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Research Article

Clinical Analysis of Neonatal Necrotizing Enterocolitis in Macao During the 10-Year Period

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Abstract

Necrotizing enterocolitis is a common neonatal gastrointestinal emergency. In the neonatal care, the incidence is high. If the disease is not early detected, the higher the chance of serious complications occurred. We reviewed the diagnosis of necrotizing enterocolitis in our hospital for retrospective analysis. The results showed 184 cases of necrotizing colitis from 2006 to 2015. We found that necrotizing enterocolitis predisposing factors are prematurity and birth weight less than 2500 grams. Breastfeeding is very important for prevention.

Keyword: *Necrotizing Enterocolitis; Neonate; Premature; Low Birth Weight; Breastfeeding*

Introduction

Necrotizing enterocolitis (NEC) is a major gastrointestinal disorder affecting newborns in the neonatal intensive care unit (NICU) [1]. The clinical features of NEC are inflammation leading to intestinal damage. It is reported that the incidence of the disease worldwide is less than 1% to 5% of the NICU admission rate, 0.5 to 5 cases/1,000 live births [2].

NEC mainly affects low birth weight infants or preterm infants. NEC usually occurs within a few weeks after the birth of newborns and is increased when we use formula for feeding. NEC symptoms may include vomiting, diarrhea, bloody stool, feeding intolerance, abdominal swelling, lack of bowel sounds. It is difficult to distinguish between mild NEC cases and other gastrointestinal diseases (such as milk protein intolerance). Severe cases may show fluid in the peritoneal (abdominal) cavity, intestinal perforation, peritonitis (peritoneal peritoneal infection) or shock. The mortality rate of NEC is 15% to 30% [2]. Most of the NEC cases can be cured by conservative treatment, but severe cases such as complicated with intestinal perforation may require surgical removal of dead intestinal tissue.

The reason for NEC is not obvious. Most of NEC's cases occur individually, but the outbreaks of NEC in the neonatal care ward have been reported [3,4]. Observations of the causes of these cluster cases may be due to infection, but this cannot determine the infection is related to the NEC outbreak [2].

NEC is a neonatal severe gastrointestinal disease. Therefore, it is important to understand the epidemiology of NEC in Macau and the degree of disease to develop public health interventions to prevent the occurrence of risk factors. In this study, we reported the incidence of neonatal NEC inpatients from 2006 to 2015 and identified potential risk factors.

Between 2006 and 2015, 3.2% of newborn babies who were admitted to NICU developed into NEC. The incidence of NEC was 3.03 per 1,000 live births. Deaths occurred in 13.5% of NEC cases. About 80% of NEC cases were born in premature delivery (gestational age less than 36 weeks) or low birth weight (less than 2500 grams). The risk of the disease was negatively correlated with gestational age and birth weight. Breastfeeding is associated with a reduced likelihood of neonatal development of NEC.

Premature infants and low birth weight are significantly associated with NEC risk factors, breastfeeding has been proven to have a protective effect on NEC. The most direct and effective reduction of NEC's strategy is to actively promote the supply of breast milk to self-sufficient breast-feeding to premature children, and breastfeeding rate of NICU is lower than the general population. Long-term interventions to deal with premature infants and low birth weight are complex and require multi-sectoral cooperation.

Purpose

The aim of this study is to do the clinical analysis of NEC in Macao during the 10-year period.

Method

All infants aged 0 to 30 months who were enrolled in the NICU of CHCS Januario from 2006 to 2015 were included in our study. Newborns characteristics were extracted from our medical records, including gender, gestational age, birth weight, pregnancy (single or multiple), as well as mother age. Apgar scores, breastfeeding and maternal factors were extracted from the medical records, including alcohol consumption during pregnancy, smoking and drug use, and delivery patterns.

The comparison of these features between NEC and non-NEC infants was performed using a chi-square or Wilcoxon test. Multiple logistic regression was used to identify NEC risk factors. With $P < 0.01$ considered statistically significant and is selected to identify factors that were significantly associated with NEC.

