



## Impact of Psoriasis on Pregnancy Desire and Possible Consequences on Fertility

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**ABSTRACT** **Introduction:** Approximately half of patients affected by psoriasis are women, and the management of female patients of childbearing age is an under-investigated topic. Some studies have shown a significant decrease in births in psoriatic patients due to intimacy and pregnancy avoidance and to potential birth complications.

**Objectives:** We sought to evaluate data on reproductive health in a cohort of female patients, to compare them with similar data in the general population and to assess the impact of psoriasis, especially genital psoriasis, on pregnancy desire and the prevalence of psoriasis in the children of patients with psoriasis.

**Methods:** This retrospective observational study involved adult female patients with a diagnosis of psoriasis made during or before childbearing age. The enrolled patients were asked questions concerning fertility and previous pregnancies in relation to their dermatologic disease.

**Results:** Of 100 women enrolled, 73 reported a history of pregnancy, for a total of 170 pregnancies. The average number of pregnancies to term and the average number of children per woman ( $1.2 \pm 1$ ) were lower than the national average. The percentage of miscarriages was 18.2%, higher than the national average; in particular, women with psoriatic arthritis had a greater percentage of miscarriages (27.4%). During the pregnancies, psoriasis was mainly stable (36.1%) or improved (29.2%), even though most patients (91.5%) did not follow any treatment.

**Conclusions:** Psoriasis impacts pregnancy desire and course. The management of psoriasis in women of childbearing age is crucial to minimize its burden on this vulnerable population.

## Introduction

Psoriasis is a high-prevalence skin condition with a chronic course, multifactorial etiology, and immune-mediated pathogenesis [1]. Approximately half of the patients affected are women, who, even today, face limitations, especially therapeutic ones, due to the changes that physiologically occur during different phases of their lives [2]. Moreover, the onset of signs and subsequent diagnosis in females is generally earlier than in males, leading to significant issues in the quality of life, especially in younger patients [3]. Since women of childbearing age represent a significant percentage of psoriatic patients, the influence of psoriasis on fertility and pregnancy should be considered and adequately addressed. There is a lack of practical guidance available to help manage the scenario when a patient with psoriasis plans to become pregnant or, since 50% of pregnancies are unplanned, is pregnant [4,5].

The impact on male and female fertility is unknown; however, an American study shows a significant decrease in births in patients with psoriasis [6]. One possible reason that has been hypothesized is the avoidance of intimacy that stems from psoriasis, especially when genitals are involved, which can often cause pain, embarrassment, and discomfort [4]. Some studies suggest that there may be an increase in preterm and or low birth weight births and an increased number of spontaneous and induced abortions [7,8]. Other inflammatory and autoimmune diseases similar to psoriasis, such as rheumatoid arthritis and inflammatory bowel disease, have been associated with the same complications due to immune dysfunction, inflammatory cytokine storm, and effects on endothelial cells, with subsequent systemic and placental vasculopathy [6,9]. However, not all studies are concordant; some do not detect a significantly increased risk of infertility, congenital disabilities, and other maternal complications [6,7].

## Objectives

Our aims were to evaluate data on reproductive health in a cohort of female patients followed at the Dermatology Clinic of IRCCS San Martino Polyclinic Hospital, to compare them with similar data in the general population, and to assess both the impact of psoriasis, especially genital psoriasis, on pregnancy desire and the prevalence of psoriasis in the children of patients with psoriasis.

## Methods

### Study Design

This retrospective observational descriptive, single-center study was conducted at the IRCCS San Martino Polyclinic Hospital Dermatology Clinic from November 2021 to May 2022.

## Study Population

Patients diagnosed with psoriasis followed on an outpatient basis at the Dermatology Clinic of the IRCCS San Martino Polyclinic Hospital were enrolled according to the following criteria:

- Female sex
- Age older than 18 years
- Diagnosis of psoriasis made at or before childbearing age
- Undergoing topical or systemic therapy, either traditional or biologic
- Acquisition of informed consent.

