Skin eruptions specific to pregnancy: an overview

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Key content

- Pregnancy results in various physiological skin changes. As a consequence, some common dermatoses can present more frequently in pregnant women. In addition, there is a number of skin eruptions unique to pregnancy.
- The aetiology of physiological skin changes in pregnancy is uncertain but thought to be due to hormonal and physical changes of pregnancy.
- The four dermatoses of pregnancy are: atopic eruption of pregnancy, pemphigoid gestationis, polymorphic eruption of pregnancy and intrahepatic cholestasis of pregnancy.

Learning objectives

- To understand the physiological skin changes in pregnancy.
- To identify the skin conditions that require appropriate referral.
- To be able to take a history, to diagnose the skin eruptions unique to pregnancy, undertake appropriate investigations and first-line management, and understand the criteria for referral to a dermatologist.

Keywords: atopic eruption of pregnancy / intrahepatic cholestasis of pregnancy / pemphigoid gestationis / polymorphic eruption of pregnancy / skin eruptions

Introduction

Pregnancy is a physiological state that is associated with specific dermatoses and modification of common dermatoses. Various hormonal, immunological and haemodynamic factors that are specific to pregnancy influence the status of the skin. There have been a number of attempts to create a universal classification, however, more recently, a clinically approved classification by Ambros-Rudolph and Müllegger has been widely accepted.1 The classification recognises atopic eruption of pregnancy, pemphigoid gestationis, polymorphic eruption of pregnancy and intrahepatic cholestasis of pregnancy to be unique to pregnancy. This review provides an explanation of the possible aetiology of the physiological skin changes and skin eruptions specific to pregnancy, their diagnosis, management and implications.

Physiological skin changes in pregnancy

Most physiological skin changes are recognised to be due to hormonal (increased estrogen, progesterone and melanocyte-stimulating hormone) and physical factors but the exact aetiology is uncertain. Box 1 summarises these changes.2,3

Almost all women notice an increase in skin pigmentation during pregnancy, which is more noticeable in dark-skinned individuals. This usually fades post-delivery, but often does not disappear completely. Melasma has been reported in 75% of expectant mothers, predominantly in the second or third trimester. The condition is distressing and often persists for months and years postpartum. Treatment can prove challenging, with limited response to topical bleaching creams, hydroquinones (not licensed in the UK), retinoids and steroids, as well as chemical peels, laser treatments and dermabrasion.4 All of the above treatments are contraindicated in pregnancy and breastfeeding. Avoidance of excessive sunlight exposure and the use of broad-spectrum sunscreens are therefore essential to prevent both initial development and exacerbation of melasma.5

Stretch marks (striae gravidarum) are also a common concern. These develop as linear red–purplish areas resulting from the stretching of skin in the second trimester. Striae gravidarum (Figure 1) occur predominantly on the abdomen, breasts, thighs, lower back, buttocks and upper
arms. They are caused by the rupture of dermal elastic fibres, which explains their irreversible nature. However, they often fade in the postnatal period to thin, atrophic, hypopigmented scars. Risk factors include personal or family history, dark-skinned women and excessive abdominal distension in pregnancy. Use of emollients is helpful, but there is no evidence that preparations such as vitamin E cream, tea tree oil and so on have any special value.

### Box 1. Physiological skin changes in pregnancy

#### Pigmentation
- Linea nigra (abdomen)
- Nipples
- Axillae
- Genitalia
- Perineum
- Secondary areola (pigmented area appears around the primary areola commonly during the fifth month)
- Melasma (chloasma gravidarum or pregnancy mask):
  - Forehead
  - Malar distribution
  - Mandibular area

#### Glands
- Eccrine
  - Miliaria
  - Hyperhidrosis
- Apocrine
  - Decreased activity (improves conditions such as hidradenitis suppurativa)
- Sebaceous
  - Activity increased in third trimester but effects on acne variable
  - Montgomery tubercles (follicles) may develop (hypertrophic sebaceous glands, non-pigmented elevations in the primary areola)

#### Vasculature
- Spider naevi
- Telangiectasia
- Palmar erythema
- Varicosities:
  - Saphenous
  - Vulval/vestibular/vaginal
  - Haemorrhoidal
- Vasomotor instability, such as, flushing
- Increased hydrostatic pressure, such as, purpura
- Increased capillary permeability, such as, oedema in extremities and face

#### Connective tissue
- Striae gravidarum
- Skin tags (epithelial polyps)

Vascular changes are thought to be partly due to the increase in estrogen, causing dilatation, instability, congestion and proliferation of blood vessels that can be seen on or through the skin. The prevalence of the spider naevi is noted to be higher, 66%, in Caucasians compared with 11% in black people. They are more common in fair-skinned individuals and the usual sites include areas around the eyes, neck, face, upper chest, hands and arms. They appear in the second trimester and the majority will disappear by the third postnatal month. If treatment is required for those on the lower extremities, sclerotherapy or laser treatment can be used. All gland activity is affected during pregnancy. However, increased eccrine gland secretions towards the third trimester can cause prickly heat (miliaria) and hyperhidrosis which can contribute to pruritus.

