

# Dermatoses Of Pregnancy: A Retrospective Cohort Study In Spain

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## Research article

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# Abstract

**Background:** Dermatoses of pregnancy (DP) is a heterogeneous group of pruritic inflammatory dermatoses that occur exclusively during pregnancy and/or puerperium. The objective of this study was to assess the specific DP and non-specific dermatoses in a Mediterranean population living in Spain.

**Methods:** This five-year retrospective study included 79 pregnant women with dermatologic disease from a total of 10533 pregnancies. Obstetric and clinical variables were assessed. Physiological skin changes of pregnancy were excluded. Those dermatoses that may also be observed beyond pregnancy and puerperium were also excluded.

**Results:** The mean age was 32 years. The most common DP were: Polymorphic eruption of pregnancy (PEP) – 36%, Atopic eruption of pregnancy (AEP) – 26%, Intrahepatic cholestasis of pregnancy (ICP) – 8% and Pemphigoid gestationis (PG) – 6%. The other 24% presented non-specific dermatoses. Only in one case of PG the newborn showed comorbidity.

**Discussion:** Multiple gestations were observed in 10,3% of PEP, in association with a rapid abdominal distention. In AEP, there was a predominance of nulliparous women in the second trimester of pregnancy, an atopic dermatitis background and female newborns. In PG, there was a majority of nulliparous in the second and third trimesters. PG was the only dermatoses associated to comorbidity of the newborn. In ICP, all patients had pruritus in the palms along with excoriations, with predominance of nulliparous and multiple gestations.

## Significance:

What is already known on this subject? Pregnancy results in various physiological skin changes. As a consequence, some common dermatoses can present more frequently in pregnant women. In addition, there are a number of skin eruptions unique to pregnancy.

The etiology of physiological skin changes in pregnancy is uncertain but is thought to be due to hormonal and physical changes of pregnancy.

In Spain and all Mediterranean area, limited attention was given to Dermatitis of Pregnancy (DP) and actual data on healthcare professionals' practice on this topic did not exist.

What this study adds? This study explores the specific DP and non-specific dermatoses in a Spanish population.

## Background:

Dermatoses of pregnancy (DP) is a heterogeneous group of pruritic inflammatory dermatoses that occur exclusively during pregnancy and/or puerperium [1–4]. Currently, there are four recognized DP: Polymorphic eruption of pregnancy (PEP), Atopic eruption of pregnancy (AEP) Pemphigoid gestationis

(PG) and Intrahepatic cholestasis of pregnancy (ICP). Some studies describe the prevalence of DP that ranges from 0.5 to 2% in European Anglo-saxon (Holmes R, Ambros-Rudolph – 1, 2) and Austrian population (Ambros-Rudolph – 4) and American population (Shornick-3), but there are no case series that analyze DP in Mediterranean population.

Besides DP, physiologic skin changes and other skin diseases which are not exclusive of pregnancy can occur. Our objective is to analyze the frequency of DP and other non-specific dermatoses during pregnancy in Spanish population (Mediterranean) and compare with the literature reported.

## Methods:

A retrospective study was made from January 2014 to December 2018 in the University Hospital of Salamanca. During 5 years, we included all pregnant and postpartum women that presented with a skin disease in a tertiary hospital, excluding physiologic skin changes. Total number was 79. The study was approved by the research ethics committee of the hospital. Other dermatosis that may be seen during pregnancy and puerperium, but which can also occur in other contexts were excluded.

We assess 1) obstetric history variables a) gestational age, b) primiparous, multiparous, c) multiple gestation pregnancy d) full-term pregnancy, preterm pregnancy e) Type of delivery (eutocic / instrumental / cesarean); F.) Sex of the newborn infants (NI): Male / Female; G.) weight, h.) Markers of fetal well-being (pH and APGAR) and comorbidities. 2) Clinical variables: a.) Age of the patient; B.) Personal history; C.) Distribution and morphology of the lesions, d.) Accompanying symptoms; E.) Complementary tests (biopsy, blood test); F.) Diagnosis; G.) Evolution time (days).

The SPSS statistical software version 23 for PC was used for the statistical analysis.

## Results:

We included a total number of 79 pregnant women. The mean age was 32 (21–41). Prevalence of DP was of 0.75%. Pruritus was a constant symptom in all patients. 76% of them were diagnosed with specific DP, whereas 24% with non-specific DP. (Tables 1 and 2). The most frequent specific DP was PEP (36%) followed by AEP (26%) and PG (6%). ICP affected 8% of the patients. The most frequent non-specific DP was acute urticaria. 20% of the patients with AEP had a history of atopic dermatitis. None of the NI suffered comorbidities. Only one NI had a vesicular eruption in scalp. (Fig. 1)

