REVIEW

# PREGNANCY AND LACTATION IN PATIENTS WITH PSORIASIS

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**ABSTRACT**

*Psoriasis is an inflammatory chronic, common skin disease that represents a great burden affecting people of all ages. It has no clear cause and although there are treatments none of them can guaranty remission. This pathology has a significant negative impact on people in all countries, affecting between 0.09% and 11.43%, which means at least 100 million people worldwide. A particular category is represented by pregnant women. Although it is reported that 55% of the patients have improved symptomatology during pregnancy, 21% reported no change and 23% suffered worsening of the illness. Psoriasis can be difficult to manage due to fluctuations in hormone levels. Even if patients can experience improvements during pregnancy, most of the women report worsening in the post-partum period (4-6 weeks). Pregnancy and lactation can also interfere with specific treatment for psoriasis. Psoriasis can increase the risk of gestational, diabetes, pre-eclampsia and hypertension in pregnancy, increased risk of preterm birth, low birth weight and emergency caesarean section. In order to have a positive outcome for the mother and the baby, careful multidisciplinary management is needed. The aim of this review is to summarize the notions in the literature regarding pregnancy with psoriasis and the current treatment trend in this group of patients.*

**KEYWORDS**: *pregnancy, psoriasis, drug safety management, pregnancy outcome*

## INTRODUCTION

Pregnancy with psoriasis can be difficult to manage due to the specific changes during this period and the restrictive options for treatment. Psoriasis is a chronic inflammatory disease that affects people of all ages so it is inevitable that from the female population with this pathology some of them will carry a pregnancy. World Health Organization reported the prevalence of psoriasis between 0.09% and 11.4% worldwide [1]. It has an unclear etiology, with different factors contributing to its onset like genetic predisposition, modification in the immune system response, trauma, sunburn, stress and others [2]. Patients with psoriasis will have skin and nail lesions (characteristic for this pathology – symmetrical, plaques with red papules, good delimitation, covered with scales that have a white/silver aspect) (Figure 1) and other comorbidities such as inflammatory arthritis, nail changes, cardiovascular conditions [1]. Psoriasis is a significant burden affecting the quality of life

of the patient even it is relatively limited to a specific body surface.

In the female population the mean time of onset or diagnosis of the disease is around 28 years [3]. In this period many women are of childbearing potential and some of them can be at the first pregnancy. In the United States were reported between 9000 and 15000 births in women with moderate to severe psoriasis [4]. Although psoriasis can improve in pregnancy, worsening can occur in some patients and in the post-partum period due to the hormonal imbalance. Psoriasis represents a problem for the fetal outcome. Moderate and severe psoriasis can complicate a pregnancy from conception until delivery. There were reported preterm delivery and low birth rate in these patients [5].

Psoriatic disease (psoriasis and/or psoriatic arthritis) can be different for every patient and has a large variation regarding symptomatology and severity during pregnancy. The evolution of the disease and the impact on the pregnancy cannot be predicted ahead but it is necessary that the medical team (obstetrician, dermatologist, rheumatologist) are prepared with a treatment plan. The way of birth must be discussed due to the possibility of genital psoriasis, skin sensitivity or Koebner phenomenon in vaginal or caesarian section delivery. The post-partum period can be a difficult one because of the symptomatology flair up which needs to adapt the treatment considering the possibility of lactation.

## MATERIALS AND METHOD

The aim of this paper is to synthetize the notions in the literature regarding the management of pregnant women with psoriasis, from conception until postpartum. We searched national and international health information sources, PubMed and Cochrane database, searching for “psoriasis”, “pregnancy” and “breastfeeding”.

## RESULTS

The influence of psoriasis in pregnancy can be separated in two aspects: the impact of the illness itself and the impact of the necessary treatment. The severity of psoriasis is evaluated by the BSA (body surface area) affected and it guides the necessary treatment. It can be mild, moderate or severe. The clinical forms are represented by psoriasis plague, inverse psoriasis, erythrodermic psoriasis, pustular psoriasis, psoriatic arthritis. The pregnancy outcome depends on the clinical form and the severity of the disease.

*Psoriasis and fertility*

Psoriasis affects equally men and women, with onset before the age of 40 in approximately 70% of cases [6]. Although there are few data regarding the impact of psoriasis on men and women fertility, studies on immune mediated inflammatory diseases (including psoriasis) have shown that this pathology can impact conceiving and pregnancy especially in the active episodes [6]. In association with an unhealthy lifestyle, systemic inflammation, hormonal and metabolic comorbidities in psoriasis decrease the reproductive function [6].

