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Association between Supraventricular Tachycardia and Necrotizing Enterocolitis: A Case-Control Study

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Abstract

Background: Necrotizing enterocolitis (NEC) is the most common and fatal gastrointestinal disease encountered in the Neonatal Intensive Care Unit. Several case reports have shown an association between supraventricular tachycardia and necrotizing enterocolitis. This study aimed to determine the association between supraventricular tachycardia and necrotizing enterocolitis. **Methods:** This study was conducted from April 1st, 2016 to March 31st, 2022, at the Department of Pediatrics, Zhongnan Hospital of Wuhan University, Hubei, China. The records of 74 subjects with the diagnosis of necrotizing enterocolitis (NEC) were obtained from the hospital's medical data records. Consequently, 74 gender, gestational age, and birth weight-matched controls (babies without NEC) were recruited as controls. **Results:** Of the 74 cases, 47.3% of the cases were males, and 52.7% were females. Regarding the birth weight and gestational age, 77% of the cases had low birth weight (LBW) and 86.5% were premature. In terms of Apgar score, 93.2% of NEC cases had an Apgar score of >7 at five minutes. The median values of white blood cells, platelets, and hemoglobin of cases were 10.90 (8.09, 13.80), 227 (169.75, 295.50), and 155.6 (130.53, 170.95), respectively. No Association between supraventricular tachycardia and necrotizing enterocolitis (P = 1.00). **Conclusion:** No association between necrotizing enterocolitis and supraventricular tachycardia was found. Further multicenter-based studies examining whether there is a potential relationship exists between supraventricular tachycardia and the development of necrotizing enterocolitis are required.

Keywords

Supraventricular Tachycardia, Neonatal Arrhythmias, Necrotizing Enterocolitis

1. Introduction

Necrotizing enterocolitis (NEC) is the most common and fatal gastrointestinal disease encountered in the Neonatal Intensive Care Unit (NICU) [1] [2]. NEC is almost exclusively a disease of prematurity affecting 5 to 12 percent of babies with very low birth weight (VLBW) or with less than 1500 g birth weight resulting in major morbidity and mortality [2] [3]. The estimated fatality rates among preterm infants range between 15% and 30% [4]. The disorder has also been reported in full-term infants [2]. It is characterized by various degrees of bowel injury from epithelial damage to complete wall injury and systemic infection as its pathological hallmark [3] [5].

The pathophysiology of NEC is thought to be due to multiple factors, and its definitive etiology is yet to be found. Prematurity and low birth weights are the most frequently reported risk factors for the evolution of NEC in neonates [4] [5]. The other frequently mentioned risk factors include formula feeding, meconium aspiration syndrome (MAS), blood transfusion, and congenital heart disease (CHD) in term infants [6]. Additionally, some case reports described neonatal supraventricular tachycardia as a contributing factor to the development of NEC [7] [8].

Supraventricular tachycardia (SVT) is a diverse group of dysrhythmias that is typically described as a narrow-complex tachycardia affecting 1 per 250 to 1000 pediatric population, with onset typically occurring before the first month of life [9] [10]. It is the most prevalent illness that requires an emergency cardiac intervention in infants and poses serious global health implications [11].

Despite extensive studies conducted to determine the potential risk factors for NEC development, there are only a few case reports that suggested supraventricular tachycardia as a possible predisposing factor for the progression of NEC [7] [8] [12] [13] [14] [15] [16]. The main purpose of this study was to identify the relationship between SVT and NEC.

2. Methods

Study design and setting: This was a single-center case-control study conducted at the Department of Pediatrics, Zhongnan Hospital of Wuhan University, Hubei, China from April 1st, 2016 to March 31st, 2022. Records of 74 subjects with the diagnosis of necrotizing enterocolitis (NEC) based on (Bell's classification criteria) were obtained from the hospital's medical records [17]. Consequently, 74 gender, gestational age, and birth weight-matched controls (babies without NEC) were recruited as controls.

Inclusion & exclusion criteria: Subjects were included if they were infants less than or equal to four weeks of age, including both those born preterm and those of full-term gestational age who developed NEC. Infants were excluded if they were more than four weeks of age, had NEC diagnosis of Bell's stage I, or had a history of structural heart disease.

Full blood count: The normal ranges for white blood cells, hemoglobin and

platelets reported by our laboratory were 4.42 to 24 * 10^9/L, 127 to 204 g/L and 108 to 375 * 10^9/L, respectively [18].

Data collection: Data were collected from the electronic medical records of Zhongnan Hospital of Wuhan University. Demographic information of all participants such as gender birth weight, gestational age, Apgar score complete blood count (WBC, HB, PLT), and the history supraventricular tachycardia was recorded and saved into an excel sheet.