## Data Collection

One hundred patients were contacted to participate in an interview, conducted in person or by telephone, related to psoriasis and reproductive health. Sixty-one (61%) patients were interviewed in person during the outpatient follow-up, and 39 (39%) were contacted by telephone. After acquiring informed consent, the patients were asked 19 questions. The questions regarded the age of onset of psoriasis and current therapy, the presence of concomitant rheumatologic disease, the possible presence of genital psoriasis, pregnancy and the possible presence of children, course of pregnancy and health of children, and course of psoriasis during pregnancy. The questionnaire was structured in two parts: a first set of seven questions administered to all patients and a second set with the last 12 questions, administered only to women with a pregnancy history. The second part thoroughly investigated the course of the pregnancy by researching the type of delivery, the presence of voluntary interruptions of pregnancy (IVG) and/or miscarriages, any history of complications of the pregnancy, and the treatment carried out during the said period. Information on live-born children was also gathered, with questions regarding the presence of noteworthy diseases, including, first and foremost, psoriasis.

## Statistical Analyses

An initial analysis was performed using descriptive statistical analysis through frequencies and appropriate measures of dispersion. Continuous variables were compared using the Mann-Whitney U test to reveal any differences between the three groups (presence/absence of arthritis or presence/absence of genital psoriasis). *P*-values less than 0.05 were considered significant.

## Results

### Sample Description

A total of 100 women were enrolled; 96 patients (96%) were of Caucasian ethnicity, three (3%) of Hispanic ethnicity, and

**Table 1. Current Treatments For Psoriasis.**

Adalimumab	13 (13%)
Brodalumab	6 (6%)
Certolizumab Pegol	3 (3%)
Secukinumab	18 (18%)
Etanercept	2 (2%)
Guselkumab	9 (9%)
Ixekizumab	15 (15%)
Risankizumab	9 (9%)
Tildrakizumab	13 (13%)
Ustekinumab	12 (12%)

one (1%) of Asian ethnicity. The mean age was  $49.26 \pm 19$  years (IQR: 19; 39-58), with a minimum value of 18 and a maximum of 82. The mean age at disease onset was 21.85 years (IQR: 16; 14-30), with a minimum value of one and a maximum value of 50.

All patients enrolled (100%) at the time of the interview were on specific biologic drugs for the treatment of psoriasis. Eighteen patients (18%) were on therapy with secukinumab, 15 (15%) with ixekizumab, 13 (13%) with tildrakizumab, 13 (13%) with adalimumab, 12 (12%) with ustekinumab, 9 (9%) with guselkumab, nine (9%) with risankizumab, six (6%) with brodalumab, three (3%) with certolizumab, and two (2%) with etanercept (Table 1).

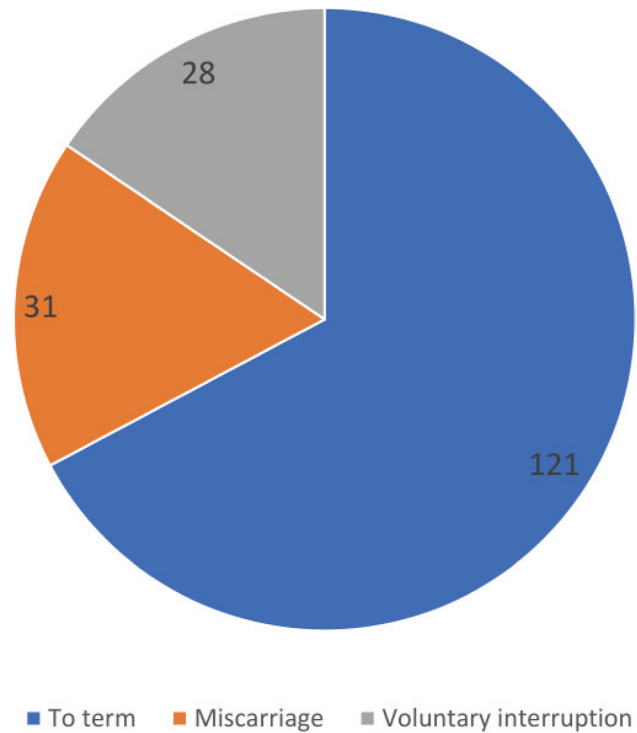
Thirty-six patients (36%), in addition to skin involvement, had psoriatic arthropathy, diagnosed by a rheumatologist. Forty-seven patients (47%) had a history of genital psoriasis.