Table 1  
Results of Clinical and Obstetric Variables of specific dermatoses

	PEP	AEP	PG	ICP
Patients number and percentage	29 (36%)	21 (26%)	5 (6%)	7 (8%)
Age	30 (24–31)	32 (23–41)	33 (28–41)	34 (25–43)
Personal History	No	Atopic D.: 4 (20%)	No	No
Symptom	Itchy 100%	Itchy 100% Pain: 5%	Itchy 100%	Itchy 100%
Distribution	Abdomen: 100% Limbs: 20% Breast: 20%	Abdomen:60% Flexion zones and limbs:40%	Abdomen:100% Limbs:100%	Palms: 100% Soles: 80% Generalized: 30%
Morphology	Papules, Urticariiform plaques and hives	Papules, scabs and scratch lesions Type E: 8 Type P: 13	Vesicles, blisters, and edematous erythematous plaques	Dermal lesions secondary to scraping (excoriations)
Supplementary tests	Biopsy: 3 Analytical: 6	Biopsy: 0 Analytical: 1	Biopsy: 5 Analytical: 4	Biopsy: 0 Analytical: 6
Days of evolution	4 (1–14)	11 (1–30)	3 (1–7)	4 (2–7)
Gestational Weeks	34 (29–38) III	22 (9–34) II	27 (22–33) II-III	34 (29–37) III
Puerperium	7 (23%)	0	1	0
Primigestas	50%	75%	100%	75%
Multiple Gestation	3	1	1	2
Full-term /premature	6% PT	19% PT	40% PT	30% PT
Type of Delivery	66% Eut; 28%CS, 6%I	77% Eut; 20% CS; 3% I	67% CS 28% Eut; 5% I	70% CS; 24% Eut; 6% I
Sex of the newborn	52% M	63% F	50% M/F	50% M/F

PEP: Polymorphic eruption of pregnancy AEP: Atopic eruption of pregnancy PG: Pemphigoid gestationis ICP: Intrahepatic cholestasis of pregnancy

M: Male; F: Female; Eut: Eutocic delivery; CS: C- Section; I: Intrumental delivery; PT: premature

	PEP	AEP	PG	ICP
Weight of the newborn	3240 (2320–4320)	2976 (2080–3600)	3040 (2800–3600)	2800 (2150–3550)
pH y APGAR	7,26 (9–10)	7,26 (9–10)	7,25 (9–10)	7,26 (9–10)
Comorbidities of the newborn	No	No	Yes	No
PEP: Polymorphic eruption of pregnancy AEP: Atopic eruption of pregnancy PG: Pemphigoid gestationis ICP: Intrahepatic cholestasis of pregnancy				
M: Male; F: Female; Eut: Eutocic delivery; CS: C- Section; I: Intrumental delivery; PT: premature				

Table 2  
NON-SPECIFIC DERMATOSIS

Diagnosis	Patients number and percentage
Acute urticaria	5 (6%)
Chickenpox	3 (4,5%)
Herpes Zoster	2 (3%)
Pityriasis rosea	2 (3%)
Lichen planus	1 (1,5%)
Gestational epulis	1 (1,5%)
Angiomas	1 (1,5%)
Ecchymosis	1 (1,5%)
Impetigo	1 (1,5%)

Almost half of pregnant women presented in her third trimester (48%), 26% in her second trimester, 15% during postpartum period and 11% in her first trimester. PEP, PG and ICP were more frequent in third trimester, though AEP also appeared in the second trimester (Table 1) 23% of PEP occurred during postpartum period (OR = 11.4, p = 0.0259, 95% CI: 1.3398 to 97.5691). 60% of the visits took place in spring and summer, particularly in August. 12% of the patients required cutaneous biopsy and 21.5% blood test. Rest of the clinical and obstetric results are shown in Table 1. Figure 2 show clinical features of a) PEP b) AEP c) PG and d) ICP.

## Discussion:

We conducted a five-year retrospective study of 79 patients in a tertiary Spanish hospital. We observed a frequency of specific DP of 0.75% which is similar to others case series. PEP was the most frequent

followed by AEP, ICP and PG and its rates are consistent with the literature [8, 6].

PEP occurs more frequently in primiparous women and multiple gestation pregnancy during the last weeks of pregnancy or immediate postpartum and male fetus [8, 10, 11]. It is associated with a higher abdominal distension in pregnant women, which can be explained by a higher incidence in multiple gestations [4, 8, 11, 12]. Overall the prognosis both of pregnant women and newborns is good. [6, 8, 12], Our study did not find more primiparous women affected (50%) but a higher frequency of multiple gestations (10.3%) occurrence in third trimester and immediate postpartum and a slightly higher ratio of male fetus (52%). Pruritus preceded the skin changes 1–2 weeks. Urticarial lesions set in the lower part of abdomen in all of patients, and in breasts and members in 20% of them. The prognosis was good in our series, and NI had a normal weigh, pH and APGAR.

