptococci
Proteus Species
Staphylococcus aureus
Non-hemolytic streptococci
Klebsiella aerogenes
Pseudomonas aureginosa

the distribution of pathogens at large in a particular nursery or neonatal intensive care unit (Baker and Barret, 1973).

Chow and colleagues (1974) actively searched for slow growing anaerobes, they found anaerobic isolates in 26% of all cases of neonatal bacteraemia. Except for clostridial sepsis and meningitis by Bacteroides fragilis, anerobic bacteraemia is usually self-limeted and rarely life threatening (Siegel et al, 1981).

Immunology

The immune system of the newborn differs from that of the infant and older child, and this difference predisposes to infections due to a wide variety of pathogens (Altemeier and Smith, 1965; Coen et al, 1969; Gotoff[b], 1974; Stossel, 1973). Abnormalities in the neonate's nonspecific defence mechanisms include defective granulocyte function(abnormal chemotaxis, phagocytosis, and bacteriocidal activity), abnormal serum opsonic activity (due to low concentrations of specific antibody, complement, and/or nonspecific opsonins, including fibronectin), and deficiencies in the classical complement pathway (Cl_q, C_3, C_5) and the properdin pathway for complement activation. Abnormalities in the neonate's specific host defence mechanism include primary (Ig^M) and secondary Ig^G) antibody response and

In most cases where evaluation is being performed on the basis of risk factors alone, it is probably reasonable to perform only blood cultures, but in the presence of clinical signs, Cerebrospinal fluid (CSF) should be obtained for culture in any infant suspected of having sepsis. (Philip[a], 1985).

Urine cultures should be performed in all newborn infants with presumed septicaemia because the genitourinary tract may serve as both a portal of entry for bacterial pathogens and a site of deposit for bacteria disseminated by the blood stream. (Speck et al, 1986). However, in view of low yield of urine cultures in early onset infection, bladder aspiration should be avoided when evaluating the unstable infant and antimicrobial therapy should not be delayed to obtain a satisfactory urine specimen. (Visser et al, 1979.

Bacterial cultures of skin, external auditory canal, umbilicus, and gastric aspirate are of little or no value in the diagnosis and treatment of neonatal septicaemia. (Speck et al, 1986).

The recently developed techniques of counterimmuno-electrophoresis, latex agglutination, staphylococcal agglutination and enzyme-linked immunosorbent assay provide simple, rapid and accurate means of detecting bacterial antigens in blood, urine and CSF. (Philip[a], 1985).

qualitative and quantitative abnormalities in circula immunoglobulins. More specifically, neonatal Ig^G is acquired transplacentally and is dependant on the gestational age of the infant and to a lesser extent the level of maternal Ig^G.

Clinical diagnosis

The difficulty in making a diagnosis of neonatal seps is largely atributable to the varied and nonspecific clinical features (Table 3) that can indicate sepsis an early stage in the course of the illness. (Speck and associates, 1986). Many noenates with these clinical features do not prove to have infection.

Laboratory Diagnosis

The diagnosis of neonatal septicaemia is ultimately based on a positive blood culture in a symptomatic infant (Speck et al, 1986). An appropriate amount of blood should be obtained from a peripheral vein under aseptic conditions. As little as 0.5 ml or less can used, although 1.0 ml generally is recommended. (Dau et al, 1979; Marks et al, 1981). Although it may be desirable to obtain two blood cultures(Gotoff[a] et al, 1970), under most circumstances a single culture seem to be satisfactory. (Franciosi[b] et al, 1972).

TABLE 3: CLINICAL FEATURES OF NEONATAL SEPSIS
(SPECK et al, 1986)

General

: Poor feeding
: Irritability
: Lethargy
: Temperature instability

Gastrointestinal:

: Diarrhoea
: Haematochezia
: Abdominal distension

Respiratory:

: Grunting
: Nasal flaring
: Intercostal recessions
: Tachypnoea/Apnoea

Haematopoietic:

: Thrombocytopaenia
: Leukocytosis
: Leukopaenia

C N S:

: Hypotonic
: Seizures
: Poor movements

Cardiovascular:

: Bradycardia
: Tachycardia
: Hypotension
: Cyanosis

Skin:

: Petechiae
: Pustulosis
: Sclerema
: Hyperemia

Indirect indicators of bacterial infection in the neonate are numerous and of differing sensitivity. These include leukopaenia (WBC less than $5,000/mm^3$), leukocytosis (WBC greater than $25,000/mm^3$), immature/total neutrophil ratio of greater than 0.2, and acute phase reactants. (Erythrocyte sedimentation rate, fibrinogen, C-Reactive Protein, haptoglobin and α1-acid glycoprotein). (Manroe et al, 1979; Philip[b], 1970).

