Title: Exploring the Relationship between Psoriasis and Pregnancy: A Systematic Literature Review

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Discussion Points:

- How does pregnancy impact the presentation of psoriasis? This literature review dives into the different hormones and genes that relate pregnancy and psoriasis, such as estrogen, progesterone and the HLA-Cw6 allele!

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ABSTRACT.

The purpose of this systematic literature review was to thoroughly examine the relationship between psoriasis and pregnancy to elucidate possible new routes of treatment. Findings from this review help close the gap in the literature on the topic as well as educate physicians and women with psoriasis who are pregnant on how psoriasis may present along the course of pregnancy and thereafter. Searches were primarily conducted in three databases: PubMed, Scopus, and Embase. Articles considered for inclusion in this literature review focused on the presentation of psoriasis during pregnancy. The literature sample obtained consisted of 14 peer-reviewed articles published from 2012-2022. As codes were identified, a master code list was developed. Second cycle coding involved categorizing of the data allowing for codes to combine and emerge as themes. Five themes were identified through categorical analysis: Immunology, general sex hormones, estrogen, progesterone, and the HLA-Cw6 allele. Collectively, these findings elucidate the individual nature of psoriasis and identify progesterone as a possible non-teratogenic therapy. Primarily, the presence of the HLA-Cw6 allele in a woman's genome along with the individual variation of estrogen receptors reinforces the researcher's recommendation for genetic testing following a psoriasis diagnosis. This genetic testing may allow patients and physicians to best understand what to expect of psoriasis during pregnancy as well as help determine the most efficacious treatment course to follow for therapy.

Key Words: pregnancy, psoriasis, HLA-Cw6, IL-23, therapy

INTRODUCTION.

Psoriasis affects millions of adults nationally-- typically around 3% of the population. It predominates in non-Hispanic white individuals and is one of the most common auto-immune disorders in the US.[1] Current treatments include topical medications (usually steroids which weaken the skin over time) and regular injectable biologics such as adalimumab (Humira), certolizumab pegol (Cimzia), and guselkumab (Tremfya).[2] Previous studies stress the possible negative teratogenic effects of continuing biologic medications during pregnancy, and recommend the use of topical treatments during this time instead.[3, 4] It is commonly believed that psoriasis symptoms tend to improve during pregnancy, however, there is limited research documenting the extent to which this occurs[3, 4] and how. The aim of this literature review was to thoroughly examine the published literature on the relationship between psoriasis and pregnancy to elucidate possible new routes of treatment. Findings from this review help close the gap in the literature on the topic as well as educate physicians and women who have psoriasis and are pregnant on how psoriasis might progress during the course of gestation and thereafter.

Background

Psoriasis is a heavily understudied disease globally. Up to 81% of countries have inadequate data on the epidemiology of psoriasis, let alone the pathogenesis behind the disease.[5] From the data that is available, it has been observed that the prevalence of psoriasis is variable geographically—it seems to be more common in high income countries and in regions with older populations.[5] The researcher theorizes this may be due to increased availability of medical resources in those regions, leading to higher rates of diagnosis. Psoriasis can be defined simply as a dysregulation of keratinocyte differentiation and proliferation.[6] These keratinocytes are responsible for early innate immune responses, which is why psoriasis is considered an auto-immune disorder—dysregulation of the body's innate immune responses leads to the body attacking itself.[6] The systemic disease of psoriasis is associated with a number of comorbidities, including metabolic syndrome, obesity, depression, arthritis, and low birth weight for pregnant women.[4] It is therefore of great interest to find a sustainable, safe treatment for psoriasis that is suitable even for pregnant women.

