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Letter to the editor

Psoriasis features associated with infertility and adverse pregnancy outcomes



Immune-mediated diseases can affect fertility and increase the risk of adverse pregnancy outcomes. The two peak ages of psoriasis onset in women are 20 to 29 years, i.e. mid-childbearing age, and 50 to 59 years. A systematic review on psoriasis and a case-control study on psoriatic arthritis did not find worse pregnancy outcomes [1,2]. However, while two recent population-based studies found no impact on fertility, increased risks of adverse pregnancy outcomes were noted [3,4].

We conducted an analytical retrospective single-center cohort study in our series of female patients with psoriasis who consulted between 2015 and 2019. We included women older than 18 years and excluded those who did not plan a pregnancy. The primary objective was to estimate the frequency of infertility and adverse pregnancy outcomes. The secondary objective was to screen for patient or disease features associated with these complications. The study protocol was approved by our hospital's ethics committee. Data collection was carried out in three steps. First, we searched the registry for eligible patients. Second, we checked their medical files. Third, we called or met them at a medical consultation. We collected details of patients and psoriasis characteristics, fertility disorders, and pregnancy outcomes. We analyzed the different associations between complications and patients' features using a *t*-test for equality of means for means, a Pearson Chi-squared test or Fisher's exact test for proportions, and a likelihood ratio test for categorical variables.

We found 120 patients eligible for the study. We excluded 39 patients who did not plan a pregnancy and 5 others who did not agree to participate in the study. Finally we studied 76 patients, all Caucasians, with a total of 240 pregnancies. Patient characteristics and descriptive data about fertility are shown in Table 1. Of note, 60.5% of patients were smokers, though no statistical correlation was found between smoking status and study endpoints (infertility, pregnancy adverse events). Ten patients (13.1%) had primary infertility, of whom 4 could never become pregnant, and 6 could never give birth to a child. We screened for conditions that might interfere with fertility or pregnancy outcomes (uterine fibroids, ovarian cysts, anti-phospholipid syndrome, deep venous thrombosis, and others), but we only included those without any identified disease after investigation. However, we did not collect data about possible genetic investigations. Primary infertility was significantly correlated only with the severity of psoriasis ($P=0.049$). The proportion of patients with primary infertility was far higher than the prevalence of primary infertility among women wishing to become pregnant in the Middle East, estimated at 2 to 3% [5]. The severity of the inflammatory state could account for the correlation between fertility disorders and psoriasis severity. This proportion may also increase if we consider infertile patients failing to become pregnant in the first 12 months of regular unprotected sexual intercourse.

Table 1

Patient characteristics and descriptive data about fertility outcomes.

Characteristic	Patients = 76
Age at onset of psoriasis	
- mean (\pm standard deviation)	33 (\pm 22)
- median (Q1, Q3)	29 (17,46)
Psoriasis, phenotype and most involved site	
- Diffuse, plaque, <i>n</i> (%)	49 (64.4)
- Diffuse, guttate, <i>n</i> (%)	7 (9.2)
- Diffuse, pustular, <i>n</i> (%)	5 (6.5)
- Erythrodermic, <i>n</i> (%)	3 (4)
- Localized, scalp, <i>n</i> (%)	6 (7.9)
- Localized, nails, <i>n</i> (%)	5 (6.5)
- Localized, inverse, <i>n</i> (%)	1 (1.3)
Psoriasis, global assessment by a physician (worst level recorded during disease follow-up)	
- Mild, <i>n</i> (%)	25 (32.9)
- Moderate, <i>n</i> (%)	24 (31.5)
- Severe, <i>n</i> (%)	27 (35.5)
Psoriasis, comorbidities	
- Psoriatic arthritis, <i>n</i> (%)	17 (22.3)
- Diabetes, <i>n</i> (%)	11 (14.4)
- Hypertension, <i>n</i> (%)	19 (25)
- Dyslipidaemia, <i>n</i> (%)	13 (17.1)
- Cardiovascular disease, <i>n</i> (%)	4 (5.2)
- Depression, <i>n</i> (%)	10 (13.1)
- Inflammatory bowel disease, <i>n</i> (%)	2 (3.3)
Psoriasis control at most patient visits: controlled, <i>n</i> (%)	46 (60.5)
Age at first planned pregnancy	
- mean (\pm standard deviation)	25 (\pm 7)
- median (Q1, Q3)	24 (20, 29)
Fertility profile	
- No pregnancy, <i>n</i> (%)	4 (5.2)
- Number of miscarriages, mean (\pm SD)	1 (\pm 1)
- <i>In vitro</i> fertilisation, <i>n</i> (%)	1 (1.3)
- Parity, mean (\pm SD)	2 (\pm 2)