Results

Between 2006 and 2015, 5701 newborns were admitted to the neonatal care unit. Of which 183 (3.2%) diagnosed as NEC. During the 10-year period, the incidence of the disease ranged from 0.88 to 4.45 per 1,000 live births (Table 1). The annual incidence of newborns in 2012 was 5.41%. The mortality rate of the disease was significantly higher than that of the non-disease (1.9 ‰). Of the 184 NEC cases, 25 died.

Year	Number of live births	NICU	NEC cases	NEC cases per 100 NICU admissions	NEC cases per 1000 live births
2006	4058	455	4	0.80	0.99
2007	7913	522	7	1.34	0.88
2008	4717	557	21	3.77	4.45
2009	4764	538	25	4.65	5.25
2010	5114	643	20	3.11	3.91
2011	5852	549	23	4.19	3.93
2012	7315	591	32	5.41	4.37
2013	6571	593	26	4.38	3.96
2014	7360	681	16	2.35	2.17
2015	7055	572	10	1.75	1.42
Total	60719	5701	184	3.23	3.03

Table 1: *Results of Univariate Analysis – Demographic Characteristics.*

Risk Factor

In 5701 newborns admitted to the neonatal care unit, all cases can be in the medical system to get the baby and maternal disease data. Of these 5,701 newborns, 184 (3.03%) were diagnosed with NEC. Subsequent analysis is based on these newborns.

About 80% of newborns with NEC are premature infants, gestational age less than 36 weeks. The risk of developing the disease is inversely proportional to gestational age (Figure 1). Pregnant weeks 28 weeks before birth, more than 10% of preterm children developed into NEC. In the 28 to 32 weeks between the baby, the proportion rose to 55.4%. Birth weight also shows an inverse relationship (Figure 2). In infants with very low birth weight (1,000 grams), 25.5% of patients were diagnosed with NEC. This proportion was 35.4% and 26.08% in infants with very low birth weight (1,000-1,500 g) and low birth weight (1,500 - 2,500g), respectively.