Achieving an accurate diagnosis of psoriasis can be arduous. It is often confused with eczema, particularly in children, because although psoriasis can present at any point in one's life, it often presents during the reproductive years (20s) or during late adulthood (50s-60s), but can occur at any age.[7] Biopsy can be used to confirm a clinical diagnosis, but it isn't suggested until several topical treatments have been tried in order to reduce possible scarring from the procedure. Mild psoriasis is defined as having affected Body Surface Area (BSA) under 10 and Psoriasis Area and Severity Index (PASI) score under 10.[4] Moderate to severe psoriasis will have one or both of these scores over 10, indicating significant surface area affected to a high level of severity.[4]

The management of psoriasis following a diagnosis is highly individualized. For some, topical creams hold the plaques at bay, using reapplication with flareups as needed. For others, the plaques are persistent or recalcitrant to topical treatments, requiring more intensive treatment. Traditional biologics have focused on reducing Th1-mediated inflammation, as it was believed that this was the primary driving factor behind lesion formation.[8] Modern therapies also include the Th17 response in their effects, specifically targeting IL-17 and

IL-23.[9] Even still, no one single therapy is a perfect fit for every patient, and particularly for pregnant women, there is a gap in intensive treatments available for use due to concern with teratogenic effects. The researcher theorizes that sex hormones could be a possible new route for treatment that would be safe for use during pregnancy, pending genetic compatibility testing.

METHODS

Role of the Researcher

The researcher recognizes personal bias in embracing a pragmatic framework. The researcher was diagnosed with moderate to severe psoriasis at the age of 22 after nearly 2 decades of dermatologic issues from the age of 4. As a patient, she struggled with numerous dermatologists and medications to find treatment, and this experience furthered the motivation to understand the pharmacology and pathogenesis behind the disease. Psoriasis during pregnancy is of particular interest to the researcher who is currently a first-year medical school and is interested in specializing in dermatology or women's health.

Search Strategy and Selection Criteria

Searches were primarily conducted between April and June 2022 in three databases (PubMed, Scopus, and Embase) available via the University of South Florida library network. Searches were also conducted in Cochrane and clinicaltrials.gov and yielded no relevant results. Articles for consideration to be included in this literature review focused on the presentation of psoriasis during pregnancy. Keywords used in the searches included *psoriasis, pregnancy, severity,* and *surface area. Estrogen* and *progesterone* were also relevant search terms used to identify the physiology behind any relationships observed. Medical subject headings (MeSH) such as *gestation, pregnancies,* and *psoriases* were used to capture any relevant articles related to the search terms. The filter for English only was used because it is the only language the researcher can speak with academic fluency. Publication dates were originally limited to 5 years in order to find current, medically relevant information, however, limited search results led the decision to increase the range to the last 10 years (2012-2022).

Database	String	Results
PubMed*	Progesterone and psoriasis	9
	Estrogen and psoriasis	38
	(severity[tiab] OR "surface area"[tiab]) AND (("Psoriasis"[Mesh] OR Psoriases[tiab] OR Plaque[tiab] OR Psoriasis[tiab]) AND ("Pregnancy"[Mesh] OR pregnancy[tiab] OR Pregnancies[tiab] OR Gestation[tiab]) AND ((y_10[Filter]) AND (english[Filter])))	57
Embase	('psoriasis'/exp OR psoriases:ti,ab OR plaque:ti,ab OR psoriasis:ti,ab) AND ('pregnancy'/exp OR pregnancy:ti,ab OR pregnancies:ti,ab OR gestation:ti,ab) AND (severity:ti,ab OR 'surface area':ti,ab) AND [2012-2022]/py	132
Scopus	(ABS(severity OR "surface area") AND ABS(Psoriases OR Pustulosis OR Psoriasis OR plaque) AND ABS(pregnancy OR Pregnancies OR Gestation)) AND (LIMIT-TO (PUBYEAR,2022) OR LIMIT-TO (PUBYEAR,2021) OR LIMIT-TO (PUBYEAR,2020) OR LIMIT-TO (PUBYEAR,2019) OR LIMIT-TO (PUBYEAR,2018) OR LIMIT-TO (PUBYEAR,2017) OR LIMIT-TO (PUBYEAR,2016) OR LIMIT-TO (PUBYEAR,2015) OR LIMIT-TO (PUBYEAR,2014) OR LIMIT-TO (PUBYEAR,2013) OR LIMIT-TO (PUBYEAR,2012))	45

Fig. 1 Table of strings used for each database searched for the purposes of the literature review. Results were counted on 5/25/2022. *PubMed searches were performed on 5/20 and the results were counted on 5/25.

