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Original Article

A clinical study of pregnancy-induced dermatoses

L. Sowmya Kothamasu, Vinma Shetty, Farzana Najmuddin, Pradyumna R Bhandary, Narendra J Shetty

Department of Dermatology, A.J. Institute of Medical Sciences, Kuntikana, Mangalore , Karnataka

Abstract

Objective To document pregnancy-related dermatoses.

Methods A hospital-based observational study was conducted in the dermatology outpatient department of a tertiary care institute. A total of 350 pregnant females were included in the study after taking informed consent. Detailed history including demographic data, chief complaints related to skin, presence of itching, skin lesions, onset in relation to duration of pregnancy, jaundice, vaginal discharge, past or family history of similar lesions, exacerbating factors, associated medical or skin disorders etc. was elicited and recorded. Relevant systemic examination and appropriate investigations were done to confirm diagnosis if required. In all cases with history of pruritus related to specific disorders of pregnancy, liver function tests were done. Data was analyzed using SPSS ver. 20.

Results Most common physiological skin changes were pigmentary (98%) followed by striae distensae (76%), glandular changes (15.4%) and vascular (10%). Nail changes were observed in 7 (2%) females. 38 (11%) patients had pregnancy-induced dermatoses. Atopic eczema of pregnancy (49.7%) was the most common condition i.e. 19 patients out of 38 which includes eczema (31.5%), prurigo (13%) and pruritic folliculitis (3.1%). followed by polymorphic eruptions (5.2%) was the most common condition followed by atopic eruptions (19.1%), herpes gestationis and intrahepatic cholestasis were observed in one (2.6%) and two (5.3%) females, respectively.

Conclusion Pregnant women are prone to suffer from a wide range of dermatological problems apart from the specific dermatoses of pregnancy. These pruritic dermatoses are unique to the gravid state. A detailed history and awareness of clinical presentation facilitate confirmation of the diagnosis and will direct the most appropriate laboratory evaluation in an effort to minimize maternal and fetal morbidity. In addition, monitoring of liver function deserves special consideration.

Keywords
Atopic eruptions, intrahepatic cholestasis of pregnancy, polymorphic eruptions, pemphigoid gestationis, pregnancy-induced dermatoses.

Introduction

Pregnancy is characterized by many physiological skin changes like striae gravidarum, melasma accompanied by hair, nail and vascular changes, which are due to hormonal effects. Along with this, the pre-existing skin conditions may either improve or exacerbate in pregnancy due to immunological changes of pregnancy. As cell-mediated immunity is depressed during pregnancy, it accounts for increased severity and frequency of skin infections such as candidiasis. There are, however, few inflammatory skin dermatoses, which are specific to pregnancy and seen only in pregnancy. Though most of these skin dermatoses are benign and resolve in postpartum

Address for correspondence
Dr. L. Sowmya Kothamasu
Department of Dermatology,
A.J. Institute of Medical Sciences,
Kuntikana, Mangalore, Karnataka
Email: sowmya258@gmail.com

period, a few can risk the fetal life and require antenatal surveillance.[1]

The dermatoses of pregnancy represent a distinct heterogeneous group of pruritic skin disorders that can be very distressing for the mother. They include polymorphic eruption of pregnancy (PEP), formerly known as pruritic urticarial papules and plaques of pregnancy (PUPPP); pemphigoid gestationis (PG), formerly known as herpes gestationis; intrahepatic cholestasis of pregnancy (ICP); and atopic eruption of pregnancy (AEP). AEP includes eczema of pregnancy (EP), prurigo of pregnancy (PP) and pruritic folliculitis (PF). Whereas PEP and AEP can be associated with severe pruritus and discomfort for the mother, PG and ICP are associated with increased fetal complications. The diagnosis and management of these pregnancy-specific disorders can be challenging due to their variation in clinical presentation and lack of definitive diagnostic tests. Early recognition of these disorders is critical to provide symptomatic care for the mother and avoid potential increased fetal risk if the diagnosis is delayed.[2]

Methods

This hospital-based observational study was conducted in the dermatology outpatient department of A.J. Institute of Medical Sciences, Kuntikana. Ethical Committee clearance was obtained.