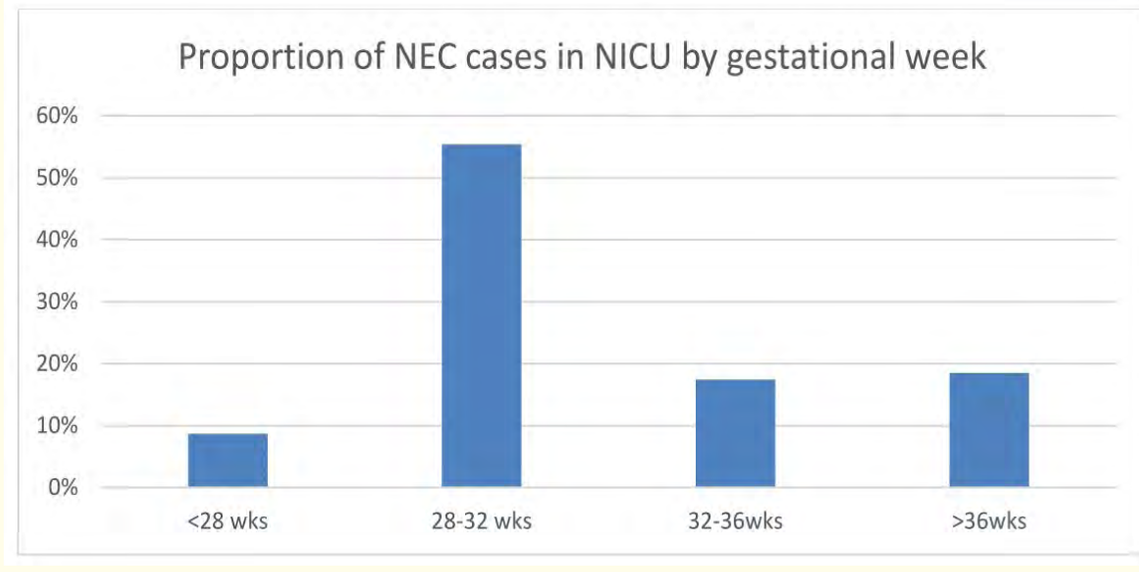

Figure 1: *Proportion of NEC cases in NICU by gestational week.*

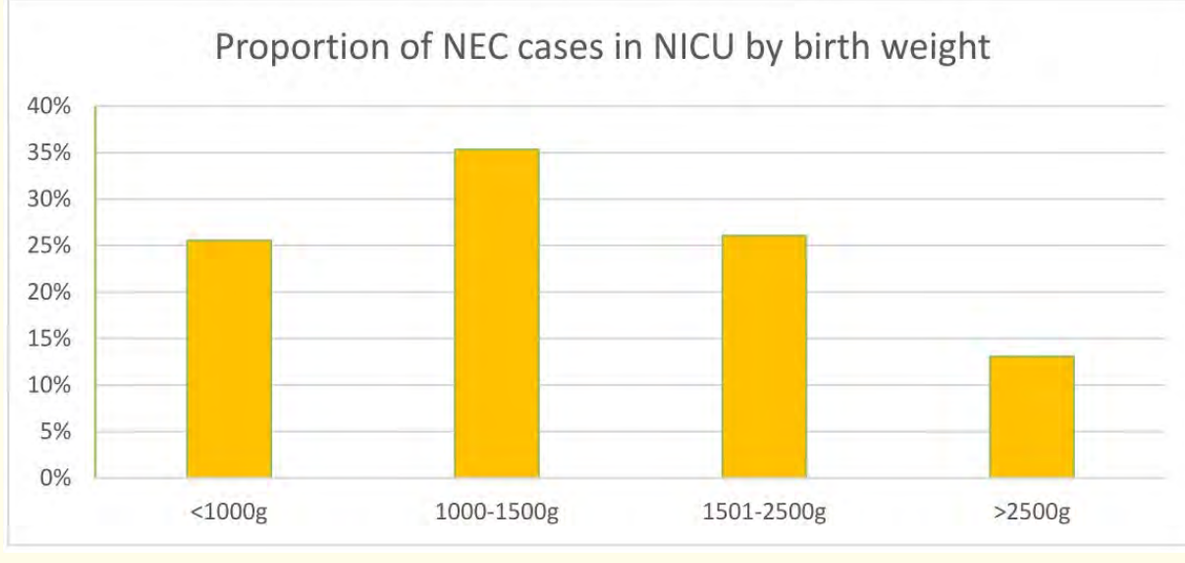

Figure 2: *Proportion of NEC cases in NICU by gestational week.*

Table 2 summarizes the characteristics of neonates with and without NEC. The neonatal factors associated with NEC were lower gestational age, lower birth weight and lower Apgar score, and we found a significantly lower rate of NEC in neonates with high breastfeeding rates. Pregnant women are age, pregnancy, smoking, drinking, drug abuse and NEC have no obvious relationship.