Inclusion and Exclusion Criteria

The researcher intended to identify articles focused on the changes in presentation of psoriasis during pregnancy. Because of the general search terms used, many articles relating to the safety of available drug treatments for psoriasis during pregnancy were found and subsequently excluded from analysis. Due to the fluctuating hormones in pregnancy, articles investigating the effects of sex hormones on psoriasis were included in the review. From the initial search results, titles and abstracts were reviewed for potential relevance. Articles were included if the article was peer-reviewed and mentioned or was about changes or factors of psoriasis presentation during pregnancy.

Coding

Data coding followed Saldaña's (2016) methods of first cycle and second cycle coding. All data sources (i.e., articles; *N* = 14) were entered into the Excel data collection matrix (Appendix A). First cycle coding began with the researcher hand coding all articles using an a priori code list adopted from Boote and Beile's (2005) Literature Review Scoring Rubric.[10]

As codes were identified, a master code list was developed. Second cycle coding involved theming of the data allowing for codes to combine and emerge as categories.[11] Coding ended with code weaving to create a narrative to see how categories and emergent themes fit together to answer the guiding questions for this review.[11]

Author	Code	Category	Theme
A. A. Simionescu, B. M. Danciu and A. M. A. Stanescu	IL23 stimulates Th17	Th17 mediation	Immunology
G. A. Vena, N. Cassano, G. Bellia and D. Colombo	psoriasis is th1 and th17 mediated	Th17 mediation	Immunology
G. A. Vena, N. Cassano, G. Bellia and D. Colombo	pregnancy decreases th17 response	Th17 mediation	Immunology
M. B. Hoffman, M. Farhangian and S. R. Feldman	Th17 and IL-23 involvement	Th17 mediation	Immunology
M. Danesh and J. E. Murase	psoriasis is th17 mediated, driven by IL-23. th1 is secondary	Th17 mediation	Immunology
M. Danesh and J. E. Murase	psoriasis is driven by IL17 producing T cells (Th17) not Th1	Th17 mediation	Immunology
M. Danesh and J. E. Murase	IL23 required for Th17 expansion	Th17 mediation	Immunology
M. Danesh and J. E. Murase	th17 is decreased in healthy pregnancies	Th17 mediation	Immunology
M. B. Hoffman, M. Farhangian and S. R. Feldman	mediated by T helper cells	T cells	Immunology

S. Hellberg, J. Raffetseder, O. Rundquist, R. Magnusson, G. Papapavlou, M. C. Jenmalm, et al.	CD4 T cells are activated in disease pathogenesis	T cells	Immunology
S. Hellberg, J. Raffetseder, O. Rundquist, R. Magnusson, G. Papapavlou, M. C. Jenmalm, et al.	P4 dampens T cell activation by affecting genes	T cells	Immunology
S. Hellberg, J. Raffetseder, O. Rundquist, R. Magnusson, G. Papapavlou, M. C. Jenmalm, et al.	STAT1 and STAT3 are enriched in disease genes	T cells	Immunology

Fig. 2 This table contains real sample codes from the master list showing how categories and themes were extracted. These codes were all taken from the "Immunology" theme to show how multiple articles can converge on the same codes and categories to elucidate a higher-order theme. Under a particular theme, there may be multiple categories. For example, under the theme "Immunology," the categories "Th17 mediation" and "T cells" were discussed.

Sample

The literature sample obtained consisted of 14 peer-reviewed articles published from 2012-2022. Six of the articles were qualitative studies and eight were quantitative studies. Articles came from a wide range of countries including the United States, Lithuania, Slovenia, Taiwan, and Great Britain.

Limitations and Delimitations

The researcher recognizes limitations in the literature review. Only the databases Embase, Scopus, and PubMed were used because they were most readily accessible as per the University of South Florida library network. After obtaining articles for review, one source was excluded because the full text of the article could not be obtained; only the abstract was available. Future research should repeat the search strategy of this paper, while also including other relevant databases to capture all pertinent information related to the topic.

Definitions

Koebner Phenomenon- presentation of a psoriatic skin lesion following trauma[12]

RESULTS.