Consecutive sampling method was followed and a total of 350 pregnant females, referred from obstetrics and gynecology OPD were included in the study after taking written informed consent. Detailed history including demographic data, chief complaints related to skin, presence of itching, skin lesions, onset in relation to duration of pregnancy, jaundice, vaginal discharge, past or family history of similar lesions, exacerbating factors, associated medical or skin disorders etc. was elicited and recorded. Complete skin examination was done in all cases to study all the physiological changes of skin and its appendages. If any specific dermatosis of pregnancy was present, the morphology of skin lesions, distribution and the sites involved were studied.

Relevant systemic examination was carried out. If any pre-existing skin disease was present, any evidence of exacerbation or remission was recorded. Appropriate investigations were done to confirm diagnosis if required. Bedside laboratory procedures like Tzanck smear, KOH mount and Gram's stain were carried out. To confirm diagnosis skin biopsy and DIF were done in a few cases. In all cases with history of pruritus related to specific disorders of pregnancy, liver function tests were done. Results were tabulated and analyzed using SPSS ver. 20.

Results

Most common physiological skin changes were pigmentary (98%) followed by striae distensae (76%), glandular changes (15.4%) and vascular (10%). Nail changes were observed in 7 (2%) females. In pigmentary conditions linea nigra (86.6%), secondary areola (74.3%) and melasma (44%) were most common. Acne was observed in 38 (11%) while nonpitting edema was present in 5.7% females (**Table 1**).

38 (11%) patients had pregnancy-induced dermatoses. Atopic eruption of pregnancy was the most common condition seen in 19 patients out of (50%) which included eczema (31.5%), prurigo (13%) and pruritic folliculitis (3.1%); followed by polymorphic eruption in 16 (42.1%) patients. Pemphigoid gestationis and intrahepatic

Table 1 Distribution of subjects based on physiological changes in pregnancy (n-350).

Physiological changes	*N (%)*
Pigmentation	343 (98)
Linea nigra	303 (86.6)
Secondary areola	260 (74.3)
Melasma	154 (44)
Naevi darkening	1 (0.3)
Pigmentary demarcation line	1 (0.3)
Striae distensae	266 (76)
Glandular changes	54 (15.4)
Acne	38 (10.9)
Montogmery's tubercule	18 (5.1)
Miliaria	5 (1.4)
Vascular changes	35 (10.0)
Nonpitting edema of feet	20 (5.7)
Palmar erythema	11 (3.1)
Spider telangectesia	5 (1.4)
Varicosities of legs	1 (0.3)
Nail Changes	7 (2.0)

Table 2 Distribution of subjects based on specific dermatoses of pregnancy (n=38).

Specific dermatoses of pregnancy	*N (%)*
Atopic eruption of pregnancy	19 (50.0)
Eczema	12 (31.6)
Prurigo	5 (13.1)
Pruritic folliculitis	2 (5.3)
Polymorphic eruption	16 (42.1)
Intrahepatic cholestasis of pregnancy	2 (5.3)
Pemphigoid gestationis	1 (2.6)

Table 3 Distribution of subjects based on associated dermatological disorders (n=38).

Specific dermatoses of pregnancy	*N (%)*
Scabies	9 (2.6)
Acne vulgaris	5 (1.4)
Acute urticaria	3 (0.9)
Polymorphic light eruption	3 (0.9)
Discoid eczema	2 (0.6)
Herpes simplex	2 (0.6)
Contact dermatitis	2 (0.6)
Psoriasis	1 (0.3)
Molluscum contagiosum	1 (0.3)

cholestasis of pregnancy were observed in 2 (5.3%) and 1 (2.6%) females, respectively (**Table 2**).

Other associated dermatological disorders are listed in **Table 3**.

Discussion

Pregnancy is associated with significant cutaneous changes, which may range from physiological changes of skin to common skin diseases occurring coincidently with pregnancy, to eruptions seen only during pregnancy or postpartum period. Complex endocrinologic, immunologic, metabolic and vascular changes associated with pregnancy influence the skin in various ways.[3]

Physiological cutaneous changes may be seen in almost all the pregnant females. Physiologic skin changes in pregnancy include changes in pigmentation (in the form of melasma, linea nigra, secondary areola, localized or generalized hyperpigmentation), vascular system (such as palmar erythema, spider angiomas, varicosities), striae distensae and endocrine function, as well as, changes in hair and nails.

