

THE ROLE OF SOME OBSTETRICAL PARAMETERS IN THE ONSET AND COURSE OF SPECIFIC DERMATOSES OF PREGNANCY

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REZUMAT

Introducere: Dermatozele specifice de sarcină reprezintă un grup heterogen de dermatoze inflamatorii pruriginoase, specific relaționate cu sarcina și/sau perioada puerperală. **Obiectiv:** Scopul acestui studiu este de a observa influența unor parametrii obstetricali în debutul și evoluția dermatozelor specifice de sarcină. **Material și metode:** În studiu au fost incluse 26 de paciente cu diagnostic clinic de PEP și AEP. S-au evaluat parametrii anamnestici, clinici și obstetricali. **Rezultate:** Pacientele cu AEP au prezentat o vârstă a menarhei semnificativ mai mică comparativ cu pacientele cu PEP ($p=0.0026$). 23.5% din pacientele cu AEP au prezentat debutul afecțiunii în trimestrul întâi de sarcină. Prezența striaelor gravidarum s-a dovedit a fi corelată pozitiv cu un ciclu menstrual neregulat, cât și cu un exces de greutate corporală. Grupul de paciente cu feți ♂ a fost corelat pozitiv cu prezența striae comparativ cu pacientele cu feți ♀ ($\chi^2=7.6, p=0.02$). **Concluzii:** O vârstă a menarhei mai mică reprezintă un indicator pentru AEP. Debutul simptomatologiei cutanate în timpul trimestrului întâi de sarcină este un indicator de diagnostic puternic pentru AEP. Un exces ponderal, în momentul diagnosticării este un indicator pentru PEP. Prezența striaelor este frecventă în PEP și se asociază adesea cu un ciclu menstrual neregulat, cât și cu un exces de greutate corporală.

Cuvinte cheie: sarcină, dermatozele specifice de sarcină, erupție polimorfă de sarcină, prurigo de sarcină, erupție atopică de sarcină, prurit

ABSTRACT

Introduction: Specific dermatoses of pregnancy are a heterogeneous group of severely pruritic inflammatory skin diseases unique to pregnancy and/or the immediate postpartum period. **Objective:** The aim of this study was to detect the influence of some obstetrical parameters in the onset and evolution of specific dermatoses of pregnancy. **Material and methods:** We included in the study 26 patients presenting with PEP or AEP and we evaluated the anamnesis parameters and also the clinical and obstetrical ones. **Results:** Women with a diagnosis of AEP have a significantly lower age of menarche than women with a diagnosis of PEP ($p=0.0026$). 23.5% of the subjects with AEP reported the onset of illness to occur during the 1st trimester of pregnancy. The presence of striae gravidarum resulted to be positively correlated with the irregularity of menstrual cycle and with a higher body-weight gain during pregnancy. The group of women carrying male fetuses presented striae more frequently than women carrying female fetuses ($\chi^2=7.6, p=0.02$). **Conclusions:** A lower menarche age is an indicator factor for AEP rather than PEP. The onset of symptoms during the 1st trimester of pregnancy is a strong diagnostic indicator for AEP. An excessive body-weight gain at the date of the diagnosis of illnesses is an indicative factor for the diagnosis of PEP. The presence of striae is frequent in PEP patients and is an associated factor with the irregularity of menstrual cycle and the excessive body-weight gain during pregnancy.

Key Words: pregnancy, dermatoses of pregnancy, polymorphic eruption of pregnancy, prurigo of pregnancy, atopic eruption of pregnancy, pruritus

INTRODUCTION

The specific dermatoses of pregnancy are a heterogeneous group of severely pruritic inflammatory skin diseases specifically related to pregnancy and/or the immediate puerperium period¹⁻³. The most recent classification of the specific dermatoses of pregnancy proposed by Ambros-Rudolph, in 2006, includes the following conditions: pemphigoid gestationis

(PG), polymorphic eruption of pregnancy (PEP), intrahepatic cholestasis of pregnancy (ICP), and atopic eruption of pregnancy (AEP).⁴ This classification scheme includes for the first time the term AEP *a new disease concept* which encompasses prurigo of pregnancy, pruritic folliculitis of pregnancy and eczema in pregnancy.