Statistical analysis: Data were analyzed using IBM SPSS version 28. Categorical data were presented as frequencies and percentages, while continuous data were displayed as median and percentiles. Since our data were not normally distributed, Mann-Whitney was used for continuous variables while the Chi-square test was used for the categorical variables. P-values less than 0.05 were considered statistically significant.

Ethical consideration: The study was ethically cleared by the ethics committee of Zhongnan Hospital of Wuhan University. Parents of all included subjects gave their informed consent for inclusion before they participate in the study.

3. Results

The total study population consisted of 148 participants comprising 74 NEC cases, and 74 matched controls. There was no statistically significant difference between the two groups in terms of gender, birth weight, gestational age, Apgar score, and history of SVT ($P > 0.05$). Of the 74 cases, 35 (47.3%) were males, and 39 (52.7%) were females. The controls consisted of 34 (45.9%) males and 40 (54.1%) females. Fifty-seven (77%) in both cases and controls were low birth weight, and seventeen (23%) cases had normal birth weight. There was a slight difference between the two groups in terms of gestational age, of which 64 (86.5%) of NEC cases were preterm, and 63 (85.1%) of the controls were born prematurely. Among the babies with NEC 93.2% (n = 69) had an Apgar score of >7 at five minutes, while in controls 89.2% (n = 66) had an Apgar score of >7 at five minutes. In terms of the history of supraventricular tachycardia, both the cases and controls had no history of SVT. Table 1 depicts the detailed demographic data. For full blood count, the median WBC was 10.90 (8.09, 13.80) among cases, and 10.33 (7.2, 13.6) among controls, ($P = 0.539$). Median platelet count was 227 (169.75, 295.5) among cases, and 233 (200.75, 277.25) among controls ($P = 0.445$). Meanwhile, median hemoglobin (Hb) was 155.6 (130.53, 170.95) among cases and 161.65 (149.93, 174.33) among controls ($P = 0.047$). Table 2 shows the detailed full blood count measurements.

4. Discussion

The present study examined the association between necrotizing enterocolitis and supraventricular tachycardia. The study population was divided into two groups, 74 cases (infants with NEC) and 74 controls (infants without NEC). Demographic characteristics such as gender, birth weight, and gestational age

Table 1. Comparison of risk between cases and controls.

		Cases (n = 74) %	Controls (n = 74) %	P-value *
Gender	Male	35 (47.3)	34 (45.9)	0.500
	Female	39 (52.7)	40 (54.1)	
Birth weight (g)	<2500	57 (77)	57 (77)	0.577
	≥2500	17 (23)	17 (23)	
Gestational Age (weeks)	<37	64 (86.5)	63 (85.1)	0.500
	≥37	10 (13.5)	11 (14.9)	
Apgar Score (5 min)	<7	5 (6.8)	8 (10.8)	0.282
	≥7	69 (93.2)	66 (89.2)	
SVT	Yes	0 (0%)	0 (0%)	1.00
	No	74 (100)	74 (100)	

SVT: Supraventricular tachycardia.

Table 2. Complete blood count levels between the two groups.

	Cases (n = 74)	Controls (n = 74)	P-value*
WBC	10.90 * 10^9/L (8.09, 13.80)	10.33 * 10^9/L (7.92, 13.6)	0.539
PLT	227 * 10^9/L (169.75, 295.50)	233 * 10^9/L (200.75, 277.25)	0.445
HB	155.6 g/L (130.53, 170.95)	161.65 g/L (149.93, 174.33)	0.047

WBC: White Blood Cells, PLT: Platelets, HB: Hemoglobin.

were compared in both groups. In terms of gender distribution, 47.3% of the cases were males, and 52.7% were females. Among the controls, 45.9% were males and 54.1% were females. The difference between the two groups was not statistically significant ($P > 0.05$). Similar results were seen in the study by Carter *et al.* In their study, they conducted a large longitudinal study with 134 infants and found that there is no relationship between gender and NEC [19]. Considering their birth weight, 77% of the cases had low birth weight (LBW) compared to 23% of them with normal birth weight. In the control group, 77% were low birth weight infants while 23% of them had normal birth weight. This indicates NEC is more common in LBW infants. The difference between the two groups was not statistically significant ($P > 0.05$). However, numerous studies revealed that NEC is related to low birth weight [4]. Although there was no statistically significant difference between cases and controls in terms of gestational age ($P > 0.05$), 86.5% of NEC cases were preterm babies while 85.1% of controls were preterm. This is supported by a study conducted by Nair *et al.* in their retrospective analysis. They presented a relationship between low gestational age and the development of NEC [20]. On Apgar score, 93.2% of NEC cases had an Apgar score of >7 at five minutes. Among the control group, 89.2% had their

Apgar score above 7 at five minutes. There was no statistically significant difference between the two groups (P > 0.05).