Seventy-three out of 100 patients (73%) had a history of previous pregnancy and were therefore selected for the study. In this subgroup, the mean age was  $53.6 \pm 12.23$  years, with a mean age at disease onset of  $23.26 \pm 12.10$  years.

### Survey Results

Regarding the women with reported pregnancy, only four (5.5%) saw their psoriasis as a limitation in pregnancy seeking. In contrast, 69 patients (94.5%) did not experience this problem. Thirty-three patients (45.2%) reported that they had suffered or still suffered from genital psoriasis. The total number of pregnancies for the whole sample was 170, with an average per woman of  $1.7 \pm 1.40$ . One hundred and twenty-one (71.2%) were carried to term with an average rate of pregnancy to term of  $1.2 \pm 1$  (Figure 1).

Among the 73 patients with a history of pregnancy, for a total number of 170 pregnancies, the number of those terminated through spontaneous abortions and voluntary interruptions of pregnancy (IVGs) was 49/170 (28.8%). The number of spontaneous abortions was 31/170 (18.2%) and the number of IVGs was 18/170 (10.6%). Among patients

**Figure 1.** Pregnancy outcomes.**Table 2. Reported Complications During Pregnancy.**

Dystocia	1 (1%)
Emergency C-section	1 (1%)
Gestational diabetes	5 (5%)
Pre-eclampsia	2 (2%)
Cholestasis of pregnancy	1 (1%)
Hyperemesis gravidarum	1 (1%)

with psoriatic arthropathy, the rate of spontaneous abortions was 17/62 (27.4%). The number of patients who reported at least one miscarriage was 19/73 (26%) in the whole population and 9/25 (36%) the subgroup of patients with psoriatic arthritis. Joint involvement in psoriasis presents a correlation with the prevalence of miscarriages, IRR 2.11 (1.12-3.99),  $P < 0.05$ . Regarding the type of delivery, out of 121 pregnancies carried to term, 77 (63.6%) were vaginal deliveries, while cesarean delivery was performed in 44 pregnancies (36.4%). Only 11/170 (6.5%) pregnancies had complications, as shown in Table 2. The mean age during pregnancy (considering the mean age in women who had reported more than one pregnancy) was  $28.9 \pm 5.29$  years, while the calculated mean age at first pregnancy was  $27.0 \pm 6.28$  years.

Regarding the course of psoriatic disease, psoriasis did not change during pregnancy in 26 patients (36.1%), improvement was reported in 21 patients (29.2%), there was a worsening of the condition in 9 patients (12.5%), and

psoriasis was still not present at the time of pregnancy in 16 patients (22.2%), exacerbating later in the postpartum period.

Regarding therapy during pregnancy, 65 patients (91.5%) did not use psoriasis-specific therapy, while only six (8.5%) continued/initiated treatment.

Regarding the presence of children, most patients carried at least one pregnancy to term. Seventy (95.9%) patients had at least one child, while only three (4.1%) did not carry to term any pregnancy. The average number of children per woman was  $1.7 \pm 0.72$ , with a minimum value of one and a maximum value of four.

The survey also considered a possible correlation between genital psoriasis and the number of pregnancies.

Of the 47 patients with genital psoriasis, 33 (70.2%) had at least one pregnancy, compared to 40/53 (75.5%) patients without genital involvement. There was no significant correlation between genital psoriasis and occurrence of pregnancy.