In the preconception period it is recommended that women respect a systemic drug-free interval for methotrexate (3 months) and retinoids (2 years) [7]. Patients considering to became pregnant should be advice to obtain a pregnancy in a period of remission or to wait an optimize control of the illness [7]. These are recommended in order to help minimize the flare-ups that can occur in some of the cases, mostly in moderate to severe ones [7].

*Impact of pregnancy on psoriasis*

Pregnancy influences the autoimmune diseases depending on the immunopathogenesis (Table 1). A study that analyzed the evolution of psoriatic women showed an improvement in more than half of the cases, but also a quarter had reported worsening [8]. If the evolution during the first pregnancy is positive, there are high chances that the following ones will have the same pattern. In a clinical evaluation of patients with psoriasis in pregnant and menstruating women was analyzed the affected BSA [9]. This study revealed that between 10 and 20 weeks of gestation there was a significantly decreasing in the psoriatic BSA and in the postpartum period there was a significant worsening in 65% of patients [9]. After 6 weeks postpartum was registered an increase of BSA.

The improvement of psoriasis in pregnancy is correlated with the increasing in

estrogen levels [9]. Other authors relate the positive evolution with the progesterone levels that may down regulate T-cell response and reduce keratinocyte-proliferation [10]. During pregnancy, the immune system changes and the T helper 17 and T regulatory cells that mediate psoriasis are down-regulated [11]. The positive evolution of symptomatology during pregnancy was reporter by patients with HLA-Cw0602 allele, whereas the non-carriers did not report remission [12].

| Study | No. of patients | Improvement | Worsening | No variation |
|---|---|---|---|---|
| Raychaudhuri et al. [8] | 91 | 56% | 26.4% | 17.6% |
| Murase et al. [9] | 47 | 55% | 23% | 21% |
| Boyd et al. [10] | 90 | 63.3% | 13.4% | 23.3% |

**Table 1 – Symptomatology evolution in pregnant patients with psoriasis**

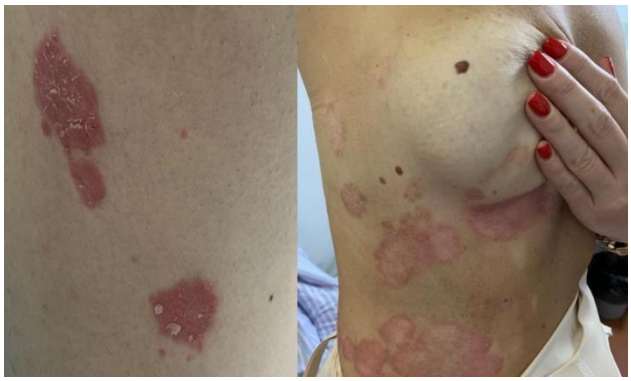

**Figure 1 – Well-defined pinkish, scaly plaques of variable sizes, thickness and shape in a symmetrical pattern on the trunk of a 30-year-old patient in the preconception period, under no treatment**

An exception for the positive evolution is represented by pustular psoriasis that usually worsen during pregnancy and is linked to impetigo herpetiformis [13]. Although it is controversial whether it is a separate pathology or a form of pustular psoriasis, impetigo herpetiformis is a very rare dermatosis that develops during last trimester, with severe maternal and fetal consequences [13]. The mechanism remains unclear but high progesterone, low calcium and reduced antileukoproteinase activity were incriminated.

*Impact of psoriasis on pregnancy*

The relationship between psoriasis and pregnancy is incompletely understood. The studies are limited, with potential bias, larger prospective studies being needed in order to assess the real impact of psoriasis and the specific drug therapy on pregnancy outcomes. Psoriasis may associate a constellation of illnesses like hypertension, obesity, depression, dyslipidemia, diabetes. A prospective study that analyzed patients with autoimmune disease reported that women with psoriasis are more likely to smoke, be depressive, gain weight and neglect prenatal multivitamins or folic acid supplements in the period before the pregnancy [13].

There are studies that focused on establishing if there is a link between the severity of psoriasis and some pregnancy complications. Moderate to severe psoriasis found to be associated with gestational hypertension, preeclampsia, cardiovascular disease and low birth weight of the newborn and preterm labor (Table 2) [14, 15].