Clinical diagnosis based on morphologic criteria is still very important for specific dermatoses of pregnancy, because unequivocal laboratory tests are only available for some of them (PG and ICP).

In Romania, the clinical criteria for a positive diagnosis of specific dermatoses of pregnancy are even more important because diagnostic tests such as DIF (direct immunofluorescence) or IIF (indirect immunofluorescence) are available only in specialized centres, specifically the ones pertaining to a Medical University. This fact makes the Romanian dermatologists to rely mostly on the clinical morphology of the condition.

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OBJECTIVE

The purpose of this study was to detect the influence of some obstetrical parameters in the onset and evolution of specific dermatoses of pregnancy, mainly atopic eruption of pregnancy and polymorphic eruption of pregnancy. Furthermore, we try to identify diagnostic clues that would help and allow the differentiation between the two diseases in daily clinic practice.

MATERIAL AND METHODS

In this retrospective study we included 26 patients in various stages of pregnancy, presenting with pruritic skin eruption (PEP, AEP). Starting with 2003, these pregnant patients were seen in the following clinics or outpatient clinics: Dermato-Venereological Clinic Timisoara, Medical Centre „Dermadent - Prof. Dr. V. Feier”, DermatoVenereology Outpatient Clinic C.F. Timisoara, Obstetric Clinic “Bega” Timisoara, Obstetric Clinic “Dumitru Popescu” Timisoara, Medical Centre „Dr. Mihalceanu”, and Medical Centre „Dr. Dorneanu”.

A full personal or medical (especially dermatological and obstetrical) history was taken. The clinical examination, where possible, included general and cutaneous features, noting particularly whether any blisters, periumbilical lesions or an eruption within the striae gravidarum were present. The patients were then classified into distinct subgroups according to the current classification⁴.

The diagnosis of **PEP** was in conformity with the clinical criteria proposed by Holmes & Black, Aronson et al, and Ambros-Rudolph et al, and was defined as the presence of: polymorphic clinical features such as: papulo-urticarial rash with urticarial plaques or non-urticarial erythema with papules or vesicles or the combination of two of them; onset of the lesions on the abdominal area within striae distansae, with periumbilical sparing, and onset of the disease in the 3rd trimester of pregnancy (second half of pregnancy) or postpartum period.^{1,5,6}

The diagnosis of **AEP** was based on the clinical criteria established by Ambros-Rudolph et al, and was defined as the presence of: eczematous and/or papular skin changes, atopic diathesis, personal or family history for atopy, and/or elevated IgE levels, and/or atopic signs throughout pregnancy, absence of other specific pregnancy-associated or not pregnancy-associated dermatoses, and onset in the first half of pregnancy.¹

Some patients were followed up throughout

pregnancy, noting the clinical evolution and the response to the treatment received. Also, the followed group of patients was reviewed at one week after the first dermatological consultation, after a month, and in postpartum period, noting birth weight, foetal sex, gestation at birth and any perinatal complications. Unfortunately, some cases were lost from evidence after the prescription of treatment so that data regarding clinical evolution and birth outcome could not be obtained.

This retrospective study uses data collected from the medical records of the subjects. The study is transversal, though some subjects were available for assessment of treatment's effects and subsequent evolution up to the end of pregnancy.

Due to the rarity of this specific group of dermatoses of pregnancy, the studied sample consists of only 26 patients. There was no free-of-illness comparison sample and subjects were divided into two sub-samples: one with AEP and one with PEP, which were subsequently compared.

Statistical processing was realized using the Statistica computer software. The performed calculations and tests included descriptive statistics: mean, median, standard deviation; simple and relative frequency count; and proportions difference significance test.

As the number of subjects is under 30, non-parametrical statistical tests were used in processing the collected data, namely: the Spearman-R correlation, the Kolmogorov-Smirnov test for comparing two independent groups. In order to assess the significant differences between frequencies, the chi-square test was used. For comparing three groups on a predictive factor, the ANOVA (one-way ANOVA) test was performed. The results were considered to be statistically significant at $p < 0.05$.