Changes are noted not only in the skin, but also in the other ectodermal structures, such as hair and nails. Increased hair growth, antenatally, is thought to be due to prolongation of the anagen phase. Acute telogen effluvium, a generalised hair shedding with diffuse non-scarring alopecia, characteristically occurs 3–6 months postpartum. Generally, recovery is spontaneous and occurs within 9–12 months, and rarely does hair density fail to recover completely.

Nails tend to grow faster during pregnancy and can become dystrophic, brittle, soft and/or pigmented. Mucosal changes include pigmentation, hyperaemia and hypertrophy, which can lead to bleeding. Pruritus in the absence of an underlying haematological or biochemical disorder is a common complaint, affecting up to 18% of pregnancies. Common sites affected include the scalp and abdominal skin. It can start as early as the third month and peaks a month before delivery. The recurrence rate in subsequent pregnancies is thought to be up to 80%.

Dermographism (Figure 2) and urticaria are also common in the last half of pregnancy. It is important nevertheless to exclude other possible cases of pruritus, such as scabies, allergic contact dermatitis, drug-induced pruritus and an exacerbation of an atopic dermatitis. The presence of skin excoriations and a glossy, polished appearance of the patient’s nails should make the physician suspect pruritus.

It is essential for the clinician to establish whether any skin-related complaint is due to a pre-existing dermatological
condition, exacerbated by pregnancy, or represents a new skin problem. A focused, detailed history (Box 2) and examination (Box 3) are key to determine whether further investigations or a referral are indicated. One needs to be aware that scratching and ulceration can alter the characteristics of the primary lesion. Pictorial records may be useful to monitor progression and response to treatment.

**Box 2.** History taking: specific questions to ask
- Duration of the disease
- Distribution and progression of the condition
- Exacerbating or relieving factors
- Associated symptoms like itching, burning, pain, weeping and redness
- Family history of skin disorders
- Social history, such as, job, travel
- Past medical history, such as, asthma, hay fever
- Drug history and allergies
- Past dermatological problems
- Previous treatments tried for this condition
- Impact of condition on quality of life

**Box 3.** Examination
- **Distribution**
  - Site
  - Symmetry:
    - Symmetry suggests endogenous cause
    - Non-symmetry suggests an exogenous cause e.g. infection, irritant or contact dermatitis

- **Description of primary lesion**
  - Shape
  - Size
  - Colour
  - Margin
  - Surface
  - Type of lesion – papule, pustule, wheal, vesicle, bulla

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**Dermatoses of pregnancy**

The ability to distinguish between dermatoses of pregnancy is of utmost importance, as some (intrahepatic cholestasis of pregnancy and pemphigoid gestationis) can cause morbidity and mortality of mother and fetus, such as intrauterine growth restriction, preterm delivery and stillbirth.

Table 1 summarises the four dermatoses of pregnancy featured in this review. Patient information about dermatoses can be downloaded from the British Association of Dermatologists, the American Academy of Dermatology and the New Zealand Dermatological Society websites.

**Intrahepatic cholestasis of pregnancy**

Intrahepatic cholestasis of pregnancy is also known as obstetric cholestasis, cholestasis of pregnancy, jaundice of pregnancy or pruritus/prurigo gravidarum.

Unlike other dermatoses, this condition presents initially with itching and results in secondary skin changes as a result of pruritus. In England, intrahepatic cholestasis of pregnancy is recorded to be 0.7% in multi-ethnic populations and in 1.2–1.5% of women of Indian–Asian or Pakistani–Asian origin. Its prevalence is known to be determined by genetic, hormonal and environmental factors, and varies between populations worldwide. It is responsible for some of the most intense itching.

Cholestasis-related pruritus is most severe at night and mainly affects the hands, feet and pressure sites. Post-inflammatory hyperpigmentation caused by scratching may occur on the back with sparing in the middle. Pruritus disturbs the sleeping pattern, thus severely affecting the quality of life and general health of a pregnant woman.