The increased inflammatory activity encountered in psoriasis can lead to cytokine imbalance and endothelial dysfunction. The consequences are represented by the vascular modifications both systemically and local (placental modifications) [13]. The administration of systemic drug therapy during pregnancy for severe psoriasis lead to similar risk of low birth weight as the general population. This suggests that the risk is correlated with the disease itself [16].

| **Study** | **No. of patients** | **Pregnancy outcomes** (statistically significant) |
|---|---|---|
| Cohen-Barak et al. [14] | 35 women<br>(68 deliveries) | Spontaneous abortions<br>Macrosomia<br>Premature rupture of membranes<br>Hypertensive disease associated with pregnancy |
| Ben-David et al. [17] | 84 women<br>(145 deliveries) | Recurrent abortion<br>Chronic hypertension<br>Cesarean delivery |
| Yang et al. [16] | 1463 women with diagnosis of psoriasis<br>645 mothers with severe psoriasis | Newborn low birth weight |
| Lima et al. [18] | 122 women<br>(162 pregnancies) | Preterm birth<br>Low birth weight |

**Table 2 – Pregnancy outcome with psoriasis**

*Management of psoriasis in pregnancy and lactation*

For a couple that is trying to conceive it is recommended that they are on a remission period and the systemic treatments were stopped in advance. In this period, for the obstetrician and dermatologist the main concern is represented by the drug safety in order to avoid the teratogenic effect and other adverse risks. The therapy needs to be adjusted to have the best results with the minimum impact on pregnancy and lactation. The data are limited due to ethical reasons. Information was drawn from studies that evaluated the same agents in larger populations with other inflammatory disease [5].

For this category of patients, topical therapy can be indicated. Emollients and topical steroids are considered safe in pregnancy. Also, women can opt for UBV phototherapy.

In moderate to severe cases systemic therapy can be needed but there are limited data regarding their use in pregnancy [19]. Methotrexate and acitretin are strictly forbidden in pregnancy. The systemic treatments that are used in a relatively confident way [20] are represented by systemic corticosteroids, cyclosporine, and biologic therapy.

Even if corticosteroids are not used in common psoriasis, they can be used in patients with arthritis or impetigo herpetiform [13]. It may be used in pregnancy, with avoidance in the first trimester [21]. The use of corticosteroids in pregnancy was associated with congenital malformation especially when it was administrated in early pregnancy [21]. Prednisone and prednisolone gave the smallest fetal risk due to the limited transplacental passage [22]. It must be taken in consideration that the use of corticosteroids for a long period of time increases the risk of preterm labor and delivery, premature rupture of membrane and the usual maternal side effects like hypertension, preeclampsia and eclampsia [13].

Cyclosporine is considered to be the safest drug for psoriasis in pregnancy (does not have an absolute contraindication in pregnancy) [13]. The advantage is represented by the passive placental blood barrier cross with no mutagenic or teratogenic proprieties [13]. Most of the date regarding cyclosporine comes from registries of transplant recipients who receive this drug but in higher dose. There was an association with preterm birth and low birth weight but it was not clear if it was a side effect or the result of the underlying disease and comorbidities [13].

The biologic therapy is the most indicated treatment for psoriasis. In pregnant patients is important the placental barrier crossing and the excretion in the breast milk. The major antibody class that passes the placenta is represented by Immunoglobulin G [11]. In this category are included adalimumab, infliximab, etanercept. Certolizumab can be an option because it is a pegylated antigen-binding fragment antibody that cannot be actively transported through the placenta [23]. The use of anti-tumor necrosis factor (TNF) alpha in pregnancy is considered safe in the first half until 22-24 weeks [24].

A very important thing is that the women with biologic agents treatment in pregnancy and

especially the third trimester must be informed that levels of anti-TNF agents were detected at birth and the clearance can take until 1 year. This means that there is a possibility of an impaired immune response in the newborns. [25, 26]

Regarding breastfeeding while using biologic agents, most medication indications advise against breastfeeding. The recent data shows that in breast milk are detected low levels of TNF-alpha and so they can be safe in nursing [27]. Even so, the newborn levels of anti-TNF agents are even lower because of the protein degradation during digestion [13]. Regarding the use of other biologic agents there are no data available on the safety during nursing.

## CONCLUSION

In women with psoriasis is necessary a carefully conception planning in order to have a successful and uncomplicated pregnancy. Remission or stabilized psoriasis must be achieved before conception. An expectative approach or topical treatment must be considered for the mild forms of psoriasis during pregnancy. For severe or complicated cases of psoriasis, systemic therapy may be needed and the advantages and disadvantages will be evaluated for each patient. Cyclosporine and biological therapy should be carefully considered during pregnancy and/or breastfeeding, but may be a treatment alternative. Well controlled trials are needed to study the impact of biological therapy on women with psoriasis during pregnancy and breastfeeding.

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