Findings

After completing the coding process for the 14 articles included in this review, five themes were identified through categorical analysis of the data: Immunology, general sex hormones, estrogen, progesterone, and the HLA-Cw6 allele. Collectively, these findings elucidate the individual nature of psoriasis. Primarily, the presence of the HLA-Cw6 allele in a woman's genome along with the individual variation of estrogen receptors supports the researcher's recommendation for genetic testing following a psoriasis diagnosis. This genetic testing may allow patients and physicians to best understand what to expect of psoriasis during pregnancy as well as help determine the most efficacious treatment course to follow.

Sex Hormones

Given that keratinocytes are the main cell type of epidermis, it is helpful to explore the factors that affect cell differentiation. Keratinocytes are responsible for regulating early innate immune responses, and androgens specifically are involved in skin cell pigmentation, aging, proliferation, wound healing, and inflammation[6]. Sobolev et. al found that there are significant differences in levels of sex hormones between psoriasis patients and healthy controls.[13] Estradiol (E2) and progesterone (PG) were significantly higher in healthy subjects whereas testosterone levels were sharply risen in psoriasis patients. This is bolstered by data from post-menopausal psoriasis patients who have further reduced E2 and PG levels and increased testosterone levels compared to post-menopausal healthy controls, reinforcing the role of sex hormones in psoriasis.
The relationship of psoriasis with sex hormones goes even further, impacting ovarian reserve (the remaining follicular pool). Patients with psoriasis have been found to have higher FSH levels, particularly, a higher FSH/LH ratio than healthy controls.[14] AFC (antral follicle count) was also reduced. Although these findings did not correlate with the severity of disease, diminished ovarian reserve can lead to POF, or premature ovarian failure. Tuğrul et. al explains that ovarian antibodies attack the ovarian reserve, causing autoimmune oophoritis.[14] This is clinically relevant for women with psoriasis who are having trouble conceiving, and the altered sex hormone levels are associated with poorer pregnancy outcomes as well. Therefore, it is of interest for physicians to recommend reproductive fertility testing for women who have been diagnosed with psoriasis to identify possible sex hormone deficits that can be addressed during pregnancy to address both psoriasis presentation and pregnancy outcomes.

Estrogen

The role of estrogen is highly debated in the pathogenesis of psoriasis. Oral contraceptives have been shown to decrease the severity of psoriasis, but the exact mechanism is unknown.[3, 8, 13, 15] Estrogen is known to have both immune dampening and immune activating properties.[6, 16] At high doses, estrogen has been found to improve the symptoms of psoriasis, whereas at low doses it is considered inflammatory;[15] however, this finding contradicts the effects of oral contraceptives which are typically low-dose estrogen. Pharmacologically, in the context of psoriasis, estrogen upregulates Th2 cells and downregulates Th1 and Th17 cells.[8] This promotes T cell conversion into T regulatory cells, which helps prevent symptoms.[6] Estradiol also inhibits IL-1B production, which inhibits IL-17 producing cells (which are key in psoriasis pathogenesis).[17] Furthermore, Cemil et. al found that a serum estradiol of less than 43.7pg/mL is indicative of a currently worsening PASI

(Psoriasis Area and Severity Index) score.[18] There is an inverse correlation between serum estradiol and PASI score, indicating that this version of estrogen is protective against psoriasis.[18] Cemil et. al theorizes that the reason for this phenomenon is that estrogen inhibits induction of an enzyme that is key in DNA replication and therefore cell proliferation.[18] Thus, in a period of high estrogen such as pregnancy, one can expect their psoriasis symptoms to improve.[8]

Even in male patients, estrogen level is inversely correlated with psoriasis severity.[15] This is likely due to the fact that estradiol (E2) and estriol (E3) receptor activation both show antioxidant effects and radical scavenging activity, reducing the detrimental angiogenesis needed for keratinocyte and sebocyte differentiation and proliferation (plaque formation).[6] However, a study conducted by Lin and Huang in 2016 shows that in vivo, E2 increases the effects of TNF-alpha on angiogenesis, and VEGF expression can be induced by E2.[15] Higher levels of VEGF lead to more severe psoriatic presentation and increased intimal thickness along with increased vascularization, which is detrimental for ovarian reserve and makes women lose their ovarian follicles faster.[14] This contradictory data pushes the hypothesis that the variability of different estrogen receptors in women could account for why psoriasis symptoms may improve for some during pregnancy but not others.[19] There are an infinite number of estrogen receptor combinations and presentations on a woman's cells, and so estrogen therapy can be suitable for some and detrimental for others. In such case, further studies should be done regarding genetic testing for those with psoriasis to determine if estrogen-based treatments could be a viable option for the patient.