	Non-NEC	NEC	p-value
Variable	N = 5517 (%)	N = 184 (%)	
Infant Characteristic			
Gestational age (week)			
< 28	160 (2.90%)	16 (8.7%)	< 0.01
28 - 31+6	442 (8.01%)	102 (55.43%)	
32 - 35+6	1660 (30.08%)	32 (17.4%)	
> 36	3255 (58.9%)	34 (18.47%)	
Birth weight			
< 1000g	180 (3.3%)	47 (25.54%)	< 0.01
1000 - 1500g	220 (4%)	65 (35.43%)	
1501 - 2499g	1490 (27.0%)	48 (26.08%)	
> 2500g	3627 (65.7%)	24 (13.05%)	
Sex (female)	2386 (43.2%)	81 (44.02%)	
Small of gestational age			
No	4017 (73.0%)	132 (71.74%)	
Yes	1490 (27.0%)	52 (28.26%)	
Apgar at 1 minute, median	9.02 ± 1.03	7.78 ± 2.33	< 0.01
Apgar at 5 minute, median	9.04 ± 0.98	8.04 ± 1.48	< 0.01
Pregnancy type			
single	4523 (81.9%)	140 (76.1%)	0.04
multiple	994 (18.1%)	44 (23.9%)	
Maternal Characteristics			
Age			
< 20	275 (5%)	11 (5.9%)	0.25
20 - 24	772 (13.9%)	28 (15.2%)	
25 - 29	1380 (25%)	52 (28.3%)	
30 - 34	2041 (37%)	70 (38.0%)	
> 35	1049 (19.1%)	23 (12.6%)	
Breastfeeding	2868 (51.9%)	70 (38.0%)	<0.01
Caesarean delivery			
No	2648 (47.9%)	82 (44.6%)	0.36
Yes	2869 (52.1%)	102 (55.4%)	
Smoking during pregnancy			
No	5209 (94.4%)	174 (94.6%)	0.8
Yes	308 (5.6%)	10 (5.4%)	
Alcohol consumption during pregnancy			
No	5197 (94.2%)	169 (91.8%)	0.24
Yes	320 (5.8%)	15 (8.2%)	
Drug use during pregnancy			
No	5258 (95.3%)	175 (95.1%)	0.96
Yes	259 (4.7%)	9 (4.9%)	

Table 2: *The condition between the Non-NEC and NEC group in NICU.*

Multivariate logistic regression analysis showed that NEC risk factors were lower gestational age, low birth weight, lower Apgar score, and no breastfeeding (Table 3). The risk of developing NEC in preterm infants born at less than 28 weeks of age was 9.57 and 6 times higher in preterm infants from 28 weeks to 35 weeks, compared with full term infants (> 36 weeks). Compared with the birth weight of 2,500 grams of the fetus, the birth weight of less than 1000 grams of newborns and birth weight between 1000 grams and 2499 grams have higher risk of 39 times and 10 times for developing NEC. Breastfeeding babies have a 40% lower risk of estimating NEC.

Variable	Odds Ratio	(95%Confidence interval)	p-value
Gestational age (week)			
< 28 vs 36+	9.57	(5.65 - 16.21)	< 0.01
28 - 35 vs 36+	6.1	(4.35 - 8.57)	< 0.01
Birth weight (g)			
< 1000 vs 2500+	39.46	(28.27 - 55.08)	< 0.01
1000 - 2499 vs 2500+	10.33	(7.17 - 14.88)	< 0.01
Breastfeeding	0.57	(0.42 - 0.76)	< 0.01

Table 3: *Risk factor of NEC- logistic regression analysis.*

Discussion

This study is similar to other epidemiological reports, NEC mainly affect premature children, the risk factors of NEC were significantly correlated with gestational age and birth weight. The cause of NEC is still poorly understood. Premature infants due to poor gastrointestinal motility and digestive function, intestinal circulation regulation is weak, intestinal barrier function and immune defense development is immature and thus increase the risk of suffering from NEC; other factors include hypoxic ischemic injury, formula feeding and Pathogenic bacterial colonization [2]. In addition, NEC babies are also more likely to get a lower 1 minute Apgar score. Apgar provides an overall assessment of the physical condition of the newborn at birth. This shows that NEC is more common in sick newborns.

Clinically, NEC is classified according to the Bell stage criteria [5], the first stage is suspected, and the second and third phases are identified and advanced. In our current research. Of these newborns, 103 (56%) were in the first phase of NEC, 56 (30.5%) in the second stage, and 25 (13.5%) in the third. The average symptom onset was 4.2 days ± 3.0 was the earliest day when the patient developed symptoms on the first day of life, and 81% of the patients developed symptoms at the first 7 days of life. The sooner the condition occurred, the more serious the situation occurred. This is similar to that reported in other literature [6].