Obstetric cholestasis has been linked to stillbirth, premature birth, meconium passage, fetal distress, delivery by caesarean section and postpartum haemorrhage, but some of this evidence is of poor quality. Monitoring of liver function and bile acids in patients with suspected obstetric cholestasis is crucial as it allows monitoring and exclusion of other conditions. Consideration should be given to carrying out investigations such as a viral screen, liver autoimmune and pre-eclampsia screen and liver ultrasound to rule out other causes.

If liver function improves or worsens very rapidly then this condition becomes less likely and other diagnoses need to be sought. It is not possible at present to predict poor outcome from deranged biochemistry levels and therefore there are no specific cut-off points for delivery. However, a link between outcome and bile acid levels is suspected and is the focus of current research.

No evidence-based antenatal surveillance techniques are available currently in prevention of stillbirth and perinatal complications as ultrasound scans and cardiotocography are not reliable in preventing intrauterine death which is usually
<table>
<thead>
<tr>
<th>Dermatoses of pregnancy</th>
<th>Areas affected</th>
<th>Risk factors</th>
<th>Recurrence risk</th>
<th>Management</th>
<th>Pregnancy outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intrahepatic cholestasis of pregnancy</td>
<td>Scalp, anus, vulva and abdominal skin</td>
<td>Indian–Asian or Pakistani–Asian ethnic origin, previous obstetric cholestasis</td>
<td>60–70% in future pregnancies</td>
<td>Ursodeoxycholic acid, Topical emollients, Sedating antihistamines, Water-soluble vitamin K</td>
<td>Increased risk of stillbirth, Increased risk of PPH, Increased risk of fetal distress, Increased risk of premature birth (mostly iatrogenic), meconium passage and caesarean section</td>
</tr>
<tr>
<td>Atopic eruption of pregnancy</td>
<td>Face, neck, chest and extensor surfaces of the limbs and trunk</td>
<td>Family history of atopy</td>
<td>Limited data</td>
<td>Topical emollients, Topical anti-pruritics, Topical steroids, Antihistamines, Ultraviolet light, Topical acne treatment</td>
<td>No adverse effect on mother or fetus</td>
</tr>
<tr>
<td>Polymorphic eruption of pregnancy</td>
<td>Abdominal striae with periumbilical sparing</td>
<td>Nulliparity, multiple pregnancies, Any cause of overdistension of skin</td>
<td>Rarely recurs</td>
<td>Topical steroids (first-line), Topical emollients, Antihistamines, Oral steroids</td>
<td>No adverse effect on mother or fetus</td>
</tr>
<tr>
<td>Pemphigoid gestationis</td>
<td>Appears around umbilicus unlike PEP, Can progress to trunk, extremities, palms and soles with mucosal sparing</td>
<td>Recognised correlation with the haplotypes HLA-DR3 and HLA-DR4, Other autoimmune conditions</td>
<td>May recur in subsequent pregnancies, with earlier onset and increasing severity, Also may recur with oral contraception/ menstruation</td>
<td>Topical/oral corticosteroids, Antihistamines, Antibiotics, Immunophoresis, Immunosuppressants</td>
<td>IUGR, Preterm labour, Self-limiting skin lesions in neonate</td>
</tr>
</tbody>
</table>

IUGR = intrauterine growth restriction; PEP = polymorphic eruption of pregnancy; PPH = Postpartum haemorrhage; ? = limited evidence
The role of monitoring fetal movements has not been assessed in women suffering from obstetric cholestasis. Early intervention such as induction of labour is not routinely recommended. Postnatal resolution of liver function should be carried out after 10 days as biochemistry may worsen in the immediate postnatal period. Recurrence risk is thought to be 45–90%.

Ursodeoxycholic acid is reported to be the only known effective treatment of intrahepatic cholestasis, which not only reduces maternal pruritus and liver function, but is also said to improve prognosis for the fetus, although the data are not robust. It is reported to have a good safety profile at the dose of 15 mg/kg a day as a single dose or in two divided doses. It is licensed in the UK for the treatment of gallstones and biliary cirrhosis at the dose of 8–12 mg/kg in two divided doses or as a single dose, and pregnancy and lactation are on the list of contraindications. Topical emollients may be used which may provide some relief from pruritus although no good-quality evidence exists to support their use. Sedating antihistamines may help with sleep at night but are unlikely to have a major effect on pruritus. It has been suggested that a discussion with the woman should be had about the use of water-soluble vitamin K to prevent clotting abnormalities related to the hepatic effects of obstetric cholestasis. However, there is a small theoretical risk of neonatal haemolytic anaemia, hyperbilirubinaemia and kernicterus. The patient’s consent for unlicensed treatments needs to be obtained.