MATERIALS AND METHODS

A prospective study was conducted from October 1987, through December 1987 at the University Teaching Hospital (UTH), Lusaka, Zambia.

Study Population

376 hospital born infants admitted to the Neonatal Intensive Care Unit(NICU) of UTH were studied for development of signs and symptoms of neonatal septicaemia. Pertinent clinical and laboratory data were recorded on each patient. Certain high risk categories(prolonged rupture of fetal membranes, longer than 24 hours, maternal fever or other evidence of maternal infection, foul-smelling amniotic fluid or malodorous baby) and certain clinical features(Refer to Table 3), developing in the infant after birth, have been well documented previously (Speck et al, 1986) and provided the basis for initiating investigation for systemic infection.

When a newborn with suspected sepsis was identified, sepsis work-up (SWU) included blood, cerebrospinal fluid and urine (suprapubic sample) cultures (the last two were occasionally deferred), a white blood cell count and differential, platelet estimate, immature/total neutrophil ratio, C - reactive protein, α_1-acid glycoprotein and haptoglobin. Table 4 shows normal

TABLE 4: NORMAL VALVES AND PROBABLE RANGE OF SOME ACUTE - PHASE REACTANTS DURING SYSTEMIC INFECTION IN NEONATES(PHILIP[a], 1985)

Reactant	Normal Level		Usual Range with Systemic Infection
	1-2 Days	3-7 Days	
C - Reactive Protein(mg/dl)	<1.6	<1.0	30 - 20.0
Haptoglobin (mg/dl	<25	<50	25 - 200
α1 - acid glycoprotein (mg/dl)	<50	<75	50 - 250

values and probable range of some acute phase reactants during systemic infection in neonates (Philip[a], 1985). Other investigations like chest radiographs, surface cultures and serology tests were performed when indicated.

Collection of Blood

Blood was drawn for culture from the femoral vein after careful swabbing of the skin, at the venipuncture site, with 70 per cent isopropyl alcohol. One to two millilitres of the blood specimen was inoculated in a blood culture bottle containing 25 ml of medium.

An extra sample of blood was taken for the other studies included in the sepsis work-up.

Laboratory Studies

All bacteriological and other investigations were handled by the U.T.H. routine laboratories. The broth used in blood culture bottle contained Brain Heart Infusion Agar (Calf brain 12.5 gm, Beef heart 5.0 gm, Proteose peptone 10.0 gm, Sodium Chloride 5.0 gm. Dextrose 2.0 gm, Disodium Phosphate 2.5 gm and Agar Oxoid L 11 10.0 gm; dissolved in one litre of distilled water and autoclaved at 121^{o}C for fifteen minutes; p^{H}7.4). The blood cultures were initially subcultured on blood agar plate and MacConkey's Medium after twelve to 18 hours of incubation at 37^{o}C. Blood cultures were checked daily for cloudiness. Subculture

plates were examined every twelve hours for visible growth and subcultured again at 48 hours and 72 hours after the initial inoculation. Organism identification was done by standard microbiological methods (Norton 1982). Antibiotic susceptibility was expedited by the disc diffusion technique.

Criteria for proven Early-Onset Neonatal Septicaemia

Designation of infection status had to be made retrospectively, since all babies investigated were considered at risk for, and/or demonstrated clinical evidence of sepsis. Those neonates whose blood cultures were positive within seventy-two hours of incubation were considered proven. Early-onset neonatal septicaemia was defined as sepsis occuring within five days after birth. (Philip[a], 1985). The late-onset disease occurs thereafter, till 28 days after birth.

Data Analysis

Only the data of early-onset neonatal septicaemia cases are presented and analyzed.