Progesterone

Unlike estrogen, progesterone is more unanimously known to have anti-inflammatory properties.[6] In the context of psoriasis, progesterone (P4) has been shown to dampen T cells and downregulate STAT1 and STAT3, all of which are involved in the pathogenesis of psoriasis. Following conception, P4 elevates in the woman to establish and maintain pregnancy, which may contribute to the decreasing severity of psoriasis presentation often seen in pregnancy. P4 therapy reduces preterm risk and has been shown to reduce inflammation in animal models of autoimmune disorders such as multiple sclerosis, and should be explored as a possible mild, non-teratogenic treatment option for psoriasis as well.[16]

Immunology

The pathogenesis of psoriasis relies primarily on the activation of CD4 T cells.[7, 16] Specifically, psoriasis is Th1 and Th17 mediated, both of which are pro-inflammatory types of cells. IL-23 is required for Th17 expansion, which is why many new psoriasis biologic therapies have begun to target IL-23.[3, 8, 17] The genes STAT1 and STAT3 are enriched in disease states, and P4 progesterone dampens T cell activation and psoriasis symptoms by downregulating them.

Physiologically, pregnancy decreases the Th17 response.[8, 9] This is because the woman's body sees the fetus as an allograft—and in order to not reject the fetus as a foreign transplant, the woman's immune responses must be dampened. Given that psoriasis is Th17 mediated, a decreased Th17 immune response biologically reduces the presentation of psoriasis symptoms.

HLA-Cw6 Allele

The HLA-Cw6 allele has been identified by geneticists in increasing the susceptibility and severity of psoriasis. Specifically, the allele is associated with type 1 early-onset psoriasis, and it works by mediating T helper cells.[20] Having a single HLA-Cw6 allele increases patient risk of psoriasis by 10x, while being a homozygous carrier increases the risk by 20x. The allele occurs most often in people who identify as Caucasian or White, which is concurrent with psoriasis prevalence statistics.[3, 20] Homozygote carriers have also been found to score higher on the PASI scale, indicating a higher level of psoriasis severity. Carriers have been seen to have more plaques on the arms, legs, and trunk, as well as being more susceptible to the Koebner phenomenon (lesion presentation after trauma). The allele is also associated with stress, obesity, and higher rates of strep infection.[20]

Carriers of the HLA-Cw6 allele have reported more relief from psoriasis during pregnancy than their non-allele-carrying counterparts.[9] They also experience more frequent remissions during pregnancy.[20] Unfortunately, this means that women who are not HLA-Cw6 positive are more likely to experience unchanged or worsened symptoms of psoriasis during pregnancy. This furthers the interest for genetic testing following a psoriasis diagnosis to understand the patient's HLA-Cw6 status and better inform prognosis and treatment options.

Pregnancy

Depending on her genotype, a woman's psoriasis is usually stable or improves during pregnancy.[3, 4, 8, 9, 16] Many biologic treatments are considered teratogenic, and so acceptable treatments for psoriasis during pregnancy; common treatments are topical corticosteroids to help fight the outbreaks when they happen.[3] Most improvement in presentation occurs early in pregnancy, between 10 and 20 weeks of gestation (vena). The maternal immune system adapts in order accept the fetal allograft, improving many autoimmune disorders in addition to psoriasis.[7] Danesh et. al reported that the psoriatic lesions studied decreased by 83.8% during the course of pregnancy.[8] This relationship between psoriasis and pregnancy is bolstered by the evidence post-partum; up to 70% of women experience post-partum flareups for psoriasis.[8] In most cases, BSA (Body Surface Area) affected also increases significantly by 6 weeks post-delivery.[3, 4, 8] This data supports the hormonal and immunological pathogenesis behind psoriasis, while providing insight on new ways we can educate and treat psoriasis-affected women who are pregnant.

