

A Study of Erythema Toxicum Neonatorum and Its Predisposing Factors

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Abstract Erythema toxicum neonatorum is one of the commonest skin lesions observed in neonates. Despite this lesion being common, its etiology and predisposing factors remains elusive. This study was designed to evaluate various neonatal and maternal factors which predisposes to the development of erythema toxicum neonatorum. A cross-sectional case control study was conducted in Manipal Teaching Hospital, Pokhara, Nepal, where 200 newborns with erythema toxicum neonatorum and 200 newborns as controls were sampled for neonatal and maternal variables which may predispose to erythema toxicum neonatorum. Neonatal variables studied were: gender, birth weight, gestation, mode of delivery, whether the baby was born through meconium stained amniotic fluid and if the newborn had received a bath after delivery. Maternal variables studied were: parity, maternal smoking and history of atopy in the mother. Odds ratio and 95% confidence interval (CI) were used to calculate the odds and risks of developing erythema toxicum neonatorum. Higher odds of developing ETN was observed in neonates weighing more than 2500 grams [OR= 3.58; 95% CI (1.92; 6.67)], term gestation [OR= 4.03; 95% CI (1.94; 8.39)], and those neonates born through meconium stained amniotic fluid [OR= 6.882; 95% CI (1.53; 30.91)]. A number of studies have shown a significant relationship between normal birth weight and term neonates as predisposing factors in the development of erythema toxicum neonatorum. However, what our study adds is that there was a higher risk of acquiring erythema toxicum neonatorum in babies born through meconium stained amniotic fluid.

Keywords: *erythema toxicumneonatorum, meconium stained amniotic fluid, neonates*

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1. Introduction

Erythema toxicum neonatorum (ETN) is recognized as a non-infectious, transient benign cutaneous lesion that commonly occurs in neonates worldwide. One of the first physicians to document this condition was a 15th century German pediatrician by the name of Bartholmaeus Metlinger [1]. Later in the 18th century, William Smellie, a Scottish obstetrician concluded that ETN was a result of meconium on the neonate's skin [1,2]. Though this is one of the commonest skin rash observed in neonates, its etiology still remains elusive. Many theories have been postulated as a possible mechanism for this eruption: prolonged contact of the meconium with the skin, vigorous removal of vernix caseosa, mechanical/chemical irritants, intestinal toxins, allergens, a transient graft versus host reaction by maternal lymphocytes, hormonal influences and a cutaneous immune reaction to commensal microflora [3,4,5,6,7].

Historically speaking, ETN has been given several names: erythema papulatum, erythema dyspepticum, erythema neonatorum allergicum and urticarial neonatorum [1]. All these names reflect the factors thought to be responsible for the development of ETN. Finally, the present name, erythema toxicum neonatorum, was given by an Austrian pediatrician Karl Leiner in 1912 [1,8].

Erythema toxicum neonatorum is characterized by small pinkish red macules which may or may not have a central papule or pustule [3]. The lesion occurs on all parts of the body but tends to spare the palms and soles [9]. The onset is typically after the first day of life and it resolves spontaneously within a week without sequelae [3,10]. Pediatricians are invariably the ones to notice this common eruption particularly in post natal wards and faced with the task of counseling parents about the benign nature of this skin lesion whose exact etiology and predisposing factors still remains unidentified. We undertook this study with the intention of gaining a better understanding of various neonatal and maternal parameters which may contribute to the eruption of this rash. We hope that this study will help us gain a better insight to the predisposing factors of ETN.

2. Materials and Methods

This cross sectional case control study was carried out in the post natal ward of Manipal Teaching Hospital, Pokhara, Nepal. The study period was from Oct 2013 to May 2014. During the study period, 200 neonates with ETN were recruited for the study, and as controls, 200 neonates without ETN were also sampled. In all the

studied newborns, the following variables were recorded: baby's gender, birth weight, gestational age, mode of delivery, whether the neonate was born through meconium stained amniotic fluid (MSAF), whether the baby had received a bath after birth and maternal information (number of previous pregnancies, maternal smoking, and maternal history of atopy). The newborns were examined after the third day of life as ETN usually develops after the first day of life. In all cases, diagnosis of ETN was made on clinical basis.

Data was collected and analyzed using SPSS for Windows version 16.0. Odds ratio and its 95% CI was calculated to observe for strength of relationship between ETN and the variables.

3. Results

A total of 400 neonates were included in this study; two hundred cases of ETN and 200 controls without ETN. Table 1 depicts various neonatal and maternal factors and its odds of developing the suspected predisposing factors. With respect to neonatal factors, statistically significant higher odds of developing ETN was seen in neonates with >2500 grams birth weight, term gestation and those born through MSAF. Gender, mode of delivery, and giving babies a bath following birth were not associated with increased risk of developing ETN. Also, maternal variables such as maternal smoking, maternal history of atopy and parity of the mother did not statistically significantly increase the odds of developing ETN.

