EPIDEMIOLOGY OF NECROTISING ENTEROCOLITIS IN MALAYSIAN NEONATES

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ABSTRACT

Over a 21-month period, 108 of 45,770 neonates born in the Maternity Hospital, Kuala Lumpur, developed necrotising enterocolitis (NEC). The incidence of NEC was 2.4 per 1000 livebirths or 2.7 per 100 special care nursery (SCN) admissions in this Hospital. There was no significant difference in the incidence between the sexes or among the different races. NEC was most common (9.4%) in the very low birthweight (VLBW: neonates weighing less than 1500 grams) and the preterms of less than 34 week gestation (8.4%). 54.6% of the patients developed the condition during the first week of life. NEC occurred throughout the year in our nursery with clustering of cases intermittently. The case fatality ratio of the condition was 28.7%. NEC accounted for 5.7% of our Hospital's neonatal (<28 days of life) and postneonatal (≥28 days of life) deaths. There was no significant difference in the rates of occurrence of placental praevia, prolonged rupture of amniotic membranes, maternal pregnancy-induced hypertension, birth asphyxia, apnoea, respiratory distress, patent ductus arteriosus and exchange blood transfusion in neonates with NEC and those in the control group. Our findings on Malaysian neonates were comparable with those reported in the literature on neonates in developed countries.

Keywords: necrotising enterocolitis, epidemiology, Malaysian neonates

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INTRODUCTION

Necrotising enterocolitis (NEC) is a life-threatening gastrointestinal disease of the newborns of unknown aetiology. Its incidence among Caucasian neonates was reported to be between 1 and 7% of neonatal intensive care unit (NICU) admissions (1-7). There were studies which suggested that prolonged rupture of foetal membranes, respiratory distress and umbilical vessel catheterisation (1,8-10) predisposed neonates to NEC. However, other workers failed to confirm them (2, 11-15).

There were very few reports on the epidemiology of this condition in non-Caucasian babies (1,16). It was not certain whether this paucity of information was due to under-reporting, high rates of early neonatal deaths before the condition could develop or a truly low incidence of NEC among the non-Caucasians.

The objectives of this study were to determine the incidence of NEC among Malaysian neonates and to ascertain whether the common perinatal factors predisposed the Malaysian neonates to this condition.

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PATIENTS AND METHODS

1) Descriptive Epidemiology

The study was carried out prospectively over 21 months, between January 1987 and September 1988, in the Maternity Hospital, Kuala Lumpur. The diagnosis of neonatal NEC was made only if the following criteria were met: (1) the presence of any of these clinical features (abdominal distension, bloody stool, lethargy, recurrent apnoea, temperature instability), and (2) evidence of intramural gas (pneumatosis intestinalis) on abdominal radiographs, and/or (3) findings at laparotomy or autopsy. Onset of NEC was defined as the day on which clinical features of the disease first manifested. All neonates diagnosed to have NEC were referred to the surgical team for joint management. The case notes of all neonates admitted to the special care nursery (SCN) were reviewed and those diagnosed to have NEC were included in the study. Death due to NEC was defined as death directly resulted from complications of acute illness or from sequelae of NEC or therapy. Data on the total livebirths were obtained from the hospital perinatal census.

2) Analytical Epidemiology

A case-control study was also carried out at the same time in an attempt to identify the risk factors associated with NEC. One control case matched to each NEC case by race, sex, mode of delivery, gestation (+ 1 week), birthweight (+ 100 gram) and birthday (+ 1 week) was randomly selected from neonates admitted to the SCN. Neonates with multiple congenital abnormalities were excluded. Perinatal factors present in the 2 groups of neonates were compared.

STATISTICAL TEST

Categorical variables were compared by Chi-square test, with Yates correction when more than one-fifth of the cells had expected values of less than 5. A value of $p<0.05$ was considered to be statistically significant.

