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ORIGINAL ARTICLE

Dermatologic findings in preterm newborns - a cross-sectional study

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Abstract

Objective: To determine the frequency of dermatological diagnoses in preterm newborns and the associated perinatal factors. **Methods:** This is a cross-sectional analytical study with a convenience sample and prospective data collection, carried out between November 2017 and May 2018. Were examined 151 premature and late preterm neonates admitted to the neonatal intensive care unit in a hospital of tertiary care level. The studied population was evaluated to evidence, describe and photograph the dermatological diagnoses present up to 28 days of life. **Results:** The frequency of dermatological diagnoses was 99.3%, being the most observed: lanugo in 128 newborns (84.7%), salmon spot in 115 (76.1%), sebaceous hyperplasia in 89 (58.9%), physiological flaking in 74 (49%), mongolian stain in 54 (35.7%), Epsteins pearl in 43 (28.4%), traumatic skin lesions in 42 (27.8%), milia cyst in 40 (26.4%), jaundice in 36 (23.8%) and toxic erythema in 20 (13.2%). Participants with a higher gestational age had a higher frequency of salmon spot, toxic erythema, mongolian spot, sebaceous hyperplasia, milia cyst and Epsteins pearl. **Conclusion:** Dermatological diagnoses were frequent and those of older gestational age had a higher frequency of physiological changes and birthmarks. Traumatic skin lesions were among the 10 most frequently observed, reinforcing the need to implement protocols for neonatal skin care, with emphasis on premature infants.

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INTRODUCTION

The first four weeks of life are called the neonatal period, a phase characterized by the maturation and adaptation of the newborn, during which dermatologic findings abound¹.

The skin is a complex and dynamic organ that performs vital functions, acting as a barrier between the body and the environment to protect us against ultraviolet radiation, prevent the invasion of pathogens, regulate body temperature, and allow sensory perception. The barrier function depends on the maturation of the stratum corneum, the most superficial layer of the epidermis, which is more developed in full-term newborns². The fact that skin is still developing in preterm newborns results in greater susceptibility to skin disorders. Most of them are benign and physiological transitory dermatoses, however, it is important to differentiate them from the ones that are pathological and indicative of disease^{1,3}.

The prevalence of dermatologic findings in the neonatal period ranges from 67.3% to 95.8%⁴. In studies carried out in Brazil, the following findings have been described within 72 hours of birth: lanugo, sebaceous hyperplasia, Mongolian spot, physiological scaling, erythema toxicum neonatorum, salmon patches, cutaneous erythema, and milia^{4,5}. Reginatto et al. selected 2,839 neonates in their study, but excluded 309 because they required neonatal intensive care. Only 7.7% (194) of the 2,530 newborns included were preterm infants. The study by Krüger et al. included 350 neonates, 98% of which full-term newborns. There is no Brazilian study that exclusively evaluated preterm infants requiring neonatal intensive care, factors that commonly constitute the exclusion criteria in epidemiological studies on the dermatologic evaluation of newborns.

Early recognition of skin diseases in newborns is of fundamental importance for accurate diagnosis, treatment, and parental counseling. This study aimed to determine the frequency of dermatologic findings and associated perinatal factors in preterm infants.

MATERIALS AND METHODS

This analytical prospective cross-sectional study included 151 newborns seen from November 2017 to May 2018. The sample collected by convenience included all late preterm newborns in rooming-in care and preterm infants admitted to the Neonatal Intensive Care Unit (NICU) of a tertiary referral hospital. The institution's Research Ethics Committee approved the study.

The study included preterm infants with ages of up to 28 days, whose parents or guardians signed an informed consent form. Neonates whose parents or guardians were not present at the time of evaluation or who were discharged before the authors of the study contacted their parents/guardians were excluded. Data collection and clinical observation were carried out in the morning on weekdays. Preterm infants were assessed when they were clinically stable.

The included subjects were evaluated based on a standard research protocol designed to establish the frequency of dermatologic findings until 28 days after birth. Infants with dermatologic findings were photographed with a Panasonic Lumix® camera, model FZ38.

The findings were described based on clinical appearance and newborns were examined without clothes by a pediatric dermatologist, who examined skin, mucous membranes, and skin appendages. The examinations were performed at the bedside, in a warm environment, with appropriate lighting, and in the presence or absence of the mother or guardian.

Patient charts were reviewed for the following data: name; sex; age (hours since birth); prenatal data (maternal gestational risk factors, maternal serology tests, use of medication); birth data (gestational age, delivery route, need for resuscitation, 1- and 5-minute Apgar scores, weight, weight for gestational age) and newborn comorbidities (clinical conditions diagnosed before or after birth).