The significance of differences between group was determined by using the Chi square test, or Fischer's exact probability test.

Definitions

The gestational age of infants were estimated on admission to the N.I.C.U. by the record of maternal menstrual history, external physical characteristics and neurologic examination of infants.

Apgar score at one minute was determined by the midwife or the doctor who delivered the baby.

Ante-natal care referred to a positive maternal history of at least a single visit to an ante-natal clinic and possession of a current ante-natal card.

RESULTS

The three hundred and seventy-six patients studied represented 197 male and 179 female infants. They varied in gestational age from twenty-eight to forty-one weeks and in birth weight from 980 to 4,400 grams (gm). 169 infants (45 percent) were preterm. 124 babies were delivered by the abdominal route (Caesarian section) and the remainder by the vaginal route; 195 spontaneous vaginal deliveries, 36 assisted breech deliveries and extractions and 21 vacuum extractions. The reasons for admission to the N.I.C.U. included prematurity, birth asphyxia, respiratory distress, birth trauma and many others.

Eighty-one patients had a sepsis work-up (SWU). There were thirty-eight cases of proven early-onset neonatal septicaemia. Of these, 32 were delivered vaginally and consisted of 19 male and 13 female infants. The remaining six neonates delivered abdominally had an equal sex distribution. Table 5 shows some of the characteristics of the cases.

Delivery method, early-onset septicaemia and mortality

Table 6 gives the incidence of early-onset neonatal septicaemia, mortality and case fatality rates by different methods of delivery. A higher rate (12.7 percent) of early-onset septicaemia was noted among neonates delivered vaginally than those delivered abdominally (4.8 percent).

TABLE 5: CLINICAL DETAILS OF BABIES WITH DOCUMENTED EARLY-ONSET SEPSIS

Case	Age at SWU*	Birth Weight(gm)	Sex	Route of Delivery	Positive Culture	Survived (S) or Died(D)
1	10 Hrs	1820	M	Vaginal	Blood	S
2.	2 Days	1500	F	Vaginal	Blood	S
3.	5 Days	1580	F	Vaginal	Blood	S
4.	16 Hrs	2060	M	Vaginal	Blood	S
5.	2 Days	1400	M	Vaginal	Blood	D
6.	1 Day	2100	M	Vaginal	Blood	S
7.	1 Day	1320	F	Vaginal	Blood	D
8.	3 Days	1600	M	Vaginal	Blood	D
9.	1 Day	1380	M	Vaginal	Blood	S
10.	2 Days	2300	F	Vaginal	Blood	S
11.	14 Hrs	1700	M	Vaginal	Blood	S
12.	2 Days	1380	M	Vaginal	Blood	S
13.	16 Hrs	1100	F	Vaginal	Blood	D
14.	3 Days	2800	M	Vaginal	Blood	S
15.	1 Day	1920	F	Vaginal	Blood	D
16.	2 Days	2200	M	Vaginal	Blood	S
17.	2 Days	1800	M	Vaginal	Blood	D
18.	1 Day	1800	M	Vaginal	Blood	D
19.	6 Hours	2500	M	Vaginal	Blood	D
20.	1 Hr	1300	M	Vaginal	Blood	D
21.	2 Days	3200	F	Vaginal	Blood	D

2.	3 Days	3700	M	Vaginal	Blood	S
3.	16 Hrs	1200	F	Vaginal	Blood	D
4.	1 Day	1040	F	Vaginal	Blood	D
5.	8 Hrs	1360	M	Vaginal	Blood	D
6.	2 Days	1460	F	Vaginal	Blood	S
7.	1 Hr	1840	F	Vaginal	Blood	D
8.	4 Days	2700	M	Caginal	Blood	S
9.	2 Days	2200	M	Vaginal	Blood	S
0.	3 Days	2090	F	Vaginal	Blood/Urine	D
1	2 Days	1830	M	Vaginal	Blood	S
2.	1 Day	1780	F	Abdominal	Blood	S
3.	2 Days	2360	M	Abdominal	Blood	S
4.	13 Hrs	2040	F	Abdominal	Blood	S
5.	1 Days	2120	M	Abdominal	Blood	S
6.	4 Days	3200	F	Abdominal	Blood	S
7.	1o Hrs	2000	M	Abdominal	Blood	D
8.	2 Days	3440	F	Vaginal	Blood	S

