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MYRIAD OF CUTANEOUS CHANGES IN PREGNANCY: A STUDY IN TERTIARY CARE HOSPITAL IN NORTH INDIA

Dermatology

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ABSTRACT

Background: The skin changes in pregnancy can be either physiological, changes in pre-existing skin diseases or development of new pregnancy specific dermatoses. Though cutaneous changes in pregnancy are a common occurrence but very limited data is available on females in North India.

Aims: The objective was to study the clinical spectrum of cutaneous manifestations in pregnant females, to differentiate between the physiological and pathological skin changes and categorize these as dermatoses specific and non-specific to pregnancy.

Methods: In this cross-sectional observational study 200 patients presenting with cutaneous complaints irrespective of their parity and gestational age were included. Thorough examination and relevant investigations were done wherever necessary.

Results: Pigmentary changes were the most common physiological change observed. Linea nigra in 129 patients (64.5%), darkening of areolae in 113 (56.5%) cases and melasma, the most common physiological change of cosmetic concern was seen in 109(54.5%) cases. Most common complaint was pruritus 123 cases (61.5%). Co-existence of physiological and pathological dermatoses was common among our patients. Specific dermatoses of pregnancy included 44 cases (22%), most common was Atopic Eruption of Pregnancy 26 (13%) cases followed by polymorphic eruption of pregnancy 14 (7%) cases and Intrahepatic cholestasis of pregnancy and Pemphigoid gestationis 2 (1%) cases each. We encountered only one (0.5%) case of Uncertain Dermatoses of pregnancy (Impetigo Herpetiformis).

Conclusion: Physiological changes are the most common dermatoses associated with pregnancy. Co-existence of physiological and pathological dermatoses is common. Most common cutaneous complaint with which pregnant females present is pruritus. The specific dermatoses of pregnancy which have a poor prognosis are fortunately of rare occurrence, but early recognition and prompt treatment is crucial to improve maternal and fetal prognosis and minimize morbidity.

KEYWORDS:

Pregnancy, Cutaneous changes, Physiological changes, Pregnancy specific dermatoses

Introduction:

Pregnancy is a physiological state of female (Roth,2009) with profo und immunological, metabolic, endocrine and vascular changes which make the pregnant woman susceptible to changes of the skin and appendages, both physiologic and pathologic.(Paunescu,2008) The skin changes in pregnancy can be either physiological (hormonal), changes in pre-existing skin diseases or development of new preg nancy specific dermatoses. Though various studies have been done on cutaneous changes in pregnancy in different parts of the world, but very scanty literature is available on females in North India. This observational study was done in Punjab to ascertain the incidence and clinical characteristics of mucocutaneous changes in pregnancy and the influence of pregnancy on the course of various dermatoses in 200 patients presenting with cutaneous complaints irrespective of their parity and gestational age. The aims of this study were to study the clinical spectrum of cutaneous manifestations in pregnant females, to differentiate between the physiological and pathological skin changes and categorize these as dermatoses specific and non-specific to pregnancy.

Methods:

In this cross-sectional observational study, data was collected from 200 pregnant women with skin problems, attending Dermatology OPD and Obstetrics and Gynaecology OPD and ward of our tertiary care hospital for a period of 2 years. Written informed consent was taken from each patient enrolled in the study. In every case detailed history including the personal history, past, obstetrical history in previous pregnancies was noted.

Thorough clinical examination was carried including general physical examination, cutaneous examination including mucosa, scalp and nails, per speculum examination was done whenever required. Routine and specific investigations were done wherever necessary.

Results:

A total of 200 pregnant females with a mean age of 24.2 years (range: 18-40 years) were included in the study, out of which one hundred and fifteen cases (57.5%) were gravida one, 57 cases (28.5%) gravida two, 15 cases (7.5%) gravida three, 12 cases (6%) gravida four and 1case (0.5%) was gravida seven (i.e. more than 5). More than half of the cases were primigravida. Earliest gestational age at which the patients presented with cutaneous complaints was 4 weeks, in some cases, the time of first presentation was as late as 39 weeks.