RESULTS AND DISCUSSIONS

Average age in the studied group was 29.18 years old and the majority of the patients were between 26 and 30 years old. (Table 1) It is unanimously accepted that PEP occurs in women of childbearing age, but there are no studies to establish the frequent age or interval of age for specific dermatoses of pregnancy. Of interest, the age of the subjects from the studied sample did not prove to be a differentiating factor for diagnosis (average age for AEP group = 29.35 years, average age for the PEP group = 29.0 years, $p > 0.1$).

Due to the fact that in the medical literature there are no comparison studies between menarche age and clinical parameters, we thought that these

correlations would be helpful for the practitioners. In the medical literature the normal age for menarche is between 11 and 15 years old, but it varies from country to country. It generally begins at about 12 to 13 years old.⁷

Table 1. Age distribution in the studied sample.

Age group	Number of subjects		% of total number (in each sample)	
	AEP sample	PEP sample	AEP sample	PEP sample
20 to 25 years	2	2	11.8	22.3
26 to 30 years	8	3	47.0	33.3
31 to 35 years	7	3	41.2	33.3
36 to 40 years	0	1	0.0	11.1
Total	17	9	100%	100%

In the studied sample, the results indicated that women with a diagnosis of AEP have a significantly lower age of menarche than women with a diagnosis of PEP ($p = 0.0026$). Also, we correlated the clinical form of the disease (AEP or PEP) with the menarche age. (Fig. 1) The results showed a statistical significant difference ($p = 0.01$) in the menarche age of women presenting AEP E-type (lower age), as compared with women with other dermatosis of pregnancy, especially women with PEP, with urticarial type. On account of these data we can conclude that a lower menarche age can be an indicator towards a diagnosis of AEP, especially E-type, rather than PEP.

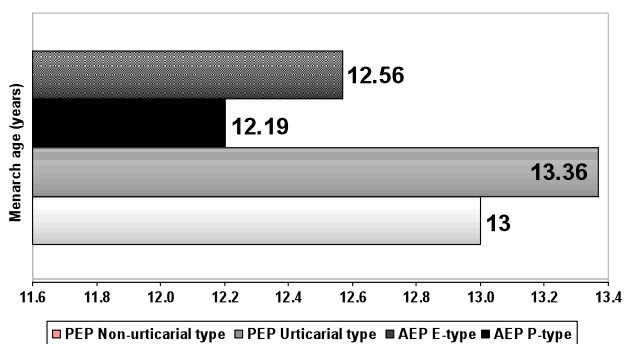


Figure 1. Average menarche age (years) and the clinical form/type of the disease.

None of the PEP's patients have experienced the onset of symptoms during the 1st trimester of pregnancy, while 23.5% of the subjects with AEP reported the onset of illness to occur during the 1st trimester of pregnancy. The difference between the two proportions regarding the frequency of onset

during the 1st trimester of pregnancy is statistically significant ($p = 0.016$), indicating that the onset of symptoms during the 1st trimester of pregnancy is a strong diagnostic indicator for AEP. Also, according to Ambros-Rudolph, an earlier onset is characteristic for AEP, in 75% of cases appearing before the third trimester of pregnancy.¹

In PEP cases, the illness onset was in the last weeks of the 2nd trimester and also in the 3rd trimester of pregnancy. This result outlines the fact that PEP onset is most frequent in the last part of pregnancy. There are also studies which show the fact that PEP usually begins late in pregnancy with the exception that the period is typically between 36 and 39 weeks of pregnancy.² The disease can also occur as early as the second trimester or as late as the postpartum period, typically in the first 2 weeks after delivery (in 15% of cases).⁸

In the studied sample, women with a diagnosis of PEP have acquired a larger body-weight during pregnancy than women with AEP. The increase in body-weight during pregnancy, at the date of the illness's diagnostic, has proven to be significant for the diagnosis. The higher incidence of excessive maternal weight gain among the patients with PEP suggests the fact that is characteristic for the diagnosis.