SWU = Sepsis work-up

22.	3 Days	3700	M	Vaginal	Blood	S
23.	16 Hrs	1200	F	Vaginal	Blood	D
24.	1 Day	1040	F	Vaginal	Blood	D
25.	8 Hrs	1360	M	Vaginal	Blood	D
26.	2 Days	1460	F	Vaginal	Blood	S
27.	1 Hr	1840	F	Vaginal	Blood	D
28.	4 Days	2700	M	Caginal	Blood	S
29.	2 Days	2200	M	Vaginal	Blood	S
30.	3 Days	2090	F	Vaginal	Blood/Urine	D
31	2 Days	1830	M	Vaginal	Blood	S
32.	1 Day	1780	F	Abdominal	Blood	S
33.	2 Days	2360	M	Abdominal	Blood	S
34.	13 Hrs	2040	F	Abdominal	Blood	S
35.	1 Days	2120	M	Abdominal	Blood	S
36.	4 Days	3200	F	Abdominal	Blood	S
37.	1o Hrs	2000	M	Abdominal	Blood	D
38.	2 Days	3440	F	Vaginal	Blood	S

SWU = Sepsis work-up

ABLE 6: INCIDENCE AND MORTALITY OF EARLY-ONSET SEPTICAEMIA AND RELATION TO ROUTE OF DELIVERY

oute of Delivery	Incidence of Septicaemia Infected/Total = %	Mortality Rate Deaths/Total = %	Case Fatality Rate Deaths/Cases = %
aginal n = 252	32/252 = 12.7	15/252 = 5.9	15/32 = 46.9
*SVD n = 195	26/195 = 13.3	13/195 = 6.7	13/26 = 50
Breech n = 36	5/36 = 13.9	2/36 = 5.6	2/5 = 40
Vacuum n = 21	1/21 = 4.8	0	0
bdominal n = 124	6/124 = 4.8	1/124 = 0.8	1/6 = 16.7

SVD = Spontaneous Vaginal Delivery

This difference was statistically significant (X^2, = 4.81; P = 0.02). Within the group of neonates vaginally delivered, identical rates of sepsis was seen in the breech and spontaneous vaginal deliveries, whereas vacuum extractions exhibited a decreased rate. Indications for caesarian section in the six septicaemic infants delivered abdominally included fetal distress (3), cord prolapse (1) and previous caesarian delivery (2). Four of these were emergency sections and the latter two electives.

There were sixteen deaths out of the thirty-eight cases of proven early-onset neonatal septicaemia. 15 deaths occured among the vaginally delivered babies representing mortality and case fatality rates of 5.9 and 46.9 per cent respectively, in contrast to the mortality rate of 0.8 per cent and case fatality rate of 16.7 per cent among those delivered abdominally. The difference in the mortality rates between the two routes of delivery was significant (X^2, = 4.21; P = 0.040).

Aetiology

Table 7 identifies the aetiologic agents found in the thirty-eight cases of proven early-onset neonatal sepsis. All the causative organisms reported were cultured from the blood. In two cases the same organism was isolated from the blood and the cerebrospinal fluid.

TABLE 7: NATURE OF ISOLATES

Isolates	Number of Isolate(%)
Gram Positive	6 (15.8)
Staphylococcus aureus	1 (2.6)
Staphylococcus albus	3 (7.9)
Streptococcus, non-hemolytic	2 (5.3)
Gram Negative	32 (84.2)
Escherichia coli	5 (13.1)
Serratia marcescens	2 (5.3)
Enterobacter hafniae	9 (23.7)
Enterobacter cloacae	6 (15.8)
Enterobacter spp	7 (18.4)
Citrobacter diversus	2 (5.3)
Klebsiella spp	1 (2.6)

Gram negative enteric bacterial accounted for the majority of cases (84.2%), Enterobacter species being the single most common causative organism. One isolate of E. Coli and five isolates of Enterobacter species were found in the babies with sepsis delivered abdominally. Enterobacter cloacae was isolated from the single death reported out of the five septicaemic cases caused by E. Coli. Most of the gram negative enteric bacteria showed in vitro sensitivity to Gentamycin and Cefotaxin.