The AEP is a benign pruritic dermatosis of unknown etiology that appears during first and second trimester. It is more frequent in multiparous women with atopic background or elevated IgE [6, 8, 10]. Typically, lesions are monomorphic papule-nodules or eczematous. [6, 8, 10, 11]. Diagnosis of AEP is clinical and supported by an elevation of IgE [8]. Biopsy is not specific and immunofluorescence is negative [6, 10, 11]. Papule-nodules can persist few months after delivery [8, 11]. AEP lasted more days than the others DP (mean of 11 days). It was not related to any comorbidity, as it is shown in other studies [8, 10, 11] although one suggest a slight decrease of NI weigh [13]. In our case series, there was a predominance of primiparous women (75%) in her second trimester; that makes sense when we think that AEP is more frequent in women with atopic background or elevated IgE, so prompt to this disease. 20% of them had suffered from atopic dermatitis (Table 1). In all the cases, there were rubbing and scratching lesions due to the severe pruritus. In 8 patient's lesions were predominantly type E (eczematous) whereas in 13 were type P (papules).

PG is an autoimmune bullous DP predominantly in the 2nd and 3rd trimester and/or immediate postpartum. Urticarial lesions became bullae due to the action of antibodies that binds the NC16A site of BP180-collagen XVII (an hemidesmosome protein) [10, 11]. Some authors described a predominance of PG in multiparous women [10] although it has not proved in other reports [8]. PG is associated with bad fetal prognosis [8, 12]. There was higher frequency of PG in the 2nd and 3rd trimester in our case series. All of them had very pruritic erythematous-edematous plaques that evolved to vesicles and bullae in periumbilical region, spreading to the rest of the body and affecting palms and soles [6, 8, 10, 11]. All the patients with PG in our study were primiparous with no predominance of any NI sex. Despite PG is associated with bad fetal prognosis, in our study PG only was associated with preterm delivery (40%) but with normal NI weigh, pH and APGAR. Occasionally, NI present bullae [8] as in one case that exhibited a self-limited vesicular eruption in scalp (Fig. 1).

ICP manifests as a generalized pruritus in the 3rd trimester presenting rubbing lesions. It usually starts in palms and soles and then affect the rest of the body [6, 8, 11]. It occurred in the third trimester and scratching signs were visible. Some authors indicated its association with multiple gestations [6]. It is well-known the defect of bile acids excretion in these patients [8]. Serum Bile acids, transaminases, and

sometimes bilirubin, are elevated. [6, 8, 11]. Some studies showed a bad fetal prognosis due to respiratory distress in 12–22%, meconium in 25–45% and preterm delivery in 12–22% of cases, along with fetal death in utero and intracranial hemorrhage. We find that all the patients with ICP had pruritus in palms, 80% in soles and 30% generalized. We observed a predominance in primiparous women maybe because there are less multiparous women in our society, and no prevalence of any NI sex. We only observed preterm delivery in 30% of affected women. Apart from that, NI weigh, pH and APGAR were normal.

## Conclusion:

Patients profile with specific DP in our Spanish case series is similar to other reported studies. PEP is the most frequent DP. Except ICP and PG, specific DP were not associated with poor fetal prognosis. Third trimester and summer months (particularly August) were the most frequent periods in which DP take place. All DP, except PEP, were more frequent in primiparous women, as we said before maybe it is due to the less and less multiparous women in the today society. However, this also could be explained because primigravida women were more frequent than multiparous women in our study. We registered a much higher percentage of patients with PG and ICP had c-sections compared to those with PEP and AEP, this could be explained with the fear to extend the pregnancy that the obstetricians could have in those diseases due to the serious obstetric consequences that we can find in both. We detected a prevalence of DP of 0.75% similar to the literature reported. More studies are needed in order to assure the results found in our case series.

## Abbreviations

DP: Dermatoses of pregnancy; AEP: Atopic eruption of pregnancy; PG: Pemphigoid gestationis; ICP: Intrahepatic cholestasis of pregnancy; NI: newborn infants.

## Declarations:

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Authors's Contributions: MGF.: writing the article; DBD.: statistics of the article, ADV.: translation of article, JC.: Conceived and supervisor of the study design. All the authors were involved in review of the draft manuscript. All the authors approved the final version for submission. Ethics approval and consent to participate: All participants gave written consent to participate. The study was approved by the research

ethics committee of the hospital. Consent for publication: All participants gave written consent to anonymised quotes being used in publications.

COMPETING INTERESTS: The authors' declare no competing interests relating to the study.

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## Figures



**Figure 1**

Vesicular Eruption in newborn scalp of a PG's mother



**Figure 2**

Clinical features of a) PEP (black arrows: Urticarial lesions) b) AEP (black arrows: monomorphic papule-nodules and star: eczematous lesions) c) PG (black arrow: erythematous-edematous plaques that evolved to vesicles and bullae in periumbilical region) and d) ICP (rubbing lesions that manifests as scratching excoriations).