Table 1. Analysis of Various Neonatal and Maternal Factors in The Development of ETN

Variable	Erythema Toxicum Neonatorum		Odds Ratio (OR)	95% CI
	No (N= 200)	Yes (N= 200)		
Gender	n (%)	n (%)		
Male (233)	117 (50.2)	116 (49.8)	1.02	(0.69; 1.52)
Female (167)	83 (49.7)	84 (50.3)		
Birth Weight				
< 2500 gm (60)	45 (75)	15 (25)	3.58	(1.92; 6.67)*
>2500 gm(340)	155 (45.6)	185 (54.4)		
Gestation				
Preterm (45)	35 (77.8)	10 (22.2)	4.03	(1.94; 8.39)*
Term (355)	165 (46.5)	190 (53.5)		
Mode of Delivery				
Vaginal (250)	119 (47.6)	131 (52.4)	0.77	(0.52; 1.16)
Cesarean (150)	81 (54)	69 (46)		
Parity				
Single (249)	133 (53.4)	116 (46.6)	1.43	(0.96; 2.16)
Multi para (151)	67 (44.4)	84 (55.6)		
Maternal Smoking				
No (375)	186 (49.6)	189 (50.4)	0.77	(0.34; 1.75)
Yes (25)	14 (56)	11 (44)		
MSAF				
No (385)	198 (51.4)	187 (48.6)	6.88	(1.53; 30.91)*
Yes (15)	2 (13.3)	13 (86.7)		
History of maternal Atopy				
No (375)	185 (49.3)	190 (50.7)	0.65	(0.28; 1.48)
Yes (25)	15 (60)	10 (40)		
Bathing of Baby				
No (248)	134 (48.2)	114 (51.8)	0.79	(0.52; 1.21)
Yes (122)	66 (54.1)	56 (45.9)		

4. Discussions

In this study we attempted to evaluate the predisposing factors contributing to ETN. Five neonatal and three maternal parameters were analyzed to assess for its strength of relationship to ETN.

4.1. ETN and Gender

The results of this study showed that there were 116 (49.8%) males and 84 (50.3%) females ETN. There was no statistically significant difference in odds of developing

ETN with regards to gender of new born [OR = 1.02; 95% CI (0.69; 1.52)]. This is similar to the findings of a study conducted in Karnataka, India, where they found it to be almost equal among the sexes [11]. However, this conclusion was not supported by Liu et al in China, who have reported a predominance of ETN in males [12].

4.2. ETN and Birth Weight and Gestation

The risk of developing ETN was higher in babies who were of normal weight; neonates who were > 2500 grams had a higher probability of having ETN [OR = 3.858; 95% CI (1.92; 6.67)] than those neonates who were < 2500 grams. Similarly, odds of developing ETN were also

statistically significant in relation to gestational age, where it was predominantly observed in term neonates [OR = 4.03; 95% CI (1.94; 8.39)]. Our findings support those of Liu et al and Ferahbas et al [12,13]. In fact, in a study done by Dash et al, there were no occurrences of ETN in preterms [14]. The explanation for this finding may be explained by the hypothesis that complete maturation of the fetal immune system is required for development of these rashes and therefore in preterms there is immunological immaturity of neonatal skin responses [13,15].

4.3. ETN and Mode of Delivery

In the present study, the odds of developing ETN was higher in babies born via vaginal route compared to those born via Cesarean section; however, it was not statistically significant [OR = 0.77; 95% CI (0.52; 1.16)]. Jain et al in Uttar Pradesh, India and Khoshnevisasl et al in Zanjan, Iran, found a significant relationship between ETN and delivery by Cesarean section [16,17], whereas Monteagudo et al and Sadana et al noted a significantly higher ETN in those babies born vaginally [10,18]. Studies have also demonstrated a positive correlation between severity of ETN and total duration of labor in cases of vaginal deliveries [12]. It was postulated that occurrence of ETN may be associated with prolonged contact with vaginal secretions which possibly acts as an allergen [1,12].

4.4. ETN and MSAF and Bathing of the Baby

The results of our study revealed a statistically significant higher risk of developing ETN if the neonate was born through meconium stained amniotic fluid [OR = 6.88; 95% CI (1.53; 30.91)]. It was postulated centuries ago that meconium on the baby's skin acts as an irritant which contributes to the development of ETN [1]. We added this variable to our study to study for a possible association and found the odds to be higher, but we were unable to make similar comparisons because of lack of literature. Later, in the 1960s, Keital et al postulated that removal of vernix caseosa can lead to skin lesions such as ETN [6]. With the intention of testing this theory, we examined the relationship of ETN with bathing of the baby, but there was no such significant difference in the occurrence of ETN and whether the baby had received a bath or not.

4.5. ETN with Maternal Parameters

Regarding maternal parameters such as smoking, parity and maternal history of atopy, we were unable to confirm any relationship between them and ETN. Studies conducted by El-Moneim et al and Ekiz et al looked into relationships between maternal smoking and various skin lesions but they too were unable to establish a connection [19,20].

Though the influence of parity in ETN was not evident in our study, Liu et al found a higher frequency in first pregnancy births, whereas Sachadeva et al noted an increase in this condition with second or subsequent pregnancies [12,15].

A survey of relatives of neonates was conducted to see for an association between ETN and family history of atopy by Keital et al [6]; they too like us were unable to conclude an existence to such a relationship. There are

concerns however, that childhood ETN may lead to atopic dermatitis later in life [12]. This topic needs further research to substantiate it.

5. Conclusion

Studies have been done in various countries to look into the predisposing factors and possible etiology of ETN, but so far, this is the first study done in Nepal looking into this subject (this is to the best of the author's knowledge). What this study adds is that the odds of developing ETN was higher in babies born through MSAF. We need further studies on a larger scale to corroborate our findings. In addition, we would like to encourage authors to carry out further studies to look into the relationship between ETN and development of atopic dermatitis later in life.

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Declaration of Conflicting Interests

The authors declare that there is no potential conflicts of interest with respect to the research, authorship and /or publication of this article.

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