Clinical Features

The most common presenting signs and symptoms were non-specific in nature; lethargy, temperature instability, poor feeding or vomitting, respiratory distress and irritability. Table 8 summarizes the prevalence of the common clinical features observed in the thirty-eight septicaemic infants.

Two septicaemia infants were meconuim stained and malodorous on admission and history of maternal pyrexia was present in one of them and prolonged rupture of membranes in the other. The actual duration of rupture of membranes was not specified.

TABLE 8: SUMMARY OF PREVALENCE OF CLINICAL FEATURES OF INFANTS WITH PROVEN EARLY-ONSET SEPTICAEMIA

Clinical Feature	Proportion of patients with given feature (%)
Temperature instability	21/38 (55)
Gastrointestinal symptoms	10/38 (26)
Jaundice	15/38 (40)
Respiratory symptoms	8/38 (21)
CNS* symptoms	4/38 (10)
Bleeding	4/38 (10)
Cyanosis	5/38 (13)
Lethargy	15/38 (40)

*CNS = Central Nervous System

Antenatal Care

The relationship between route of delivery, antental care and early-onset neonatal septicaemia is shown in Table 9. The development of early-onset neonatal sepsis was unrelated to antenatal care in both vaginal deliveries (X^2 = 0.162, P = 0.687) and abdominal deliveries (Fischer's test P = 0.738). The antenatal care level in the vaginal deliveries did not significantly differ from that in the abdominal deliveries (Fischer's test, P = 0.401).

Apgar Score

An Apgar score, at one minute, of less than 8 was significantly associated with higher incidence of early-onset septicaemia among the vaginally delivered infants (X^2 = 6.59, P = 0.01). This was not the case with the group of infants delivered abdominally (Fischer's test, P = 0.371). Initial Apgar score between the two routes of deliveries are shown in Table 10.

Gestation Age

The relationship between gestational age route of delivery and development of early-onset neonatal septicaemia is shown in Table 11. Among the vaginal births, the rate of early-onset sepsis in preterm infants was 18.6 per cent as compared to 4.6 per cent in full term infants in the same group. This increase in incidence of sepsis in premature infants was statistically significant (X^2 = 9.86, P = 0.001). Similarly a significant difference was noted among neonates that were abdominally delivered (Fischer's test P = 0.00121).

TABLE 9: RELATIONSHIP BETWEEN ANTENATAL CARE, ROUTE OF DELIVERY AND EARLY-ONSET NEONATAL SEPSIS

Route of Delivery	Antenatal Care: % with care	% Septicaemia in Group with Care	% Septocaemia in Group without Care
Vaginal n = 252	202/252=80.1	27/202 = 13.4	5/50 = 10
Abdominal n = 124	118/124=95	6/118 = 5.1	0/6 = 0

TABLE 10: RELATIONSHIP BETWEEN INITIAL APGAR SCORE, ROUTE OF DELIVERY AND EARLY-ONSET NEONATAL SEPSIS

	APGAR SCORE AT 1 MINUTE			
Route of Delivery	% below 8	% Sepsis in Group with 0-1-2	% Sepsis in Group with 3-4-5-6-7	% Sepsis in Group with 8-9-10
Vaginal n = 252	94/252=37.3	4/16 = 25.0	15/78 = 19.2	13/158= 8.2
Abdominal n = 124	60/124=48.3	1/9 = 11.1	1/51 = 6.6	4/64 = 6.3

TABLE 11: RELATIONSHIP BETWEEN GESTATIONAL AGE, ROUTE OF DELIVERY AND EARLY-ONSET NEONATAL SEPTICAEMIA

Route of Delivery	Incidence of Septicaemia Infected/Total = %	
	Less than 37 Wks	37 Wks & more
Vaginal n = 252	27/144 = 18.8	5/108 = 4.6
Abdominal n = 124	5/25 = 20.0	1/99 = 1.0

Birth Weight

Low birthweight was consistently associated with a higher incidence of early-onset septicaemia. This increase was significant in both vaginally (X^2 = 7.26, P = 0.007) and abdominally (Fischer's test, P = 0.003) delivered neonates. This increase was not influenced by method of delivery (Fischer's test, P = 0.672). Table 12 shows the relationship between bith weight, route of delivery and rate of early-onset neonatal sepsis.