Pigmentary alteration was seen in up to 90% of pregnant women in one of the study.[4] In our study, pigmentary changes were seen in 98% of cases, of which linea nigra was the most common, seen in 86% of cases followed by secondary areola seen in 74% of cases. Kumari *et al*.[5] reported linea nigra, and secondary areola in 91.4% and 78.4% of their cases, respectively, which is comparable to our study. Hyperpigmentation is due to elevated serum levels of MSH, estrogen or progesterone. Estrogen increases the output of melanin by the melanocytes and effect of estrogen is augmented by progesterone, resulted from melanin deposition into epidermal and dermal macrophages.

Melasma was seen in 44% of cases in our study. In most of the cases onset was in second trimester and centrofacial pattern being the most common. Muzaffar *et al*.[6] found melasma to be present in 46% of their cases similar to our study The disorder is known to be aggravated by ingestion of contraceptive pills and exposure to

sunlight.[6,7,8] Commonly melasma fades after parturition but in our study persisted in most of the patients

Striae distensae develop in up to 90% of women during the 6th and 7th month of pregnancy.[8] In our study, striae were seen in 76% of cases and were more common in multigravida (67%) than in primigravida (33%). Raj *et al*.[9] also found striae distensae in 75% of pregnant women, which is closer to that seen in our study. Lower abdomen was the most commonly involved site. Striae are mainly due to physical factors, stretching secondary to increase in the abdominal girth plays a major role.

Vascular changes result from distension, instability and proliferation of vessels during pregnancy. In our study non pitting edema was seen in 5.7%, varicosities of legs was seen in 0.3%, palmar erythema was observed in 6.3%, whereas spider nevi occurred in 3.7%. Muzaffar *et al*.[6] reported palmar erythema in 12% of their cases.

The vascular changes seen during pregnancy are related to persistently raised levels of estrogen. The placenta is a rich source of basic fibroblast growth factor, a very active angiogenic factor in pregnancy.[10]

Increased eccrine gland function leads to miliaria, hyperhidrosis, dyshidrotic eczema, and decreased apocrine gland function leads to improvement in hidradenitis suppurativa, Fox-Fordyce disease.[8] Increased sebaceous function in third trimester leads to acne (10.9%) and enlargement of sebaceous glands on the areola (called Montgomery's gland or tubercles) was observed in 5.1%.

Pregnancy may be associated with a change in physical characteristics of pre-existing nevi as suggested by some authors.[11,12] However, no such changes were observed in any of our cases.

Nail changes such as brittleness, subungual hyperkeratosis, onycholysis and leuconychia have been reported during pregnancy.[4,8,13] In our study most common nail changes are transverse grooves and brittleness of nails which are observed in 2% of females. Common hair changes seen in pregnancy are mild to moderate hirsutism and hypertrichosis. After delivery these usually resolve. There is an increased proportion of anagen growing hairs due to estrogen and androgen stimulation in the second trimester. After the end of pregnancy the follicles in which anagen has been prolonged rapidly enters catagen followed by telogen leading to telogen effluvium, which is evident for 6-16 weeks. Spontaneous recovery of hair takes 3-12 months.

Pregnancy-specific skin dermatoses include an ill-defined, heterogeneous group of pruritic skin eruptions, which are seen only in pregnancy. The first classification of dermatoses of pregnancy was proposed by Holmes and Black[14] in 1983 and included four skin conditions: 1) pemphigoid gestationis (PG, syn. herpes gestationis); 2) polymorphic eruption of pregnancy (PEP), (syn. pruritic urticarial papules and plaques of pregnancy [PUPP]); 3) prurigo of pregnancy (PP); and 4) pruritic folliculitis of pregnancy (PF).

The most recent rationalized classification was proposed by Ambros-Rudolph *et al*.[3] in 2006 which is as follows: 1) atopic eruption of pregnancy (AEP); 2) polymorphic eruption of pregnancy; 3) pemphigoid gestationis; and 4) intrahepatic cholestasis of pregnancy, described as specific dermatoses of pregnancy.