Atopic eruption of pregnancy

Atopic eruption of pregnancy (Figure 3) is also known as prurigo gestationis (Besnier), Nurse’s early-onset prurigo of pregnancy, pruritic folliculitis of pregnancy or eczema in pregnancy.

Atopic eruption of pregnancy is known to be a benign condition and the most common dermatosis of pregnancy with an incidence of 1 in 300. There is a higher incidence of atopic eruption of pregnancy in women with a family history of atopy. The pathogenesis of this condition is thought to be linked to pregnancy-specific immunological changes. Reduced cellular immunity and reduced production of Th1 cytokines (interleukin(IL)-2, IL-12, interferon gamma) stand in contrast to the dominant humoral immunity and increased secretion of Th2 cytokines (IL-4, IL-10). In 80% of cases atopic eruption of pregnancy occurs as the primary condition and in the rest of patients as an exacerbation of a pre-existing complaint. It predominantly affects women in the second and third trimester, but may also occur as early as the first trimester.

It presents as erythematous, excoriated nodules or papules on the face, neck, chest and extensor surfaces of the limbs and trunk. The diagnosis is based on clinical presentation and requires no further investigations as long as other dermatoses of pregnancy have been ruled out. Histopathology is non-specific and immunofluorescence is negative. Improvement is seen following delivery with no postnatal exacerbation. There are limited data on its recurrence in the next pregnancy. Atopic eruption of pregnancy is relatively benign and causes no adverse effects on the mother or fetus.

Treatment of atopic eruption of pregnancy is symptomatic. Oatmeal baths, emollients, topical antipruritics such as 1% menthol in aqueous cream and calamine in aqueous cream, topical steroids and oral antihistamines, and ultraviolet light may help to alleviate symptoms. Wearing soft light clothes and staying in a cool environment is recommended. Topical benzoyl peroxide preparations and erythromycin with zinc acetate lotion are sometimes effective in atopic eruption of pregnancy, which some clinicians consider to be hormone-induced acne.

Polymorphic eruption of pregnancy

Polymorphic eruption of pregnancy (Figure 4) is also known as pruritic urticarial papules and plaques of pregnancy, toxic erythema of pregnancy, Bourne’s toxaeamic rash of pregnancy, linear IgM dermatosis of pregnancy and Nurse’s late-onset prurigo.

It is a benign, self-limiting, pruritic inflammatory disorder of pregnancy with the reported incidence being between 1 in 160 and 1 in 300 pregnancies, usually presenting in the third trimester or immediately postpartum. Risk factors include...
nulliparity, multiple pregnancies and any other cause of overdistension of the abdominal skin in pregnancy. The condition initially presents with pruritic, erythematous papules commonly located within the abdominal striae and with periumbilical sparing. It progresses to the trunk and extremities, sparing the palms and soles in the majority of cases, and does not affect the face. The lesions can coalesce to form plaques or wheals, often resembling target lesions. Most of the time it resolves within 4–6 weeks from the time of onset.

The cause of polymorphic eruption of pregnancy is unknown and may be multifactorial. One hypothesis suggests that stretching of the abdomen causes damage to the connective tissue, provoking an inflammatory response. No association is noted with hormonal or immunological changes.

Most cases are diagnosed clinically without the need for invasive testing. However, skin biopsies may be needed if there is no response to initial treatment, or there is doubt as to the diagnosis. Histology shows lymphocytic vasculitis with eosinophils and oedema of the papillary dermis. Early biopsies show a prominent dermal oedema, and later biopsies reveal epidermal changes such as spongiosis, and hyper- and parakeratosis. Negative direct and indirect immunofluorescence studies help in differential diagnosis with pemphigoid gestationis.

This dermatosis is usually self-limiting and treatment is predominantly for symptom control to relieve pruritus and reduce inflammation. Topical steroids are often used as the first line of treatment and oral steroids are virtually never required. Antihistamines and emollients may also be beneficial. Induction of labour is not necessary or recommended, as polymorphic eruption of pregnancy has no impact on maternal or fetal outcome. Recurrence in subsequent pregnancies is rare.

Pemphigoid gestationis

Pemphigoid gestationis (Figure 5) is also known as pregnancy-related bullous pemphigoid, gestational pemphigoid and herpes gestationis.