Prenatal and neonatal characteristics were grouped to allow statistical analysis based on the following parameters: hours since birth: <450h or >450h; gestational age (GA): less than 28 weeks, 28 to 32, 32 to 34, or 34 to less than 37 weeks; 1-minute Apgar score: 1-6 or 7-10; 5-minute Apgar score: 1-6 or 7-10 or not evaluated (cases in which the infant was born in another institution); birth weight: <1000g, 1000 to 1499 g, 1500-2499 g, 2499 g-4000 g; weight versus GA: small for gestational age (SGA), adequate for gestational age (AGA), or large for gestational age (LGA)⁶⁻⁹.

Data were presented as mean values, medians, and frequencies. Statistical analysis was performed on the R Core Team 2018 software package (R: A Language and Environment for Statistical Computing. R Foundation for Statistical Computing, Vienna). Pearson's chi-squared test, Fisher's Exact test, and the Mann-Whitney test were performed.

RESULTS

A total of 230 preterm infants were born during the study period, of which 151 were included. Eighty-seven (57.6%) were females and 62 (41.1%) were males. The mean GA at the time of evaluation was 33.5±2.28 weeks; additional data from the newborns are shown in Table 1. The mean birth weight was 2081±665 g (540 to 3600 g). A total of 119 (78.8%) were considered AGA, 22 (14.6%) were graded as SGA, and ten (6.6%) were graded as LGA.

Comorbid conditions were found in 125 (82.8%) mothers (Table 2). The main ones were endocrine conditions (43%), hypertension (33.8%), and infectious disease (17.9%).

At the time of physical examination, the median time since birth was three days (4 hours to 27 days). At least one dermatologic finding was recorded in 150 (99.3%) newborns, and 146 (96.7%) had two or more of such findings. The findings fell into the following categories: physiological alterations (physiological scaling, Epstein pearls, Bohn's nodules, sebaceous hyperplasia, milia, and lanugo) in 144 (95.4%) newborns;

Table 1. Distribution of characteristics in the included newborns.

Characteristics		n (%)
Gestational age (weeks)	<28	4 (2.6)
	>28 and <32	18 (11.9)
	≥32 and <34	38 (25.2)
	≥34 and <37	91 (60.3)
Hours since birth [†]	<450	143 (94.7)
	≥450	8 (5.3)
Sex	Female	87 (57.6)
	Male	62 (41.1)
	Indeterminate	2 (1.3)
1-minute Apgar score	<7	64 (42.4)
	>7	85 (56.3)
	Unknown [#]	2 (1.3)
5-minute Apgar score	<7	11 (7.3)
	>7	138 (91.4)
	Unknown [#]	2 (1.3)
Weight	<1kg	8 (5.3)
	>1 and <1.5 Kg	20 (13.2)
	>1.5 and <1.5 Kg	78 (51.7)
	>2.5 and <4kg	45 (29.8)
Category (weight vs. GA*)	SGA**	22 (14.6)
	AGA***	119 (78.8)
	LGA****	10 (6.6)
Resuscitation maneuvers	Performed	78 (51.7)
	Not performed	73 (48.3)

NOTE: [†] at the time of skin examination; [#] patients born in other hospitals, information not available; *GA = gestational age; **SGA = small for gestational age; ***AGA = adequate for gestational age; ****LGA = large for gestational age.

Table 2. Maternal epidemiological characteristics.

Characteristics		n (%)
Maternal serology	Positive	18 (11.9)
	Negative	133 (88.1)
Delivery	Vaginal	48 (31.8)
	Cesarean section	103 (68.2)
Gestational risk factor	Present	125 (82.8)
	Absent	26 (17.2)
	Endocrine*	65 (43)
	CH/PIH**	51 (33.8)
	Infeciosas	27 (17.9)
	Smoking/Alcohol drinking/Drugs	25 (16.5)
	Gynecologic-obstetric***	17 (11.2)
	Previous surgery	13 (8.6)
	Neuropsychiatric	11 (7.3)
Maternal Comorbidities	Asthma	7 (4.6)
	Previous fetal death	6 (4.0)
	Cardiovascular	4 (2.7)
	Orthopedic	1 (0.7)
	Rheumatologic	1 (0.7)
	Hematologic	1 (0.7)

NOTE: * Diabetes and thyroid disease**CH: chronic hypertension/ PIH: pregnancy-induced hypertension.**** Placental abruption, cervical incompetence, gynecological cancer.

birthmarks (salmon patches, port-wine stains and Mongolian spots) in 133 (88.1%); and benign pustular and vesicular lesions (miliaria, toxic erythema and neonatal pustular melanosis) in 25 (16.6%).