Among the 200 cases studied, majority had more than one cutaneous manifestation at a time. 72 cases (36%) had only one skin manifestation, 50 cases (25%) had two skin conditions, whereas 65 cases (32.5%) had 3 and 13 cases (6.5%) had 4 skin manifestations at the time of presentation.

Almost all cases presenting to us had one or the other physiological skin change in pregnancy, 44 (22%) had specific dermatoses of pregnancy. Pigmentary changes were the most common physiological change observed. Linea nigra [Figure 1] was present in 129 patients (64.5%) followed by darkening of areolae seen in 113 (56.5%) cases.

The most common physiological change of cosmetic concern was melasma 109(54.5%) cases [Figure 2], centrofacial pattern of melasma

was most common, seen in 74(67.9% of melasma cases), malar in 30 (27.5 % melasma patients) and mandibular in 5 (4.6% of melasma cases).

FIG 1 Linea nigra with striae

FIG 2 Melasma (Cholasma)

This was followed by striae 100 (50%) cases [Figure 1], the lower abdomen and thigh were involved in 42 (21%) cases, only lower abdomen in 29 (14.5%) cases, striae on abdomen, thigh and breast were seen in 27 (13.5%) and on abdomen and breast in 2(1%) cases. In our study, 25% of patients with striae were primigravida and 75% were multigravida.

Pruritus (without any cause) was present in 16 (8%) cases. Other miscellaneous conditions noted were acne 6 (3%) cases, xerosis, hirsuitism, vascular lesion (pyogenic granuloma) and telangiectasia in 1 patient (0.5%) each. [Table 1]

Table 1: Physiological changes in pregnancy:

Physiological change	No. of Patients	Percentage
Striae	100	50
Melasma	109	54.5
Xerosis	1	0.5
Telangiectasia	1	0.5
Hirsutism	1	0.5
Acne	6	3
Pruritus	16	8
Vascular	1	0.5
	235	

Among the dermatoses affected by pregnancy there were 139 conditions, out of these infections were most common 120 (86.33%). There were 20 cases (10%) of bacterial infections, there were syphilis 19 (9.5%) cases and furuncle 1case (0.5%). The cases testing positive for non treponemal serological tests were confirmed using specific treponemal tests and diagnosed as having Syphilis only if treponemal tests were positive in significant titre thus ruling out false positives. Among those having fungal infections there were total 51 (25.5%) cases, including tinea 24(12%) cases, vulvovaginal candidiasis 20 cases (10%) and pityriasis versicolor 7 cases (3.5%).Total of 38 cases (19%) of viral infections included warts (HPV) 22 cases (11%), 4 cases of herpes i.e. HSV- oral 3(1.5%) and genital herpes 1(0.5%) case. There were 6 cases (3%) of chickenpox, 4 (2%) cases of pityriasis rosea and 1 case(0.5%) of molluscum contagiosum. There were 11 cases (5.5%) of scabies included under parasitic infections.

Other conditions were urticaria 5 cases (3.6%), contact dermatitis 3 (2.2%) and connective tissue diseases (Systemic sclerosis) 2cases (1.4%) and one case (0.7%) each of eczema, genodermatoses (Neurofibromatosis), drug reaction due to ART in HIV positive patient, vasculitis, verrucous hemangioma [Figure 3] and sebaceous cyst. Here the percentage was calculated out of total number of dermatoses affected by pregnancy (139) as many patients had overlapping of various conditions and infections.

FIG 3 Verrucous hemangioma on trunk

Specific dermatoses of pregnancy included 44 cases (22%). All of these cases had pruritus. Among these, most common was Atopic Eruption of Pregnancy 26 (13%) cases followed by Pruritic urticarial papules and plaques of pregnancy 14 (7%) cases and Intrahepatic cholestasis of pregnancy and Pemphigoid gestationis 2 (1%) cases each. There was only one case of Pruritic folliculitis of pregnancy included under AEP.

One hundred and twelve (56%) cases had Generalised pruritus. Among the pregnancy unrelated primary causes accounting for 68 (34%) cases, majority were infections (fungal infections like tinea and vaginal candidiasis, viral infections and scabies) accounting for 45 (22.5%) cases. For 16 (8%) cases no primary cause could be found and these cases were assigned to be of pruritus associated with pregnancy. There were 23 cases with genital pruritus, majority, 20 (10%) cases of them had vaginal candidiasis [Figure 4] as etiology.