AEP is the most common pregnancy-induced dermatosis in our study and observed in 49.7%.

AEP is a benign pruritic disorder of pregnancy, which includes eczematous and/or papular lesions in patients with an atopic diathesis after exclusion of the other dermatoses of pregnancy.[3]

Results are in accordance with Vaughan-Jones *et al*.[15] who had reported a high prevalence of atopic eczema in pregnancy for the first time. The reason for increased incidence of atopic eczema in pregnancy was cited to be due to immunological changes in pregnancy. In a retrospective study on 505 pregnant patients Ambros-Rudolph *et al*.[16] confirmed these findings.

In present study eczema was observed in 11 (28.9%) females. In our study 7 (70%) patients had first episode of atopic eczema during pregnancy and remaining 4 (30%) patients with AEP had exacerbation of pre-existing atopic dermatitis. The eruption was seen more commonly in primigravida and skin lesions started during early pregnancy in first and second trimester. Lesions usually involve trunk and limbs but can affect all parts of the body.

Pregnancy has specific immunological changes characterized by lack of strong maternal cell mediated immune function and Th1 cytokine production stands in contrast to dominant humoral immunity and increased secretion of TH2 cytokines.[17] So the exacerbation of preexisting atopic dermatitis, as well as, first manifestation of atopic changes can be explained by a dominant TH2 immune response that is typical for pregnancy.

Maternal prognosis is good as lesions respond quickly to therapy. Fetal health is unaffected but later on there might be a risk of developing atopy in the infant.

In present study, prurigo of pregnancy was seen in 13% patients. Also called as Besnier's prurigo, has been reported to occur in approximately one in 300 pregnancies.[3] Most of our patients presented with lesions over the extensor aspect of legs and upper arms. Four of our patients presented in second trimester and one in third trimester.

It is characterized by pruritic, often excoriated papules and nodules on the extensor surfaces of the legs and upper arms The time of onset is variable can occur in all trimesters. The etiology and pathogenesis is not known, although there is sometimes a history of atopy.[15] There are no recognized adverse effects for the mother or fetus. The eruption usually resolves soon after delivery as it did in all of our five patients. Histopathology of PP is nonspecific and usually shows chronic, inflammatory cell infiltrate.

Pruritic folliculitis of pregnancy was seen in 5.2% patients in our study. This finding is consistent with the study done by Puri *et al*.[18] Commonly seen in the second and third trimester of pregnancy it affects an estimated one in 3,000 pregnancies.[19] Contrary to its name, pruritus is not a major feature and it may be mistaken for acne or microbial folliculitis.[20,21] PFP is considered as a form of steroid acne and characterized by multiple, pruritic, 2- to 4-mm, follicular monomorphic papules or pustules typically on the shoulders, upper back, arms, chest, and abdomen. The diagnosis is made clinically after excluding other more common rashes. Histologically the condition is characterized by sterile folliculitis. The skin lesions clear spontaneously at delivery or in the postpartum period. It is not associated with morbidity to the mother or fetus. Small case series have failed to implicate immunologic dysfunction or elevated androgen levels.[22,23,24] Wilkinson *et al*.[23] suggested that PFP might be a form of hormonally-induced acne, caused by end-organ hypersensitivity to increased serum levels of sex hormones during pregnancy.

Pruritic urticarial papules and plaques of pregnancy (PUPPP) is benign self-limiting pruritic inflammatory disorder that usually affects primigravida in the last weeks of pregnancy or immediately postpartum.[3] Also known as toxemic rash or polymorphic eruption of pregnancy. In our present study, it was seen in 16 (42.1%) patients. Of these 13 (81.3%) patients were primigravida and 3 (18.7%) were multigravida. This is in contrast to the figures quoted by Puri *et al*.[18] (62%) and Das *et al*.[25] (24.5%). Pruritic urticarial papules and plaques occurs in 1 of 160 pregnancies, and is more common in white women.[26] Classically, this disease occurs in primigravida, and the incidence is higher in multiple gestations (i.e. 0.5% of single births, 2.9% of twin pregnancies, and 14% of triplets).[27] Usually intensely pruritic papules start within striae distensae and later spread to involve the trunk and extremities.[28,29]