A recent study performed by Siahaan *et al.* also found no significant relationship between NEC and Apgar score [21].

For the full blood count, our study presented a median of 10.90 for WBC among NEC case, and a median of 10.33 among controls. The difference between the two groups was not statistically significant (P > 0.05). Platelet count of a median of 227 among case group, and median of 233 among controls were found. There was no statistically significant difference seen between cases and controls (P > 0.05). This disagrees with previous studies describing the role of hematological disorders in NEC development. A review conducted by Song *et al.* stated that both increased WBC and thrombocytopenia may have a role in the development of NEC [22]. On the other hand, the study reported hemoglobin (Hb) of a median of 155.6 among the NEC group and a median of 161.65 among the controls. There was a significant statistical difference (P = 0.047) between the two groups. A recent cohort study performed by Cai *et al.* concluded that decreased hematocrit concentrations may predict NEC occurrence [23]. It is possible that a decrease in HC could cause ischemic and hypoxic damage to the body, which results in the redistribution of blood and microcirculation disorders, which in turn could affect the intestinal tract of children adversely [24].

Based on the history of SVT, there is no association between supraventricular tachycardia and necrotizing enterocolitis. Since no previous observational studies examined this area, this study was the first case-control study examining the association between SVT and NEC with the largest sample size. However, a few published case reports found an association between SVT and NEC. The first case report was reported by Cale *et al.* in 1995. In their study, the infant developed extensive necrotizing enterocolitis on day 8 after prolonged SVT [7]. The subsequent case was reported in 1998 by Khalak *et al.* in their study, a premature newborn with supraventricular.

Tachycardia developed NEC within 28 hours of starting enteral feeding [8]. More than a decade later, Hanna, described NEC in the second week of life in a preterm infant with a history of repetitive SVT and enteral feeding [14].

In 2017, Saini J, *et al.* published another case report. In their article, they stated two near-term infants, one of them with intrauterine growth restriction (IUGR), and one large for gestational age who developed NEC following episodes of SVT [13]. Nakib *et al.* in 2018, reports a full-term baby who was on breastfeeding and diagnosed with NEC preceded by SVT [15]. Mecarini *et al.* also presented a case in 2020. Their published report described a moderate preterm baby who developed NEC in the third week of life after recurrent SVT [16].

A recent case reported by H. Akduman *et al.* stated a full-term infant born by cesarean section and diagnosed with NEC on the 22nd of life following episodes of SVT 14 hours prior to the NEC [12]. A newly published case report presented a preterm newborn with isolated supraventricular tachycardia followed by ne-

crotizing enterocolitis [25].

In an attempt to explain the association between supraventricular tachycardia and necrotizing enterocolitis, several theories have been proposed. The blood flow to the intestine is supplied by the superior and inferior mesenteric arteries as well as celiac artery, and Ischemia is a well-recognized and a significant risk factor for the development of NEC [26].

The diving reflex, which redistributes cardiac output to maintain the blood supply to the essential organs such as the brain and the heart, is one mechanism of intestinal hypoperfusion associated with necrotizing enterocolitis [27]. The published case reports suggest that repeated attacks of SVT may lead the development of NEC through mesenteric blood flow disturbances [7] [12] [13] [14] [15] [16] [28]. This may result from the raised vascular resistance reducing blood supply to the mesentery and leading reduced tissue perfusion, hence injury to the intestinal mucosa [2]. The generation of oxygen-free radicals during stabilization of cardiac output through management of SVT may induce reperfusion tissue injury to the bowel. Prolonged tachycardias may also result in hemodynamic compromise, however some authors believe that NEC can also occur in infants affected by SVT in the absence of considerable hemodynamic instability [15] [16].

5. Conclusion

In summary, this study found that necrotizing enterocolitis was slightly more common in females than males. Premature birth and low birth weight were also associated with the increased risk of developing NEC. No association between necrotizing enterocolitis and supraventricular tachycardia was found. Further multicenter-based studies examining whether there is a significant association exists between supraventricular tachycardia and the development of necrotizing enterocolitis are required.

Study Limitations

This study has a number of limitations. It is a retrospective study with a small sample size, a possibility of selection bias, only one center was involved, it may not be generalizable to all infants in China, and a matched control group was included.

Declarations

Ethics Approval and Consent to Participate

This research was authorized by the Ethics Committee of Zhongnan Hospital, Wuhan University, in agreement with the Helsinki Declaration and the Protocol of Helsinki's rules and directions for medical research on children. Before participating in the study, the parents of all newborn infants provided their informed consent for their participation. Patients' confidentiality was maintained throughout the duration of the study.

Authors' Contribution

Ali Omar Jimale conducted data collection and manuscript drafting. Zakaria Ahmed Mohamed performed the analysis of the data. Dongchi Zhao conceived the study and supervised the entire process of the study.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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