The ten most frequent findings were lanugo, in 128 (84.7%) newborns; salmon patches in 115 (76.1%); sebaceous hyperplasia in 89 (58.9%); physiological scaling in 74 (49%); Mongolian spots in 54 (35.7%); Epstein pearls in 43 (28.4%); traumatic skin lesions in 42 (27.8%); milia in 40 (26.4%); jaundice in 36 (23.8%); and toxic erythema in 20 (13.2%). Figure 1 shows the most frequent findings. Less frequent findings included port-wine stain; miliaria; contact dermatitis; acrochordons; Bohn's nodules; intertrigo; infantile hemangioma; cutis marmorata; adnexal polyps; supernumerary nipple; branchial cyst; seborrheic dermatitis; ungual dystrophy; collodion baby; and lesions with unconfirmed diagnosis. Table 3 lists the skin alterations and their frequencies of occurrence.

The most frequent skin alterations were correlated with maternal and newborn characteristics. Findings salmon patches, toxic erythema, Mongolian spot, sebaceous hyperplasia, milia, and Epstein pearls were more frequent in individuals with higher gestational ages, i.e., infants born closer to the end of full-term pregnancy (Table 4). The frequency of occurrence of physiological scaling, lanugo, jaundice, and traumatic skin lesions was not statistically different between infants with different gestational ages.

When the distribution was evaluated in relation to birth weight, we found that greater birth weight was linked to higher frequency of occurrence of salmon patches ($p=0.032$), Mongolian spots ($p=0.001$), toxic erythema ($p=0.029$), milia (0.049), Epstein pearls ($p=0.041$), and lanugo ($p=0.044$).

Table 3. Frequency of dermatologic findings in preterm infants.

Dermatologic finding*	n	(%)
Lanugo	128	84.7
Salmon patches	115	76.1
Sebaceous hyperplasia	89	58.9
Physiological scaling	74	49.0
Mongolian spots	54	35.7
Epstein pearl	43	28.4
Traumatic skin lesions	42	27.8
Milia	40	26.4
Jaundice	36	23.8
Toxic erythema	20	13.2
Finding pending diagnosis	10	6.6
Contact dermatitis	8	5.2
Miliaria	6	3.9
Bohn's nodules	5	3.3
Hemangioma	3	1.9
Acrochordon	2	1.3
Cutis marmorata	2	1.3
Supernumerary nipple	2	1.3
Ungual alterations	1	0.6
Seborrheic dermatitis	1	0.6
Intertrigo	1	0.6
Port-wine stain	1	0.6

* 146 (96.7%) of the included newborns had two or more dermatologic findings.



Figure 1. A. Sebaceous hyperplasia. B. salmon patch. C. Epstein pearl. D. lanugo. E. physiological scaling. F. Mongolian spot.

Table 4. Presence of dermatologic finding relative to gestational age and birth weight.

Parameter	Dermatologic finding	Presence GA* ± SD**	Absence GA ± SD*	p
Gestational Age (GA)	Toxic erythema	35.1 ± 1.1	33.3 ± 2.4	0.004
	Salmon patches	34.1 ± 2	33.0 ± 2.9	0.045
	Epstein pearls	35.0 ± 1.2	33.4 ± 2.5	0.001
	Milia	34.3 ± 1.1	33.4 ± 2.5	0.003
	Sebaceous hyperplasia	34.3 ± 1.6	33.1 ± 2.9	0.047
	Mongolian spot	34.5 ± 1.6	33.4 ± 2.5	0.008
Birth Weight (grams)		Birth weight (min-max)	Birth weight (min-max)	
	Milia	2.300 (1.235-3.530)	1.945 (540-3.600)	0.002
	Toxic erythema	2.675 (1.790-3.530)	1.945 (540-3.600)	<0.001
	Mongolian spot	2.322 (1.010-3.530)	1.920 (540-3.600)	0.001
	Epstein pearls	2.260 (1.235-3.455)	1.912 (540-3.600)	0.004

*GA: Gestational Age; **SD: Standard deviation.

The relationship between birth weight and GA was also evaluated, with salmon patches found more frequently in preterm infants graded as AGA ($p=0.04$).

DISCUSSION

Several authors have reported elevated frequencies of dermatologic findings in newborns¹⁰⁻¹². However, few studies have evaluated this data in preterm infants, especially the ones admitted to NICUs^{13,14}. Indeed, admission to an NICU is often used as an exclusion criterion. The assessment of preterm newborns in NICUs requires caution. Examiners must

be accustomed to the neonatal intensive care environment and avoid untimely handling and exposure of infants. Despite methodological differences, the frequency of dermatologic findings (99.3%) in our study was similar to that described in previous studies, i.e., with proportions greater than 90%^{4,5,12}. This reinforces the importance of neonatologists and pediatricians recognizing skin alterations, avoiding unnecessary investigations that might disturb the parents or delays in recognizing potentially serious conditions.