Lastly, the study investigated the presence of significant diseases in the children of mothers with psoriasis. Fifteen patients (21.4%) reported health issues in at least one of their children, while 55 patients (78.6%) reported having healthy children. Of the 15 patients with at least one affected child, nine (12.9%) reported a child with psoriasis.

## Discussion

The study of reproductive health in psoriatic women is a hugely developing area of research. More and more scientific evidence correlates the skin condition with alterations in reproductive life. In particular, systemic inflammation, the increase in comorbidities, and the psychological impact of psoriasis have been studied. Psoriasis is a disease characterized by lesions of visible skin; since many of the patients affected are young women, this leads to a significant impact on their quality of life.

The first objective of this study was to evaluate the available data on the reproductive health of women with psoriasis and to compare them with similar data from the general population. Data analysis showed a total number of 170 pregnancies, 121 of which carried to term. The average index of pregnancies to term in the entire sample was  $1.2 \pm 1$ , which is lower than the reported national average over the past 50 years. Similarly, the average number of children per woman was  $1.2 \pm 1$ , also lower than the national average. These results could be primarily due to the systemic inflammatory condition, leading to a deficit in placental immune modulation and consequently more issues in pregnancy [10]. Additionally, the psychological condition of patients, who are often unwilling to have children or have difficulties in conception due to discomfort and pain, should not be

overlooked [4]. Relative to maternal age, the survey found an average age of conception of  $28.9 \pm 5.29$  years, which, compared to the average in the general population, does not present significant differences.

Another significant finding from the study was that the percentage of miscarriages was 18.2% of the total number of pregnancies (95% CI: 13.2–24.7%). This data point, when compared with the general population, which over the years has had a miscarriage rate of about 10–14% [11], is higher. Moreover, of the 73 patients with a history of pregnancy, 26% also had a history of miscarriage, which is significantly higher than the available data in the general population (IRR: 1.86; 95% CI: 1.26–2.74;  $P = 0.005$ ). This finding highlights that patients with psoriasis have more miscarriages. The reasons that could explain this finding are the increase in inflammatory cytokines, and particularly TNF- $\alpha$ , which have been associated with an increased risk of miscarriage [10], the teratogenic effect of many drugs used to treat psoriasis [4], and the increase in maternal age, which is associated with an increase in comorbidities including metabolic syndrome, anxiety or depression, alcohol abuse, and smoking, factors with a known detrimental effect on pregnancy [4]. The latter finding also agrees with recently published studies, thus favoring the condition's link with increased miscarriages [12].

Furthermore, the rate of miscarriages in patients with psoriatic arthropathy was much higher than in patients with only cutaneous disease: 27.4% (95% CI: 17.9–39.6) vs 13% (95% CI: 17.9–20.6), respectively. The comparison between the two groups proved significant with IRR: 2.11 (1.12–3.99).

This difference may be explained by the fact that patients with psoriatic arthritis present a disease with a more significant systemic impact, leading to increased comorbidities and aggravating the inflammatory condition [13]. In addition, patients with psoriatic arthritis often require special therapies, which negatively impact conception and the physiological course of pregnancy [14].

Relative to the number of cesarean deliveries, the number of pregnancies carried out by surgical delivery in the sample was 44 (36.36%), which is aligned with the available data in the general population. Recent studies show that this percentage is slightly higher in patients with psoriasis [12]. This is most likely due to more significant complications during delivery such as preeclampsia and abnormalities at the placental level caused by the inflammatory vasculopathy and the different maternal-fetal relationship [10,12,15].

The survey also provided data on the prevalence of complications in pregnancy. The rate of serious complications was 6.5%, which is lower than the reference rate in the general population, (25.4%) [11]. This finding also does not appear to agree with the literature, which defines psoriasis

as a possible causative/aggravating factor in pregnancy complications [15]. In the study, this result could be ascribable to the limited number of patients in the sample and to the fact that being a retrospective study, the accuracy of specific data may only be partially reliable.