The periumbilical region, face, palms, and soles are usually spared. Occasionally vesicles, purpura, targetoid, eczematous, or polycyclic lesions are seen. It rarely recurs in subsequent pregnancies, but when it does it is often less severe.[30] The exact etiology is not known. A relationship to skin distension has been proposed due to the higher prevalence of PUPPP in multiple gestations and in women with increased weight gain during pregnancy, or the condition may represent a cutaneous response to the presence of circulating fetal cells that have invaded maternal skin.[31,32] Another theory has been proposed that stretching of the skin damages the connective tissue causing subsequent conversion of nonantigenic molecules to antigenic ones, leading to skin eruption.[33,34]

Histological findings are non-specific and the immunofluorescence studies are negative. Disease is self-limiting and lesions resolve near term or in the post partum period. The fetal and maternal prognosis is excellent.[35] Most of the patients obtain relief with the use of moderate potent topical corticosteroid, topical calamine and systemic antihistamines

Pemphigoid gestationis (PG) was observed in one (2.6%) patient. It is similar to those encountered by Das *et al*.,[25] an Indian study done in Kolkata. PG is a rare autoimmune bullous disease that is associated with pregnancy and rarely with trophoblastic malignancy or molar pregnancy.[36] Incidence of HG is approximately 1 in 50,000 pregnancies.[37] Commonly manifest in the late pregnancy (mean of 21 weeks)[38] or immediate postpartum but can appear in any of the three trimesters. In 75% cases flare is seen at the time of delivery, which is a typical feature.[39]

PG tends to recur in subsequent pregnancies, with usually earlier onset and increasing severity. It begins with the sudden onset of intensely itchy, urticarial lesions, which are found on the abdomen in 50% of cases. At this stage, it is very difficult to distinguish this disease from PUPPP. The lesions then progress to a generalized bullous eruption that usually spares the mucous membranes, palms and soles.[40]

Biopsy results reveal a subepidermal blister with an eosinophil-predominant infiltrate. The infiltrate is localized to the dermal-epidermal junction and perivascular areas. Direct immunofluorescence (DIF) is the most sensitive and specific assay for differentiating PG from PUPPP. Performed on perilesional skin, DIF shows a linear band of C3 and/ or IgG at the basement membrane. Salt-split skin studies demonstrate antibody binding to the roof of the vesicle.[41]

Intrahepatic cholestasis of pregnancy or pruritus gravidarum (seen in 5.3% of patients) is caused by maternal intrahepatic bile secretory

dysfunction. Two cases were reported in this study. The first, a primigravida presented in the third trimester with severe itching over the extremities and mild elevation of serum bile acids (normal serum bilirubin levels). The second was multigravida who presented at the end of second trimester and had reported history of similar eruption in previous pregnancy.

Results are similar to that of an Indian study conducted in Kolkata (5.2%).[25] Incidence is reported to be 0.02% to 2.4% world wide.[42] A genetic predisposition for this disorder has been described. This disease is characterized by intense generalized pruritus usually seen in 3rd trimester of pregnancy in about 70% of cases.[43] Although constant, the pruritus is classically much worse at night. It may be most severe on the palms and soles. The important feature of intrahepatic cholestasis is the absence of primary lesions and excoriations are the only cutaneous finding.[44]

Most sensitive marker of ICP is elevation of serum bile acids. Jaundice is present in a minority of patients. Symptoms tend to dissipate within days of delivery, but there is a tendency toward later development of gallbladder disease in these women. There is a potential for recurrence in subsequent pregnancies or with OC use. Fetal risk is also a matter of concern. It includes fetal distress, stillbirths and preterm delivery due to placental anoxia.[45]

Conclusion

Pregnant women are prone to suffer from a wide range of dermatological problems apart from the specific dermatoses of pregnancy. This study emphasizes the need for a scrupulous and meticulous search for dermatological diseases instead of a casual cursory examination and dismissing the patients with symptoms attributing them to the normal course of pregnancy. These pruritic dermatoses are unique to the gravid state. A detailed history and awareness of clinical presentation facilitate confirmation of the diagnosis and will direct the most appropriate laboratory evaluation in an effort to minimize maternal and fetal morbidity. In addition, monitoring of liver function deserves special consideration.

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