

# Erythema Toxicum Neonatorum: A Retrospective Review

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## ABSTRACT

**Objectives:** To describe clinical manifestations, differential diagnosis, and treatment outcome of Erythema Toxicum Neonatorum in healthy newborns at King Hussein Medical Center and Queen Rania Children's Hospital.

**Methods:** The medical records review was conducted for patients with clinical diagnosis of Erythema Toxicum Neonatorum who were treated at King Hussein Medical Center and Queen Rania Children's Hospital dermatology clinics between February 2008 and September 2012. Extracted data include duration of pregnancy, type of delivery, age, sex, cutaneous rash characteristics, associated clinical conditions, laboratory investigations, skin biopsy, and treatment. Simple statistical analyses (mean, frequency, and percentage) were used to describe the study variables.

**Results:** The study included 152 patients, 88 males and 64 females with a male to female ratio of 1.4:1. The age at onset of the rash ranged from one to 11 days (mean age was 4 days). All subjects were products of hospital-based deliveries. The erythematous and papular type was the commonest (73.7%). History of drug intake during pregnancy was found in about two thirds of cases (66%). Four subjects (2.64%) had lymphadenopathy and five (3.22%) had moderate fever. Tzanck smear was done in 17 subjects with severe skin rash. Skin biopsy was done in four patients. About half cases received oral antihistamine treatment and the rashes disappeared over 24 to 36 hours. Follow up was done for four weeks.

**Conclusion:** Erythema Toxicum Neonatorum is a self-limiting disease and without long term sequelae. More efforts are needed to raise awareness of this condition amongst health care professionals to avoid unnecessary investigations and treatment as it is sometimes misdiagnosed as bacterial infection.

**Key words:** Erythema Toxicum Neonatorum, Newborn.

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## Introduction

Erythema Toxicum Neonatorum (ETN) is the most common, transient benign self-limiting asymptomatic skin rash in healthy newborns.<sup>(1-4)</sup> The incidence of ETN is controversial and ranges from 15% to 70% of newborn infants.<sup>(5-8)</sup> In general, there is no gender or racial

predilection.<sup>(5,7)</sup> However, a recent large prospective study involving 1,000 neonates found a higher prevalence of ETN in Caucasian newborns and those with greater gestational age and higher birthweight, and with vaginal delivery.<sup>(8)</sup> ETN is characterized by small erythematous macules with or without central papules or pustules (Fig. 1, 2).<sup>(1,4,5)</sup> The onset is

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**Fig.1:** Erythematous papules over face.



**Fig.2:** Erythematous papules (and pustules)

typically during the first 48 hours after birth and the lesions usually last for two to three days, although the pustular eruption may persist longer.<sup>(2,5,6,9)</sup> The most characteristic of ETN is the flea bite picture with a minute white yellow papule on an erythematous base. The pustular variant is seen in about 30% of cases. Lesions often begin on the face and spread to affect the trunk and limbs.<sup>(8)</sup> Palms and soles are characteristically not affected. The rash usually resolves without permanent sequelae.<sup>(1,4,7,10)</sup> Typical lesions are usually easily diagnosed; therefore laboratory investigations are often not necessary.<sup>(5)</sup> However when investigation are performed, peripheral blood smear show eosinophilia in 18% of cases;<sup>(4,11)</sup> and this is usually more evident when the eruption has a predominant pustular component. The pathology of ETN is usually performed in a limited number of cases. The papular lesions are characterized by eosinophils infiltration of the outer root sheath of hair follicles.<sup>(4,5,9,12,13)</sup> The pustular lesions show intrafollicular accumulation of eosinophils immediately below the stratum corneum.<sup>(10)</sup> Tzank cytological smear of the pustule content demonstrates inflammatory cells, more than 90% of which are eosinophils.<sup>(5,9,14,15)</sup> The cause of the ETN is not yet established, although multiple theories have been proposed. Leiner coined the term 'Erythema Toxicum Neonatorum' in 1912 and he linked the condition to gastrointestinal disturbances.<sup>(5,10)</sup> Mayerhofer and Lypolt-Knajnovic found blood eosinophilia as well as eosinophils in pustules and they proposed allergy as a mechanism.<sup>(4,5,7,11,15)</sup> This theory gained weight as the administration of antihistamines to affected babies was found to reduce the duration of the rash by half.<sup>(5)</sup> The possibility that ETN

could be a graft versus host reaction through maternal-baby lymphatic system was suggested by Bassukas in 1992.<sup>(5,6,9,15)</sup> Erythema could also be secondary to the newborn skin reaction to mechanical and heat stimulation.<sup>(4,7,15)</sup> Increased level of immunological and inflammatory mediators suggests that ETN may also be an immune system reaction.<sup>(1,4,5,7,11,16,17)</sup> The aim of this review was to describe epidemiology, clinical manifestations, differential diagnosis, and treatment outcome of erythema toxicum neonatorum in healthy newborns at King Hussein Medical Center and Queen Rania Children's Hospital.