DISCUSSION.

This systematic literature review elucidates the individual nature of psoriasis. There are several factors affecting the presentation of psoriasis during pregnancy, ranging from genetic to hormonal. Overall, a woman with psoriasis who is pregnant should expect some improvement during early pregnancy, maintaining that improvement throughout the course, and then worsening symptoms post-partum.[3, 4, 8, 9, 16] Current biologic medications available for psoriasis have limited data in showing safety of use during pregnancy, therefore, it may be of interest to explore the use of natural sex hormones as a possible route of safe treatment.[7] Based on this literature review, progesterone seems like a strong candidate for possible non-teratogenic psoriasis treatment. Its use is already being tested in mouse models and is so far successful, and elevation of progesterone levels is already required for pregnancy maintenance in women.[16] A low dose supplement could be a more efficacious treatment for pregnant women who are suffering from moderate to severe psoriasis and don't want to go back to non-preventative topical treatments. Topical treatments can be very effective for mild psoriasis, however, in more severe cases, interventional treatment is recommended in order to help prevent plaque formation—topical treatments are used only after the lesion is already formed and painful. Finding a biologic treatment that is safe for pregnancy would alleviate the symptoms of millions of women worldwide. The effectiveness of a sex hormone treatment route may be determined via genetic testing, which the researcher recommends following a psoriasis diagnosis. Genetic testing will allow physicians to understand what treatments the body will respond to best, as well as advise on expectations of psoriasis presentation throughout life and pregnancy. It will help map receptor distribution to identify candidacy for specific drugs, as well as inform on patient HLA-Cw6 status to manage disease expectations. Future research may focus on other periods of life where one may experience hormonal changes in relation to psoriasis—for example, puberty. Furthermore, elucidating the differences in psoriasis presentation between men and women will allow physician scientists to better understand the pathogenesis behind psoriasis to develop more effective treatments against the disease.

The findings of this review provide the foundation for an investigation the researcher will conduct following this literature review. The researcher aims to complete a clinical study that investigates the *amount* of change in BSA affected by psoriasis during pregnancy. This will allow for the creation of patient education materials that can be distributed to women of reproductive age upon a psoriasis diagnosis. Ultimately, the findings from this review help close the gap in the literature on the topic of psoriasis during pregnancy and provide a foundation for further study on the progression of psoriasis during pregnancy, which may lead to possible new treatments and enhanced patient education on this topic.

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SUMMARY - ACCELERATING TRANSLATION

The purpose of this systematic literature review was to thoroughly examine the relationship between psoriasis and pregnancy to elucidate possible new routes of treatment. Findings from this review help close the gap in the literature on the topic as well as educate physicians and women with psoriasis who are pregnant on how psoriasis may present along the course of pregnancy and thereafter. Searches were primarily conducted in three databases: PubMed, Scopus, and Embase. Articles considered for inclusion in this literature review focused on the presentation of psoriasis during pregnancy. The literature sample obtained consisted of 14 peer-reviewed articles published from 2012-2022. Data coding followed Saldaña's (2016) methods of first cycle and second cycle coding. All data sources (i.e., articles; *N* = 14) were entered into the Excel data collection matrix. First cycle coding began with the researcher hand coding all articles using an a priori code list adopted from Boote and Beile's (2005) Literature Review Scoring Rubric.[10] As codes were identified, a master code list was developed. Second cycle coding involved categorizing of the data allowing for codes to combine and emerge as themes. Five themes were identified through categorical analysis: Immunology, general sex hormones, estrogen, progesterone, and the HLA-Cw6 allele. Collectively, these findings elucidate the individual nature of psoriasis and identify progesterone as a possible non-teratogenic therapy. Primarily, the presence of the HLA-Cw6 allele in a woman's genome along with the individual variation of estrogen receptors reinforces the researcher's recommendation for genetic testing following a psoriasis diagnosis. This genetic testing may allow patients and physicians to best understand what to expect of psoriasis during pregnancy as well as help determine the most efficacious treatment course to follow. The findings of this review provide the foundation for an investigation the researcher will conduct following this literature review. The researcher aims to complete a clinical study that investigates the *amount* of change in BSA affected by psoriasis during pregnancy. This will allow for the creation of patient education materials that can be distributed to women of reproductive age upon a psoriasis diagnosis. Ultimately, the findings from this review help close the gap in the literature on the topic of psoriasis during pregnancy and provide a foundation for further study on the progression of psoriasis during pregnancy, which may lead to possible new treatments and enhanced patient education on this topic.