Gender

The relationship between sex and early-onset septicaemia (Table 13) in this study was random in infants vaginally delivered (X^2, = 0.5687; P = 0.450) and in those abdominally delivered (Fischer's test, P = 0.580). This relationship was unaffected by the route of delivery (Fischer's test, P = 0.502).

Laboratory Studies

The distribution of postive results of acute phase reactants and total white cell counts in the septicaemic infants is given in
Table 14. The immature/total neutrophil ration was reported with so much irregularity that it was not analyzed.

TABLE 12: RELATIONSHIP BETWEEN BIRTH WEIGHT, ROUTE OF DELIVERY AND EARLY-ONSET NEONATAL SEPSIS

Route of Delivery	Birth Weight(Grams) % with Septicaemia 1,000 - 1,500	% with Septicaemia 1,501 - 2,500	% with Septicaemia 2,501 & above
Vaginal n = 252	11/48 = 22.9	16/106 = 15.1	5/98 = 5.1
Abdominal n =	0/3 = 0	5/28 = 17.9	1/93 = 1.1

TABLE 13: RELATIONSHIP BETWEEN SEX, ROUTE OF DELIVERY AND EARLY-ONSET NEONATAL SEPSIS

	Incidence of Septicaemia Infected/Total = %	
Route of Delivery	Male	Female
Vaginal n = 252	$19/_{130} = 14.6$	$13/_{122} = 10.6$
Abdominal n = 124	$3/_{67} = 4.5$	$3/_{57} = 5.3$

TABLE: TOTAL WHITE CELL COUNTS AND ACUTE PHASE REACTANTS AT TIME OF ONSET OF EARLY-ONSET SEPSIS

Test	Postive Test with Proven Sepsis	(%
*WBC $<5,000$ or $>25,000$/cu mm	6	(15.8)
C-Reactive Protein	17	(44.7)
Haptoglobin	13	(34.2)
α1 - Acid glycoprotein	11	(28.9)

*WBC (White Blood Cell Count) not determined in 5 cases.

DISCUSSION

The following limitations encountered in this study, may be a potential source of bias. Perinatal events for each subject were recorded by the attendant Midwife. Some of the data was incompletely recorded. Consequently certain important vatiables such as duration of rupture of fetal membranes were not included in the data analysis. Irregularities in the availability of specimen bottles and other materials did exist also. The autopsy rate in our NICU is very low and none was performed during the study to determine whether septicaemia was the primary or secondary cause of death among the cases. The literature, on the subject, available in the UTH Medical Library was limited.

Because of the lack of specific presenting signs and symptoms in neonatal septicaemia, knowledge of conditions predisposing to the development of infection in the newborn infant becomes important. At the earliest signs of illness in the high risk infants, specimens for bacteriologic examinations should be obtained and if indicated, appropriate antimicrobial therapy instituted (Overall Jr., 1970). The division of neonatal sepsis into early and late onset groups has been well described (Gluck et al, 1966; Gotof[a] et al, 1970).

Although there has been variation in the definition of early-onset neonatal septicaemia, there is a general consensus that it is the early rather than late onset disease that is associated with peripartum events(Hurley et al, 1981; Davies, 1985; Placzek et al, 1983).

The difficulties in identifying the true incidence of neonatal sepsis have been reviewed by Siegel and Coworkers (1981). The monthly statistics compiled for the Ministry of Health shows that the incidence of neonatal (ear-y and late onset) in the UTH NICU among hospital born infants is approximately 20 per 1,000 live births (per month) and a case fatality rate of 40 per cent. Chintu and associates (1976) recorded an incidence of neonatal septicaemia of 36 per 1,000 admissions to the UTH NICU.