## Methods

The medical records of patients with clinical diagnosis of erythema toxicum neonatorum who were treated at King Hussein Medical Center and Queen Rania Children Hospital dermatology clinics between February 2008 and September 2012 were reviewed retrospectively. Extracted data include duration of pregnancy, type of delivery, age, gender, cutaneous rash characteristics, associated clinical conditions, laboratory investigations, skin biopsy, and treatment. Simple statistical analyses (mean, frequency, and percentage) were used to describe the study variables.

## Results

The study included 152 patients, 88 males and 64 females with a male to female ratio of 1.4:1. The age at onset of the rash ranged from 1 to 11 days (mean age of 4 days). All study subjects were product of hospital based deliveries and all were breastfed. Table I shows the study parameters and clinical manifestations with the

**Table I:** Demographic data and clinical manifestation among the study group.

Entity	No.	%
Sex		
Males	88	57.9
Females	64	42.1
Erythematous and papular type	112	73.7
Pustular type	40	26.3
Skin rash with lymphadenopathy	4	2.6
Skin rash with moderate fever	5	3.2
History of drug intake during pregnancy	96	63.1
Complete blood count	17	11.2
Tzanck smear	17	11.2
Skin biopsy	4	2.6
Antihistamine therapy	78	51.3

erythematous and papular type being the commonest (70.15%). Mothers of 96 patients (63.16%) admitted drug (unspecified) intake during pregnancy. High eosinophil count was evident in complete blood count (CBC) and in Tzanck cytological smears from the pustules of 17 patients with severe pustular skin rash.

Histological examination showed typical subcorneal and intrafollicular accumulation of eosinophils in skin biopsy of four patients with severe skin rashes, who also had fever and lymphadenopathy. Seventy-eight (51.3%) cases were treated with oral antihistamine in the form of dimethindene maleate in a dose of 10 drops three times daily for seven days; the rash disappeared within 24-36 hours. Follow up was done for four weeks, with no permanent sequelae in any of the involved subjects.

## Discussion

Most of our cases had the onset of ETN two to three days after delivery. However, four cases started at nine days of age. Delayed onset in full term infants, as late as 10 days of age, has been observed by other studies.<sup>(5, 6)</sup> This study showed predominance of male patients with a ratio of 1.4:1. This is not in agreement with most studies,<sup>(5,10,14)</sup> but similar results have been observed in others.<sup>(2,4,11)</sup> The most common skin rash type was erythematous and papular (73.7%) followed by the pustular type (26.3%) and this is similar to other studies.<sup>(5,6,10)</sup> Lymphadenopathy was noted in four subjects (2.6%), who also had fever and severe skin rash. The main differential diagnosis in these cases was bacterial infection. Complete blood count from these patients

showed peripheral eosinophilia and pus cultures yielded negative results. Tzanck cytological smears and skin biopsy were performed in these patients, where the diagnosis of ETN was confirmed and the lymphadenopathy disappeared with time.

The presence of lymphadenopathy in patients with ETN has not been reported previously and is not expected due to the non-infectious nature of the condition. Its presence in these subjects triggered further investigations in the affected patients, but infection was not confirmed and the patients' condition improved without antibiotic treatment. Tzanck smear and CBC were also done in 13 more patients with moderately severe skin rash, in whom these tests showed the characteristic eosinophil content of the pustules and peripheral eosinophilia on differential blood count. As the diagnosis of ETN was clinically evident in the rest of the subjects, skin biopsy and Tzanck smear were deemed unnecessary. Although erythema toxicum neonatorum appears to be a common condition in newborns, its pathogenesis is still largely unknown.<sup>(17)</sup> This theory of allergy is further supported by increased eosinophils in blood and in affected tissues as evident in Tzanck smears and skin biopsies. It is suggested that leukotriene B<sub>4</sub> and eosinophil chemotactic factor play an important role in attracting eosinophils to the skin.<sup>(5,16)</sup>

A limitation of our study was its retrospective nature as this hindered the possibility of performing any further laboratory tests.

## Conclusion

ETN is a common generally benign self-limiting condition in the newborn. It is frequently misdiagnosed as bacterial infection; therefore, a dermatological consultation is helpful to avoid unnecessary treatment and investigation, which are only needed in a small number of cases. A future larger prospective study is advised to help assess theory of allergy and further uncover the mysteries of this condition.

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