RESULTS

During the 21-month study period, 45,770 livebirths were born in the hospital and 3,962 neonates were admitted to the SCN. 108 neonates (2.4 per 1000 livebirths or 2.7 per 100 admission to SCN) developed NEC. There was no significant difference in the incidence of NEC between the two sexes ($0.1>p>0.05$) or among the different racial groups ($0.5>p>0.1$) of neonates admitted to the SCN (Table I). NEC significantly affected a larger proportion (9.4%) of VLBW babies and those (8.4%) of gestation less than 34 weeks ($p<<<0.001$). 69.4% of neonates with NEC weighed less than 2500 grams and 67.6 percent of the affected babies were preterm. There was also significantly more neonates affected in the group delivered by breech (7%) than by other modes of delivery ($p<0.001$).

Table I
BASIC DATA OF NEONATES WITH AND WITHOUT NECROTISING ENTEROCOLITIS IN THE SPECIAL CARE NURSERY, MATERNITY HOSPITAL, KUALA LUMPUR. (JANUARY 1987-SEPTEMBER 1988)

	Total no. of admissions	Neonates with NEC No.	(%)
Sex	2209	51	(2.3)
Male	1746	57	(3.3)
Female	7	0	(0.0)
unknown			
Race			
Malay	2404	66	(2.7)
Chinese	835	18	(2.2)
Indian	650	23	(3.5)
Others	73	1	(1.4)
Birthweight (grams)			
500 - 999	111	3	(2.7)
1000-1499	348	40	(11.5)
1500-1999	625	32	(5.1)
2000-2499	535	12	(2.2)
2500-2999	771	9	(1.2)
3000-3499	817	9	(1.1)
3500-3999	366	3	(0.8)
4000 and above	38	0	(0.0)
Gestation (weeks)			
24-27	51	1	(2.0)
28-30	202	20	(9.9)
31-33	286	24	(8.4)
34-36	626	28	(4.5)
37-41	2668	34	(1.3)
⩾ 42	129	1	(0.8)
Mode of delivery			
SVD*	2374	58	(2.4)
Forceps	168	3	(1.8)
Vacuum extraction	156	0	(0.0)
LSCS**	979	29	(3.0)
Breech	285	20	(7.0)

Note: * SVD = spontaneous vertex delivery
** LSCS = lower segment Caesarean section

Table II
AGE OF ONSET OF NECROTISING ENTEROCOLITIS

Age (weeks)	Neonates with NEC No.	(%)
1	59	(54.6)
2	35	(32.4)
3	7	(6.5)
4	6	(5.6)
5	0	(0.0)
6	0	(0.0)
7	1	(0.9)

54.6% of the neonates developed NEC during the first week of life (Table II). The incidence was rare after the fourth week of life. The disease occurred throughout the year in our nursery with intermittent clustering of cases. Table III shows that NEC accounted for 5.7% of this Hospital's total neonatal (<28 days of life) and postneonatal (= or >28 days of life) deaths. A significantly large number of deaths (8.2%) in the VLBW neonates were caused by NEC (0.05>p>0.2).

Table III
RELATIVE CONTRIBUTION OF NECROTISING ENTEROCOLITIS TO NEONATAL AND POSTNEONATAL DEATHS IN THE MATERNITY HOSPITAL, KUALA LUMPUR (JANUARY 1987-SEPTEMBER 1988)

Birthweight (grams)	Total no. of deaths	Deaths due to NEC No.	(%)
500- 999	107	3	(2.8)
1000-1499	160	19	(11.9)
1500-1999	89	8	(9.0)
2000-2499	56	1	(1.8)
2500 and above	128	0	(0.0)
Total	540	31	(5.7)

The case fatality ratio of NEC among the Malaysian neonates was 28.7% (Table IV). VLBW neonates had the highest case fatality ratio among all birthweight groups.

The birthweight and gestation of neonates with NEC and those in the control group were comparable (Table V). There was no statistical significant difference in the rates of occurrence of placental praevia, prolonged rupture of foetal membranes, maternal pregnancy-induced hypertension, birth asphyxia, apnoea, neonatal respiratory distress, patent ductus arteriosus and exchange transfusion between the two groups of neonates (0.5>p>0.1).