FIG 4 Vulvovaginal candidiasis

In all, 123 cases (61.5%) had pruritus out of which, 112 had generalised pruritus and 23 had genital pruritus, including 12 patients having both generalised and genital pruritus.

Various cases with pruritus are tabulated as follows. [Table 2]

Table 2: Causes of pruritus in pregnancy

	No. of Patients	Percent
Generalized pruritus	**112**	**56**
Specific cause	44	22
Chronic urticaria	3	1.5
Infections	45	22.5
No primary cause found	16	8
Xerosis	1	0.5
Others	3	1.5
Genital pruritus	**23**	**11.5**

Discussion:

Skin and its appendages undergo various normal physiological changes during pregnancy, usually well tolerated by a pregnant female, but a few of them may be a cause for concern. (Rathore, 2011), (Rudolph, 2011). Physiological skin changes in pregnancy include changes in pigmentation (melasma, linea nigra, secondary areola, localized or generalized hyperpigmentation), alterations of the connective tissue (striae distensae) and vascular system (palmar erythema, spider angiomas, varicosities) as well as changes in hair and nails. Cutaneous manifestations in pregnancy are classified into four main categories as per the latest classification. (Kar, 2012)

1. Physiological changes associated with pregnancy,
2. Dermatoses specific of pregnancy,
3. Uncertain dermatoses of pregnancy and
4. Pre-existing dermatological conditions modified by pregnancy.

In our study, linea nigra was present in 129 patients (64.5%) followed by darkening of areolae seen in 113(56.5%) cases. The most common physiological change of cosmetic importance was melasma, observed in 109 cases (54.5%). Melasma has been reported to occur in 50-75% of pregnant women, as hormonal factors play an implicating role in its etiology.(Krupashanker,2012) . In studies done by Hassan et al (2015), Kothamasu et al(2016) and Kumari et al (2007) pigmentary changes were the most common physiological change observed followed by striae. Kumari et al (2007) reported linea nigra in 91.4% of their cases and secondary areola in 78.4%, Hassan et al (2015) reported linea nigra in 80% of cases followed by secondary areola in 75% and melasma in 64% of cases, centrofacial pattern being the commonest, seen in 67% of those with melasma.

In our study, the second most common physiological change observed was striae, seen in 100 (50%) cases. The lower abdomen and thigh were involved in 42 (21%) cases, only lower abdomen in 29 (14.5%) cases, striae on abdomen, thigh and breast were seen in 27 (13.5%) and on abdomen and breast in 2(1%) cases. Thus lower abdomen was the most common site for striae followed by thighs and breasts. 25% of patients with striae were primigravida and 75% were multigravida. Only 21.7% of primigravidas, 78.9% of gravida 2 and 100% of gravida 3 and above patients had striae.

Hassan et al (2015) reported striae in 38.7% cases out of which 41% were primigravidae and 59% were multigravidae. Striae distensae develop in up to 90% of women late in second and third trimester of pregnancy (Sachdeva, 2008). In our study majority of primigravidas presented in early half of pregnancy.

Six (3%) patients developed acne, 2 of our patients developed increased facial hair and 1 patient each had development of spider nevi and pyogenic granuloma on finger. None of our patients had any presenting complaint pertaining to nail changes.

The most important entity of this spectrum of cutaneous manife stations is the specific dermatoses of pregnancy, almost always associated with pruritus. These include 4 conditions as per the latest classification (Sachdeva,2008) Atopic eruption of pregnancy (AEP), Polymorphic eruption of pregnancy (also known as PUPPP), Pemphigoid gestationis and Intrahepatic cholestasis of pregnancy.

In our study we had 44 cases (22%) in this category, Atopic eruption of pregnancy 26 cases (59.1% among patients with specific dermatoses) was the commonest. It includes, prurigo of pregnancy 21 cases (47.7%), eczema in pregnancy 4 cases (9.1%) and pruritic folliculitis of pregnancy 1 case (2.3%) [Figure 5].