The incidence of this dermatosis is very rare, affecting between 1 in 1700 and 1 in 50 000 pregnancies, and it occurs any time after the second trimester and, rarely, immediately after childbirth.

The rash usually appears around the umbilicus as urticarial papules and plaques, which join to form bullae, extending to involve the trunk, extremities, palms and soles with mucosal sparing. Large, tense blisters can form after a few weeks around the edge of the rash or in otherwise unaffected areas of the skin.

It is believed to be an autoimmune condition with antibodies against target antigen (proteins of placenta and the skin). There is a recognised correlation with the haplotypes HLA-DR3 and HLA-DR4. A skin biopsy is necessary to make the diagnosis. Two samples must be taken from perilesional skin: one for histology and the other for direct immunofluorescence studies. Histology reveals degenerative changes in the basal cells resulting in the blister being located first in the epidermis and subsequently between the Malphigian layer and the subepidermal basement membrane. There is associated spongiosis. Direct immunofluorescence studies reveal C3 deposition along the basement membrane. Complement fixing IgG antibodies are seen in 50% of patients. Indirect immunofluorescence (blood or blister fluid) reveals circulating IgG against BP180 or bullous pemphigoid antigen 2 in the hemidesmosomes of the basal membrane zone.

Treatment focuses on symptom control with the use of topical and oral corticosteroids and antihistamines. Therapy may need to be altered prior to delivery to prevent a flare-up. Drug treatment will depend on individual circumstances.
Oral steroids can be indicated for symptomatic relief of symptoms if topical corticosteroids are not sufficient for disease control. Pregnant women are at increased risk of osteoporosis so steroids should be used with caution. Typically prednisolone 30–40 mg (0.5 mg/kg bodyweight) reduced by 5 mg every 3 days to 0. It is essential to monitor glucose and electrolytes while on treatment. Various other systemic treatments, including some antibiotics, can be helpful in recalcitrant disease. Alendronic acid is contraindicated in pregnancy. Cyclosporin appears to be safe in pregnancy. Recent data show no increased risk of malformation, preterm labour or low birthweight babies and thereby its use during pregnancy can be considered safe and effective. The American Academy of Pediatrics considers cyclosporine contraindicated during breastfeeding owing to the potential for immunosuppression and neutropenia. It is used with monitoring of renal function and blood pressure if it proves impossible to maintain disease control with less than 7.5 mg prednisolone. Immunosuppressants as steroid-sparing agents may be helpful for severe cases post-delivery. Cases unresponsive to systemic corticosteroids may benefit from immunophoresis.

Exacerbations and remissions are characteristic. The course of the disease shows frequent improvement towards delivery followed by a flare-up at the time of delivery (75% of patients). Increased blistering can occur around delivery. If the blister count increases as the expected date approaches, the dose of prednisolone may need to be introduced/increased for 7 days with monitoring. A postnatal flare-up is also common and usually resolves within 2 to 6 weeks. Unlike polymorphic eruption of pregnancy, pemphigoid gestationis may recur in subsequent pregnancies, with earlier onset and increasing severity, and also with use of oral contraception or during menstruation. There have been reported cases of intrauterine growth restriction with this dermatosis, so antenatal fetal surveillance is crucial to watch for this complication. It is prudent to increase frequency of scanning to monthly if there is suspicion of intrauterine growth retardation. There is conflicting evidence about any increased risk of preterm labour with this condition. One in ten newborns may develop mild, self-limiting skin lesions due to a passive transfer of antibodies to the fetus.

Pemphigoid gestationis is described in association with other autoimmune diseases, including Graves’ disease and other autoimmune syndromes. Women who should be referred to a dermatologist include those with:

- Pemphigoid gestationis.
- Intrahepatic cholestasis of pregnancy.

Women who should be referred to a dermatologist include those with:

- Pemphigoid gestationis.
- Polymorphic eruption of pregnancy, atopic eruption of pregnancy or a localised area of itching or skin eruption where initial management fails.
- Skin eruptions associated with systemic symptoms.

Ideally, patients with any skin eruption should be seen in a joint obstetric/dermatology clinic.

**Conclusion**

Pregnancy results in a variety of physiological and pathological changes to the skin. The latter can be divided into two categories – those that can occur outside pregnancy and those that are unique to pregnancy. Idiopathic pruritus without obvious skin eruption is a common problem.

Diagnosis and management are dependent upon a structured history and examination, and understanding of serious and/or common dermatoses that may require referral to a dermatologist.

**Disclosure of interests**

None declared.

**References**

prevalence in relation to the development of obstetric cholestasis.