Table IV
BIRTHWEIGHT-SPECIFIC MORTALITY RATES OF NECROTISING ENTEROCOLITIS IN MATERNITY HOSPITAL, KUALA LUMPUR. (JANUARY 1987-SEPTEMBER 1988)

Birthweight (grams)	Livebirths	NEC		Rates per * 1000 livebirths		C.F.R.**
		Cases	Deaths	Cases	Deaths	
500- 999	119	3	3	25.2	25.2	100.0
1000-1499	342	40	19	117.0	55.6	47.5
1500-1999	837	32	8	38.2	9.6	25.0
2000-2499	3,670	12	1	3.3	0.3	8.3
2500	40,802	21	0	0.5	0.0	0.0
Total	45,770	108	31	2.4	0.7	28.7

* Rates in indicated birthweight category
** C.F.R.: Case Fatality Rate = Deaths/Cases X100

Table V
PERINATAL AND NEONATAL FACTORS IN 108 NEONATES WITH NEC AND 108 CONTROL MATCHED NEONATES

	Neonates with NEC		Control neonates	
Birthweight (grams)				
mean	1823		1817	
standard deviation	±719		±719	
Gestation (weeks)				
mean	34.6		34.4	
standard deviation	±3.9		±4.1	
	No.	**(%)**	**No.**	**(%)**
Placental praevia	4	(3.7)	4	(3.7)
Prolonged rupture of foetal membranes > 24 hours	4	(3.7)	7	(6.5)
Maternal pregnancy-induced hypertension	16	(14.8)	11	(10.2)
Apgar score < 5 at 1 minute	8	(7.4)	9	(8.3)
Apgar score < 7 at 5 minute	5	(4.6)	8	(7.4)
Mechanical ventilation	19	(17.6)	29	(26.9)
Apnoea	6	(5.6)	3	(2.8)
Respiratory distress	50	(46.3)	60	(55.6)
Patent ductus arteriosus	5	(4.6)	4	(3.7)
Umbilical catheterisation for exchange transfusion	8	(7.4)	6	(5.6)

DISCUSSION

Data obtained from the Malaysian Statistics Department showed that the Kuala Lumpur Maternity Hospital delivered 52.8% of the total livebirths in the city in 1987. This Hospital serves both as a service hospital for the residents in Kuala Lumpur and as a referral hospital for the nearby states in Malaysia. The number of livebirths in this hospital was about three times that of most general hospitals in Malaysia. In view of the large number of neonates in this hospital, the data in this study would probably be close to the actual incidence of NEC among neonates in the Malaysian population.

Because of the strict criteria used in diagnosing NEC, we might have excluded some neonates with mild NEC. However, it was unlikely that any neonate without NEC was included. Our study showed that NEC was not rare among our sick neonates. The incidence and birthweight-specific mortality rates of this condition were similar to those reported in the developed countries. The VLBW neonates were the most commonly affected group as was found elsewhere (1-3, 17). Furthermore, as was reported by others, the common perinatal factors were not shown to be significantly more common among our NEC neonates when compared with the controls. Lawrence et al (18) proposed that the NICU environment itself was responsible for the development of NEC. This was because in the NICU, the physical isolation, cleanliness of nursing procedures and treatment with antibiotics reduced the variety of organisms with which the neonates were colonised. As a result, the few variety of organisms which remained in the neonatal gut were able to multiply without interference. The ability of the immature gut to take up macromolecules produced by the organisms in the lower ileum permitted absorption of toxins from the multiplying bacteria with resultant intestinal damage and the start of NEC.

Control studies on the types and volumes of milk given to neonates prior to onset of NEC so far did not show any of the feeding regimens to be the predisposing or protecting factors for the development of NEC (19 – 23). However, the breast milk used in these studies were either refrigerated or frozen before being fed to the neonates. Although frozen or refrigerated breast milk was known to retain some of its immunologic properties (24, 25), a study by Stevenson et al (26) showed that frozen breast milk fed to hospitalised preterm neonates was not effective in suppressing the proliferation of coliform and other potentially pathogenic organisms in the gut. Since studies on laboratory model (27) had shown that breast milk could prevent NEC, there is now a need to carry out case control studies to determine the protective role of freshly obtained breast milk fed to our sick preterm and VLBW neonates.

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