FIG 5 Atopic eruption of pregnancy

Next in frequency was polymorphic eruption of pregnancy 14 cases (31.8%) followed by Intrahepatic cholestasis of pregnancy and Pemphigoid gestationis 2 cases (4.5%) each. [Table3]

Table 3: Specific dermatoses of pregnancy.

Disease	No. of Patients	Percentage cases	Percentage Among specific dermatoses
Atopic Eruptions of Pregnancy	**26**	**13**	**59.1**
Eczema in Pregnancy (E-type)	4	2	9.1
Prurigo of Pregnancy (P – type)	21	11	47.7
Pruritic folliculitis of pregnancy	1	0.5	2.3
Polymorphic Eruption of Pregnancy (PEP)	**14**	**7**	**31.9**
Herpes Gestationis	**2**	**1**	**4.5**
Intrahepatic Cholestasis of Pregnancy	**2**	**1**	**4. 5**
Total	**44**	**22**	**100**

AEP was more severe in multigravidas and was seen in later half of pregnancy. Majority of the patients had lesions distributed on the extensor aspects of the limbs [Figure 6] and less on the trunk.

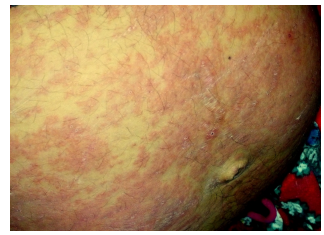
FIG 6 Prurigo of pregnancy

Ambros-Rudolph et al (2006) confirmed a high prevalence of atopic eczema in pregnancy in a retrospective two-center study on 505 pregnant patients, revealing that 80% of the affected patients experience first episode of atopic eczema during pregnancy. The eruption was seen more commonly in primigravida and skin lesions started during early pregnancy in first and second trimester.

Similarly Hassan et al(2015) observed that among the specific dermatoses of pregnancy, prurigo of pregnancy was the commonest and seen in 16 (50%) cases. Also in study done by Kothamasu et al(2016) AEP was the most common, 49.7% cases of pregnancy specific dermatoses.

The incidence of polymorphic eruption of pregnancy was 31.8 % (14 cases) among pregnancy specific dermatoses in our study [Figure 7]. The exact pathogenesis of PEP is unknown. Due to presence of prominent abdominal striae in majority of cases, it is hypothesized that stretching of the abdominal skin leads to damage to the underlying connective tissue leading to an inflammatory reaction process. It is 10 times more likely to occur in women with multiple pregnancy (twins or triplets), primigravida with male fetuses, or those who undergo rapid or excessive weight gain during pregnancy. Hassan et al(2015) observed PEP in 7 (22% of pregnancy specific cases), all being primigravidae and Kothamasu et al(2016) had 16 (42.1%) cases with PEP.

FIG 7 Polymorphic eruption of pregnancy



In study done by Kumari et al(2007) the various specific dermatoses of pregnancy, Pruritic Urticarial Papules and Plaques of Pregnancy (PUPPP) was the most common disorder (14 cases) followed by Pruritus gravidarum (5 cases). Pre-bullous stage of pemphigoid gestationis (PG) has similar features clinically and may be difficult to differentiate. Unlike in pemphigoid gestationis, the umbilical region is usually spared (Huilaja, 2014) and DIF is negative.

In our study there were 2 cases each of Pemphigus gestationis (PG) 4.5% and Intra-hepatic cholestasis of pregnancy (ICP). PG [Figure 8 (a) and 8 (b)] is a rare autoimmune subepidermal bullous dermatosis occurring during pregnancy and postpartum initially described by Dr. John Milton in 1872. (Zhao,2015). The estimated incidence is 1 in

40,000-50,000 pregnancies. The disease is probably triggered by a placental antigen that cross-reacts with skin antigens.(Ambros – Rudolph, 2006) Rarely, associated with a hydatiform mole, trophoblastic tumors, and choriocarcinoma. Nearly half of the cases develop during the first pregnancy.(LipozenČiĆ,2012)

FIG 8(A) Pemphigoid gestationis

FIG 8(B) Pemphigoid gestationis

ICP occurs due to a mild form of intrahepatic bile secretory dysfunction and is seen in the third trimester of pregnancy in about 70% of cases.(Kumari,2007) There are no primary cutaneous lesions in ICP and it presents only with secondary skin lesions caused by scratching due to intense pruritus, which represent linear excoriation marks, erosions, and scabbing [Figure 9](Warshauer,2013). In particular it involves the extensor surfaces of the extremities, but also the abdomen and buttocks.