A significantly higher incidence of early-onset neonatal septicaemia was noted among vaginal deliveries. This may be partly explained by higher rate of prematurity prevalent among the vaginal deliveries (50 per cent) as compared to the abdominal deliveries (20%). This difference was statistically significant (X^2, = 8.3, P 0.01). Such a high incidence of prematurity among vaginal deliveries denotes dealing with large number of infants who are susceptible to complications like sepsis. Prematurity is the single most important risk factor for neonatal sepsis

(Speck et al, 1986). The prematurity rate of all the babies in this study was forty five per cent. This is higher than rates reported else where(Bada et al, 1977); Gunn et al, 1970). Other authors have pointed out the importance of mechanical factors such as difficult traumatic delivery that may accompany vaginal parturition. These may result in a break in the normal skin and mucous membrane barriers to infection (Haggarty, 1961). Frazier et al (1982) in their study to evaluate effect of method of delivery on neutrophil function found impaired function among infants vaginally delivered and those infants delivered by Caesarian section with labour. Those infants delivered by caesarian section without labour had normal neutrophil function. Impaired neutrophil function is associated with increased risk of bacterial infection (Coen et al, 1969; Anderson et al 1974).

The case fatality rate of early-onset neonatal septicaemia in this study was 42 per cent. This is consistent with previous reports (Hurley et al, 1981; Franciosi[a] et al, 1973).

The increase in incidence of early-onset sepsis with birth asphyxia is statistically significant among vaginally delivered neonates in this study ($P = 0.01$). Other reports show that infants who are subjected to asphyxia at birth and who require resuscitation appear to be at particular risk for neonatal sepsis (Philip[a], 1985).

As in many other reported series, (Baker et al, 1979; Hurley et al, 1981; McCracken[b] et al, 1971) there was a significant increase in incidence of early-onset sepsis among neonates

of low birth weight (less than 2,500 gm) irrespective of route of delivery.

This present series failed to show gender predilection of early-onset sepsis in contrast to other reports that have shown that male infants are more likely to acquire and succumb to infection in an approximate ratio of 2:1 (Washburn et al, 1965).

Lack of accurate documentation of duration of rupture of eftal membranes precluded analysis of prolonged rupture of membranes to establish the relationship between this variable and the development of early-onset neonatal sepsis. Prolonged rupture of membranes i.e. longer than 24 hours has been associated with increased incidence of infection in the newborn in some reports (Speck et al, 1986, Bada et al, 1977). Other researchers have reported contrary findings (Wilson et al, 1982).

The relationship between the incidence of antenatal care and subsequent development of early-onset neonatal sepsis was random in both vaginal and abdominal deliveries. Buetow and associates (1965) reported similar findings.

Gram negative enteric bacteria were the most common causative organisms, as has been found to be the case some series (Gluck et al, 1966; McCracken[c] et al, 1966). The causal bacteria of early-onset sepsis in the neonate are usually those indigenous to the maternal genital tract(Table 2), but rarely adventitious microbes from the infected maternal

genital tract may be isolated (Hurley et al, 1981). Staphylococcus albus was isolated in three of the septicaemic infants in the present study. This organism, a skin commensal, is recognized as an important pathogen both in early and late onset sepsis (Battisti et al, 1981).

The nonspecific indicators of neonatal sepsis used in this study were total white blood cell count and acute phase reactants(Table 14). There was great variability in the value of the individual tests as has been observed by other workers (Wilson et al, 1974; Daum et al, 1979). Philip[a] and Coworkers (1985) showed in his series that combining these tests enhances their predictive value of sepsis, and that their greatest potential value is to exclude infection when uncertainty exists about the clinical condition of an infant. In this NICU we use an Acute Phase Reactant(APR) scoring system that employs c-Reactive protein, haptoglobin and alpha-1-acid glycoprotein. A score of 1 is assigned to each positive reactant. A positive APR score denotes two or all three reactants positive. 31 of the 38 case of proven sepsis (82%) in this study had at least a score of 2.

CONCLUSION

Early-onset septicaemia is a significant problem among hospital born neonates admitted to this NICU and is associated with high mortality. Vaginally delivered babies carry a significantly higher risk of developing the disease.

RECOMMENDATIONS

1. Neonates at risk of developing infection require immediate bacteriologic evaluation and prompt institution of anti-microbial therapy.

2. Vaginal delivery is an added risk in this hospital, therefore every effort must be made to carry out vaginal deliveries under strict aseptic conditions.