FIGURES AND TABLES.

Figure 1.

Figure 2.

Table 1. Search Strings Used Per Database

Database	String	Results
PubMed*	Progesterone and psoriasis	9
	Estrogen and psoriasis	38
	(severity[tiab] OR "surface area"[tiab]) AND (("Psoriasis"[Mesh] OR Psoriases[tiab] OR Plaque[tiab] OR Psoriasis[tiab]) AND ("Pregnancy"[Mesh] OR pregnancy[tiab] OR Pregnancies[tiab] OR Gestation[tiab]) AND ((y_10[Filter]) AND (english[Filter])))	57
Embase	('psoriasis'/exp OR psoriases:ti,ab OR plaque:ti,ab OR psoriasis:ti,ab) AND ('pregnancy'/exp OR pregnancy:ti,ab OR pregnancies:ti,ab OR gestation:ti,ab) AND (severity:ti,ab OR 'surface area':ti,ab) AND [2012-2022]/py	132
Scopus	(ABS(severity OR "surface area") AND ABS(Psoriases OR Pustulosis OR Psoriasis OR plaque) AND ABS(pregnancy OR Pregnancies OR Gestation)) AND (LIMIT-TO (PUBYEAR,2022) OR LIMIT-TO (PUBYEAR,2021) OR LIMIT-TO (PUBYEAR,2020) OR LIMIT-TO (PUBYEAR,2019) OR LIMIT-TO (PUBYEAR,2018) OR LIMIT-TO (PUBYEAR,2017) OR LIMIT-TO (PUBYEAR,2016) OR LIMIT-TO (PUBYEAR,2015) OR LIMIT-TO (PUBYEAR,2014) OR LIMIT-TO (PUBYEAR,2013) OR LIMIT-TO (PUBYEAR,2012))	45

1 **Table 2**. Example Coding List

2

Author	Code	Category	Theme
A. A. Simionescu, B. M. Danciu and A. M. A. Stanescu	IL23 stimulates Th17	Th17 mediation	Immunology
G. A. Vena, N. Cassano, G. Bellia and D. Colombo	psoriasis is th1 and th17 mediated	Th17 mediation	Immunology
G. A. Vena, N. Cassano, G. Bellia and D. Colombo	pregnancy decreases th17 response	Th17 mediation	Immunology
M. B. Hoffman, M. Farhangian and S. R. Feldman	Th17 and IL-23 involvement	Th17 mediation	Immunology
M. Danesh and J. E. Murase	psoriasis is th17 mediated, driven by IL-23. th1 is secondary	Th17 mediation	Immunology
M. Danesh and J. E. Murase	psoriasis is driven by IL17 producing T cells (Th17) not Th1	Th17 mediation	Immunology
M. Danesh and J. E. Murase	IL23 required for Th17 expansion	Th17 mediation	Immunology
M. Danesh and J. E. Murase	th17 is decreased in healthy pregnancies	Th17 mediation	Immunology
M. B. Hoffman, M. Farhangian and S. R. Feldman	mediated by T helper cells	T cells	Immunology
S. Hellberg, J. Raffetseder, O. Rundquist, R. Magnusson, G. Papapavlou, M. C. Jenmalm, et al.	CD4 T cells are activated in disease pathogenesis	T cells	Immunology
S. Hellberg, J. Raffetseder, O. Rundquist, R. Magnusson, G. Papapavlou, M. C. Jenmalm, et al.	P4 dampens T cell activation by affecting genes	T cells	Immunology
S. Hellberg, J. Raffetseder, O. Rundquist, R. Magnusson, G. Papapavlou, M. C. Jenmalm, et al.	STAT1 and STAT3 are enriched in disease genes	T cells	Immunology

3

4