FIG 9 Intrahepatic cholestasis of pregnancy

Cases of PG and ICP were confirmed with biopsy, DIF and S.LFT respectively. Both cases of PG presented again with post-delivery flare. Our findings were consistent with the description of Kothamasu et al(8) who observed herpes gestationis and intrahepatic cholestasis in one (2.6%) and two (5.3%) females, respectively whereas Hassan et al(2015) observed 8 cases (25%) of ICP and 1 (3%) case of PG. [Table 4].

Table 4: Comparison with recent studies

Study Year Cases	Kumari et al(9) 2007 607	Hassan et al(7) 2015 650	Kothamasu et al(8) 2016 350	Our study 2016 200
Atopic Eruption of pregnancy	2	16	19	26
Polymorphic Eruption of Pregnancy	14	7	16	16
Intrahepatic Cholestasis Pregnancy	-	8	2	2
Herpes Gestationis	1	1	1	2

In the 1st trimester (zero-12 weeks of gestation) three patients presented with vulvovaginal candidiasis, two each had scabies and urticaria. Only one patient developed chloasma during the first trimester of pregnancy.

In the 2nd trimester (13-28 weeks), 52 patients developed chloasma and 43 had striae. 16 females presented with pruritis of pregnancy, 11 had prurigo of pregnancy, eight had PUPPP, four presented with eczema one had chronic urticaria and PFP – pruritic folliculitis of pregnancy. Among infections, the most common were genital warts- 14 patients, 12 had positive serology for syphilis but no active lesions and 11 presented with vulvovaginal candidiasis. One patient presented with lesions of Impetigo herpetiformis at 26wk2d period of gestation.

In the 3rd trimester (29 weeks onwards) 59 had chloasma and 58 presented with striae. Nine had prurigo of pregnancy, six patients were diagnosed as having PUPPP, both our patients of pemphigoid gestationis presented in the 3 trimester (at 32wk 4d and 29 wk 3d), only case of ICP presented at 28weeks and 4 days of gestation. Fortunately none of our patients had fetal loss. Twelve of our patients had tinea, seven had warts and six developed vulvovaginal candidiasis. Six had positive serology for syphilis, no active lesions seen on examination.

There were six cases of chickenpox, three patients presenting in second and third trimester each and were managed according to the latest BAD guidelines.

There was only one case of Impetigo Herpetiformis [Figure 10] included under the Uncertain dermatoses of pregnancy.

FIG 10 Impetigo herpetiformis

Its pathogenesis is poorly understood, elevated levels of progesterone may play a role. Hypocalcaemia and hypoparathyroidism may contribute to disease occurrence. (Geraghty, 2011)

Conclusion:

The finely tuned, harmonious complex cascade of molecular and cellular phenomenona that the gestation brings, many signs and/or symptoms target the cutaneous layers. Our study reveals that the physiological changes are the most common dermatoses occurring in almost all the patients and were found to have an incidence similar with those of earlier studies.

The pre-existing dermatoses affected during the course of pregnancy contributed to a major number of cases in this study. Many of our patients had co-existence of physiological and pathological dermatoses. Majority of patients present with complaint of pruritus which may be physiological or pathological.

The specific dermatoses of pregnancy have a comparatively rare occurrence. Among these, Atopic eruption of pregnancy(AEP) is the most common pregnancy dermatoses followed by Pruritic Urticarial Papules and Plaques. AEP and PUPPP present with no maternal or fetal risks. Among the specific dermatoses of pregnancy, those having a poor prognosis are Intrahepatic Cholestasis of Pregnancy and Pemphigoid Gestationis and fortunately have rare occurrence (2% cases), but awareness, early recognition and prompt treatment is essential for improving maternal and fetal prognosis and minimizing morbidity.

In our study we encountered only one (0.5%) case of Uncertain Dermatoses of pregnancy (Impetigo Herpetiformis).

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