Regarding the course of psoriasis in pregnancy, the survey found that psoriasis did not change during pregnancy in 26 patients (36.1%). In 21 patients (29.2%), improvement was reported; in nine patients (12.5%), there was a worsening of the condition, and in 16 patients (22.2%), psoriasis was still not present at the time of pregnancy, exacerbating later in the postpartum period. These data agree with those in the literature, which reports that 55-56% of pregnant women with psoriasis reported improvement in pregnancy, 16-21% noticed no change, and only 23-24% worsened [16,17]. What may explain this slight difference, especially the higher percentage of patients in clinical stability is that the study is retrospective. The patients' self-assessment of the lesions may therefore have been biased, compared with an accurate specialist clinical evaluation.

Regarding therapy during gestation, 65 patients (91.5%) did not use psoriasis-specific therapy, while only six (8.5%) continued/initiated treatment. This result might be due to the fear of the consequences that therapies might have during pregnancy. Moreover, because the disease frequently tends to improve during pregnancy, there often is no need to continue with treatment. Nonetheless, a significant number of patients who experienced psoriasis worsening or stability during pregnancy still were not receiving treatment. However, it must be noted that many of the reported pregnancies occurred in the pre-biologic era, when systemic treatments were not compatible with pregnancies. Currently, certolizumab pegol, a biologic drug suitable for psoriasis during pregnancy, is available and recommended for women who are planning to conceive. However, while anti-interleukins should be discontinued when planning pregnancy, new data suggest that exposure to most biologic drugs does not cause significant harm to the fetus [18]. This allows the dermatologist to plan the most effective treatment in fertile female patients, with the possibility of switching to certolizumab in case of pregnancy diagnosis or desire.

The second purpose of the study was to assess the impact of psoriasis, especially genital psoriasis, on the ideation of motherhood. Patients with an occurrence of pregnancy were selected, and a correlation between genital psoriasis and the number of pregnancies was studied. Of 73 patients, 33 reported pregnancy with genital psoriasis involvement, with a mean of  $2.3 \pm 1.09$ . In contrast, there were 40 patients without genital psoriasis who reported at least one pregnancy, with a mean of  $2.4 \pm 1.14$ . The correlation does not show statistical significance ( $P 0.82$ ), so it emerges from our study that genital involvement does not significantly impact

reproductive life, even though the impact of this condition on sex life is known and described in the literature.

The third and final objective of the study was to assess the prevalence of psoriasis in the children of patients with psoriasis. Considering the 121 pregnancies carried to term and twin births (122 children), nine (7.37%) children had the same condition as the mother. This figure can be defined as underestimated because some of the children in the sample are still young and thus have a good chance of developing psoriasis in the future. This finding confirms sources in the literature, which show that children of patients with psoriasis are more likely to develop the disease [19]. It has been seen that psoriasis has a vital genetic component and that children from two affected parents are 50% more likely to develop psoriasis. If, on the other hand, there is only one affected parent, the probability drops to 16% (still much higher than the general Italian population, among which the prevalence is about 3%) [19,20,21].

## Conclusions

Psoriasis is a chronic disease that can impact all phases of life, including conception and pregnancy. In our retrospective study, we found that women with psoriasis had fewer pregnancies and a greater prevalence of miscarriages than the national average. In particular, women with psoriatic arthritis had a significantly higher rate of miscarriages than women without joint involvement, which may be explained by the higher levels of systemic inflammation that accompany joint involvement in psoriasis. We also confirmed the current knowledge on the course of psoriasis during pregnancy and on the hereditary transmission of psoriasis in children conceived by affected mothers. Despite the availability of new effective and, in some cases, pregnancy-safe treatments, the management of psoriasis in women of childbearing age deserves greater attention from specialists.

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