3. Accurate recording of clinical data on every patient is imperative and should be reinforced in this hospital. This would facilitate the undertaking of further enquiry into all possible factors that contribute to the high incidence of early-onset neonatal septicaemia and the increased risk associated with vaginal deliveries, in this environment.

4. Co-operation between Paediatricians and Obstetricians should be fostered by holding joint perinatal mortality meetings.

5. The APR score is a simple, rapid and useful adjunct in the evaluation of a neonate with suspected septicaemia and hence should be included in the sepsis work-up of such patients.

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APPENDICES

DELIVERY METHODS AND NEONATAL SEPSIS

DEMOGRAPHIC DATA:

NAME: .....HOSP. NO. ..... SERIAL NO.....
DATE/TIME OF BIRTH. ..... MOTHER'S AGE:.....
SEX: ..... BIRTH WEIGHT:..... FATHER'S AGE .....
DATE/TIME OF ADMISSION: ..... PARA..... GRAVIDA .....
REASON FOR ADMISSION TO NICU. LMP.....
..... ESTIMATED GESTATION .....
MOTHER'S BLOOD GROUP ..... VDRL ve/ ve/Not done
ATTENDED ANC - YES/NO HOUSE WIFE/WORKING .

NATAL HISTORY

Mode of Delivery:-

Vaginal ..... Vertex (SVD)
Breech .... delivery/extraction ... method....
Vacuum
Forceps ... high/low .... indication
Others (e.g. other maneuvers)

Caesarian Section .... emergency/elective
Indication .... previous c/s
fetal distress
maternal distress
PE/PET/HBP
obstructed labour
abruptio placentae
placenta praevia
prolapsed cord
maternal diabetes mY
maternal cardiac disease
others

Duration of labour ... 1st stage .....
2nd stage .....

Time of Rupture of membranes to time of delivery .....

Amniotic fluid .... colour .... meconium stained Yes/No
odour .... foul smelling Yes/No

Type of placenta .....
Twin/Singleton ..... if twin: mono/Dichorionic
mono/Di-ovular.

Prenatal Maternal Factors. Specify onset, duration and treatment if any.

Pyrexia .....
U.T.I. .....
Pneumonia .....
Others .....

Apgar Score: 1min ..... 5min.....

Resuscitation:

Suction ..... Nasopharyngeal ..... //
Oropharyngeal .....
Endotracheal .....
Aspirate .....meconum/blood/mucus/clear
Tracheal lavage Yes/No solution/amount used
.....

Oxygen therapy: Ambleat
dry/humidified: Bag and mask
Intubation
Mechanical ventilation

I.V. line peripheral vein
umbilical catheterization

Medications $NaHCO_3$ (4.2%) cc
Adrenaline (1:10,000) cc
Dextrose .....% cc
Naloxone cc
Others .....
.....

PHYSICAL EXAMINATION

Head circumference .....
Height/length .....
Pallor ..... present/absent
Cyanosis ..... present/absent
Jaundice ..... present/absent time of appearance .....
Respirations rate ..... type ..... Heart rate .....
Chest .....
Heart .....
Abdomen .....Liver ..... Spleen ..... Kidneys .....
Skull ..... Genitalia .....
Eyes ..... Umbilical cord .....
Ears/Nose ..... Neonatal reflexes .....
Mouth ..... Grasp .....
Neck ..... Moro's .....
Breast modules ..... Sucking .....
Sole creases .....
Hip joint .....
Any congenital abnormalities .....
Clinical gestational age .....
Other signs .....
Diagnosis .....

Management: .....
.....
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LABORATORY STUDIES

APR score (CRP, α_1 - acid Glycoprotein, Haptoglobin) done at birth, 6hrs, 12hrs, 24hrs, 8 PRN after birth.

Cultures - Blood (from peripheral vein)
- CSF
- Urine
- Tracheal aspirate
- Swabs of throat, ears, umbilicus, rectum abscess, nose &etc.
- Others

Non-specific tests
- FBC, DCC, Retic count
- Immature cell : total neutrophil ratio
- Mini ESR.
- HIV.

Others

CLINICAL PROGRESS: .....

OUTCOME: .....