Data from the Spanish psoriasis registry indicated a fertility rate among women of childbearing age with moderate to severe psoriasis which was less than half that in the Spanish population (16.3 vs. 38.6 per 1000 woman-years) [6].

Thirty-one patients (40.7%) experienced at least one miscarriage during their childbearing years. The high number of miscarriages in our series was not found in studies that examined large databases of women with psoriasis, where spontaneous abortions in first pregnancies reached 9.3% and 7% in the psoriasis and the non-psoriasis groups, respectively [3,7]. Of the 42 patients (55.25%) who planned a pregnancy after the onset of psoriasis, 38 gave birth to at least one child. In patients who became pregnant, the mean time between marriage and first pregnancy was 1.23 [1–4] years. Of the 240 pregnancies included in total, 54 (22.5%) led to miscarriage, and 186 (77.5%) led to birth, of which 46 (24.7%) were by caesarean section, 22 (11.8%) involved maternal complications (preeclampsia, labor dystocia, threatened premature labor, placenta previa, gestational diabetes), and 8 (4.3%) were marked by fetal complications (stillbirth, prematurity, tachycardia, other).

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Logically, pregnancies involving maternal or fetal complications had significantly more caesarean sections ($P=0.001$). Compared to observational and population-based studies, the proportion of maternal and fetal complications was similarly high in our series [1,3,4]. Of note, in the comparative non-psoriatic population of the Swedish register, maternal and fetal complications occurred in 6.3% and 5.3% of patients, respectively [4]. The presence of maternal complications was significantly correlated with a higher age at first planned pregnancy ($P=0.038$), an already known factor, and with psoriatic arthritis ($P=0.043$), in contrast with the results of Polachek et al. [2]. A recent study showed that increased disease activity, in rheumatoid arthritis and axial spondyloarthritis, was a risk factor for pregnancy complications [8]. As the number of patients with fetal complications was small, we felt it irrelevant to perform statistical analysis. A recent meta-analysis by Xie et al. showed that, compared with the general population, pregnant women with psoriatic diseases have a significantly higher risk of adverse maternal but not fetal outcomes [9].

The limitations of the study included its retrospective design, the absence of a control group, memory bias, and the fact that some of the patients had late onset psoriasis after the end of their child-bearing years. We did not perform a sensitivity analysis to account for the possibility of misclassification of exposure in these patients. We hypothesized that certain of these patients had discrete signs years before the psoriasis flare-up leading to diagnosis, and that most patients had susceptibility alleles predisposing to psoriasis with a subclinical effect on immune pathways. Otherwise, data were descriptive, leading to possible confounding factors that could interfere with interpretation of the results. Also, we only noted the most widely prescribed treatments during the long follow-up without identifying specific treatments given during pregnancy because the file notes might not cover the whole lifespan and patients might not precisely recall the details of their treatment during pregnancy. We could not exclude the possibility of an unexpected pregnancy occurring during use of a contraindicated systemic treatment.

In conclusion, this study provided more data suggesting that fertility and pregnancy outcomes are negatively affected in women with psoriasis.

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Disclosure of interest

The authors declare that they have no competing interest.

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