In the present study, the frequency of lanugo (84.7%) was higher than the one reported in other articles, in which frequencies of occurrence ranged from 2.8% to 38.9%^{4,11}.

Prematurity might influence the observation of this finding, as Sachdeva et al. and Wallach described^{15,16}. The incidence of lanugo was higher in newborns weighing more than 1000 g, which is in agreement with Sachdeva et al.¹⁶, in that the authors a higher frequency of occurrence of lanugo in newborns weighing less than 2500 g.

The frequency of sebaceous hyperplasia (58.9%) was similar to the one reported by Krüger et al. (66.6%)⁵, and higher than in other studies, in which it ranged from 26.1% to 48.4%^{4,11,12}. Frequency of occurrence of sebaceous hyperplasia increased with GA, as reported by Moosavi et al.¹⁷.

Regarding birthmarks, we observed salmon patches in 76.1% of the newborns, against 24.6% to 70% reported in other studies³. The incidence of Mongolian spots was 35.7%, which was lower than the levels reported by Moosavi et al.¹⁷ (71.3%) and higher than the levels described Ekiz et al.¹¹ (19%). Both salmon patches and Mongolian spots were more frequent in newborns with greater GA and birth weight, which reinforces the hypothesis developed by Reginatto et al. that birthmarks indicate skin maturity⁴.

The frequency of traumatic skin lesions (27.8%) was higher than the one reported by Reginatto et al.⁴ (2%) and Csoma et al. (18%)¹⁴. Such discrepancy may be due to the fact that in the present study, as well as in the study by Csoma et al., newborns receiving intensive care – and therefore more exposed to procedures of daily care – were included. The frequency of occurrence of traumatic skin lesions was higher in newborns weighing less than 1000 g and with a lower GA, which supports the relationship between increased vulnerability to iatrogenesis and skin immaturity.

Epstein pearls were observed in 28.4% of the newborns, a lower frequency than the one described by Khoshniveisal et al.³ (60.4%). This finding was more frequent in newborns with greater GA and in line with the reports by Moosavi et al., Haveri and Inamadar,^{17,18} which reported that Epstein pearls are more common in full-term newborns. It is important to realize that this skin alteration may have been underdiagnosed in the present study because of the difficulty in examining the oral cavity of newborns with devices such as orotracheal and oral catheters installed.

Milia was observed in 26.4% of the newborns. Khoshniveisal et al. reported a higher frequency² (42.6%), while Moosavi et al. and Kanada et al. found low frequencies (7.5% and 8%, respectively).^{17,19} Milia was more frequent in infants with greater GA, as described by Reginatto et al., and in newborns with greater birth weight, as described by Sadana et al.^{4,20}.

Toxic erythema was present in 13.2% of the included newborns, against 21% in the study by Reginatto et al.⁴ and 6.7% in the study by Monteagudo et al.²¹ when preterm infants are considered. The difference may be attributed to the relationship observed between erythema toxicum neonatorum and increased GA and birth weight, on account of the effects of greater cutaneous immune maturity.

Physiological scaling occurred in 49% of the newborns, a value close to that reported by Monteagudo et al.²¹ (41.5%) when evaluating newborns regardless of GA. The frequency found in this study was higher than the one described in the study by Monteagudo et al.²¹ (21.3%) when only preterm infants are considered. Moosavi et al. did not observe physiological scaling in preterm infants and also correlated it with maturity and greater birth weight.¹⁷

As a limiting factor, skin examinations were performed only once in each newborn, which means the frequency of occurrence of some findings may have been underestimated. This is explained by the inherent difficulties in having access to the study population, since it includes newborns requiring intensive care who are unavailable for serial examinations. Nevertheless, we observed that skin changes are frequent and influenced by parameters such as GA and birth weight.

This study described dermatologic findings in preterm infants, a population that increases annually and has a higher survival rate due to advances in NICU care, which require greater care when handled because their skin is immature and, therefore, more vulnerable to traumatic skin injuries. Neonatologists and pediatricians play a decisive role in the care of preterm infants. The knowledge and attention these professionals devote to the identification of neonatal dermatoses is required in the definition of an adequate approach, which includes guidance to parents, indication of treatment, prevention of iatrogenesis, and assist in differential diagnosis.

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