Breastfeeding has proven to be the protective factor of NEC, which is consistent with other reports [7,8]. Breastfeeding infants have a significantly lower risk of NEC than formula feeding [9,10]. Compared with formula milk feeding, human milk promotes host defense and gastrointestinal maturation [11]. The nutritional content of breast milk is more suitable for the needs of preterm children [12]. Therefore, an important strategy to reduce NEC risk is to promote the mother's own milk to provide premature infants.

It also shows that the higher the proportion of milk in the diet can reduce the risk of NEC. Mothers breastfeeding under intensive care is a daunting challenge, including the production of adequate breast milk and the maintenance of breast milk supply to newborns. We need to understand and address these barriers in order to achieve early breastfeeding for premature babies to prevent necrotizing enterocolitis from occurring.

This study only uses the NEC condition of our hospital, which does not really reflect the overall situation of patients with total necrotizing enterocolitis in Macau, limiting the possible bias in the selection of single-center studies. Preterm infants are usually in tube feeding, receiving a combination of human milk and supplemental feeding. However, the type of supplemental feeding provided is not available in this analysis, thus limiting our assessment of the association of NEC with alternative feed or supplemental feed types. A further limitation of this report is that other interventions that may affect the incidence of NEC, such as vascular access surgery and intravenous drugs, have not yet been included in the analysis.

Conclusion

In conclusion, necrotizing enterocolitis is a neonatal gastrointestinal disease that can cause serious complications. Premature infants and low birth weight are significantly associated with NEC risk factors. Breastfeeding seems to reduce the likelihood of developing NEC. Therefore, actively promoting and supporting the provision of early breast milk for preterm infants is a key strategy for the prevention and treatment of NEC. Early breast milk expression is important for premature infants. It is necessary for multi-sectoral collaboration to provide early interventions for preterm birth and low birth weight neonates to prevent serious complications.

Bibliography

1. Boccia D., *et al*. "Nosocomial necrotising enterocolitis outbreaks: epidemiology and control measures". *European Journal of Pediatrics* 160.6 (2001): 385-391.

2. Lin PW and Stoll BJ. "Necrotising enterocolitis". *Lancet* 368.9543 (2006): 1271-1283.

3. Faustini A., *et al*. "An epidemic of gastroenteritis and mild necrotizing enterocolitis in two neonatal units of a University Hospital in Rome, Italy". *Epidemiology and Infection* 132.3 (2004): 455-465.

4. Wendelboe AM., *et al*. "Cluster of necrotizing enterocolitis in a neonatal intensive care unit: New Mexico, 2007". *American Journal of Infection Control* 38.2 (2010): 144-148.

5. M J Bell., *et al*. "Neonatal necrotizing enterocolitis. Therapeutic decisions based upon clinical staging". *Annals of Surgery* 187.1 (1978): 1-7.

6. Yee WH., *et al*. "Incidence and timing of presentation of necrotizing enterocolitis in preterm infants". *Pediatrics* 129.2 (2012): e298-e304.

7. Schurr P and Perkins EM. "The relationship between feeding and necrotizing enterocolitis in very low birth weight infants". *Neonatal Network* 27.6 (2008): 397-407.

8. Kelley L. "Increasing the consumption of breast milk in low-birth-weight infants: can it have an impact on necrotizing enterocolitis?" *Advances in Neonatal Care* 12.5 (2012): 267-272.

9. Lucas A and Cole TJ. "Breast milk and neonatal necrotising enterocolitis". *Lancet* 336.8730 (1990): 1519-1523.

10. Sullivan S., *et al*. "An exclusively human milk-based diet is associated with a lower rate of necrotizing enterocolitis than a diet of human milk and bovine milk-based products". *Journal of Pediatrics* 156.4 (2010): 562-567.

11. Schanler RJ., *et al*. "Feeding strategies for premature infants: beneficial outcomes of feeding fortified human milk versus preterm formula". *Pediatrics* 103.6 (1999): 1150-1157.

12. Fox TP and Godavitarne C. "What really causes necrotising enterocolitis?" *ISRN Gastroenterology* (2012): 628317.

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