The presence of striae gravidarum was among the studied patients, as follows: 35.3% of the women with AEP, and 66.6% women with PEP. The statistical analysis with the chi-square test indicated the difference to be not statistically significant ($\chi^2 = 2.33$, $p = 0.12$).

Of interest, the presence of striae gravidarum resulted to be positively correlated with the irregularity of menstrual cycle and with higher body-weight gain during pregnancy. The correlation between striae gravidarum and the irregularity of menses is not mentioned in the literature, but the result shows that it could be considered as a predictable factor for the diagnosis of PEP. Paunescu MM et al, observe that an excessive body weight gain is a favouring factor for the presence of striae gravidarum and also for the subjectively perceived intensity of pruritus, in a severe way.⁹ The correlation between striae gravidarum and an excessive body-weight is well known in the medical literature regarding in principal the etiopathogenesis of PEP. There are theories which sustain the fact that PEP is triggered by the greatest abdominal distension with the result of destruction of the elastic fibre.² The damage of the connective tissue could therefore play a role in the etiopathogenesis of PEP.

In 16 cases, the sex of the foetus was revealed before delivery using ultrasound techniques. From the group of women carrying male foetuses, five subjects were

with AEP, and five with PEP. Statistically significant (Spearman R coefficient = 0.65, $p < 0.05$) is the fact that this group of women, carrying male foetuses, tend to have a later onset of illness, beginning with the last weeks of the 2nd trimester of pregnancy, than women carrying female foetuses (average gestational age at onset = 29.33 for female foetuses versus 33.63 for male foetuses). Concerning PEP, there are data in the literature which mention that women with male foetuses are more affected, with a male/female ratio of 2:1, contributing to the etiopathology of this disease.¹⁰

Of interest, in the studied patients with specific dermatoses of pregnancy, the group of women carrying male foetuses presented striae gravidarum more frequently than women carrying female foetuses ($\chi^2 = 7.6$, $p = 0.02$). (Fig. 2) Regarding AEP there are no data about this correlation, but in PEP there are data which explain the fact that the disease appears more often at patients with excessively body-weight gain at women carrying male foetuses.

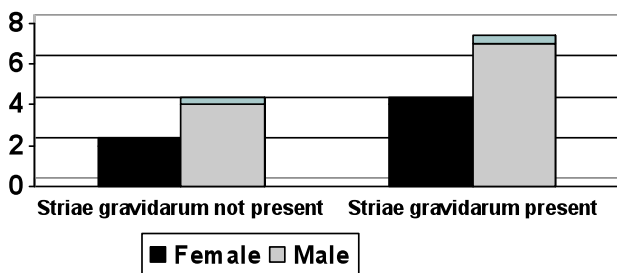


Figure 2. Presence of striae gravidarum and the gender of carried foetus.

CONCLUSIONS

1. The age of the patients is not a differentiating factor for diagnosis between AEP and PEP.

2. The menarche age is a predictive factor among the patients with dermatoses of pregnancy, indicating the cases with AEP, rather than PEP, and most important the E-types.

3. The onset of symptoms during the 1st trimester of pregnancy is a strong diagnostic indicator for AEP.

4. The PEP's onset is most frequent in the last part of pregnancy (last weeks of the 2nd trimester and the 3rd trimester of pregnancy).

5. An excessive body-weight gain at the date of the illnesses' diagnosis is an indicative factor for the diagnosis of PEP.

6. The presence of striae gravidarum is frequent in PEP patients and is an associate factor with the irregularity of menstrual cycle and the excessive body-weight gain during pregnancy.

7. Women carrying male foetuses tend to have a later onset of illness, beginning with the last weeks of the 2nd trimester of pregnancy, than women carrying female foetuses (average gestational age at onset = 29.33 for female foetuses versus 33.63 for male foetuses).

8. Of interest, women carrying male foetuses present striae gravidarum more frequently than women carrying female foetuses.

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