



Review

Vitiligo and pregnancy: How do each affect the other?

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ABSTRACT

Vitiligo is one of the dermatoses affecting the melanocytes resulting in their destruction and subsequent patchy depigmentation of the skin. It is postulated to occur due to an autoimmune problem. Despite being a disease with limited systemic involvement and lack of mortality, it has a severe psychological impact. It may have a powerfully negative effect on a patient's quality of life. The relationship between vitiligo and pregnancy is not widely acknowledged. It may be associated with adverse pregnancy outcomes such as recurrent miscarriage, prematurity, intrauterine growth retardation and pre-eclampsia. Herein, this review describes the disease's adverse effects on pregnancy outcomes and the influence of pregnancy itself on the clinical evolution and prognosis of vitiligo.

1. Introduction

Vitiligo is one of the dermatoses affecting the melanocytes resulting in their destruction and subsequent patchy depigmentation of the skin. The pathogenesis of the disease is not clear. However, the autoimmune background is the most accepted hypothesis. There is a consensus that the spectrum of autoimmune diseases is more prevalent among females. However, vitiligo has no gender predilection and may be associated with adverse pregnancy outcomes such as recurrent miscarriage, prematurity, intrauterine growth retardation (IUGR) and pre-eclampsia [1,2]. Despite vitiligo is a disease with limited systemic involvement and is never associated with direct mortality yet, it has a severe psychological impact. It may have a severe negative effect on a patient's quality of life, mainly because of the associated disfigurement resulting in stigmatization, low self-esteem and social isolation [3,4]. A recent study found that 50% of vitiligo patients are depressed [4]. Therefore, psychiatric input is crucial in the management of vitiligo patients. In this review, a comprehensive search of the available literature and reviews has been undertaken to outline the disease's adverse effects on pregnancy

outcomes and the influence of pregnancy itself on the clinical evolution and prognosis of vitiligo.

2. Autoimmune disease

Autoimmune diseases (AIDS) are known to have the female predilection and may be present before or during the reproductive age. Consequently, studying the behaviour of these diseases during pregnancy and lactation is of particular interest. It is well approved now that different AIDS have different responses to pregnancy, some showing improvement, others remain the same, and several deteriorating. The response of AIDS to the hormonal and immunological changes of pregnancy will reflect the different pathophysiology and, consequently, each disease's behaviour [5]. The risk of developing an autoimmune disease was significantly higher during the first year after delivery, then gradually tapered down. Recent studies suggest that the postpartum period warrants more heightened vigilance regarding the risks of autoimmune diseases among women [6]. The possible mechanisms for altered autoimmunity during pregnancy and postpartum, which leads to loss of the

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immunosuppressive state of pregnancy, include the hormones such as cortisol, estrogens, progesterone and prolactin, which achieve high levels during pregnancy, infections, vaccines, and stress are other possible implicated mechanisms [5].

3. Vitiligo

Vitiligo is an acquired, idiopathic skin disease characterized by circumferential cutaneous depigmented macules and patches [1]. The reported incidence of this disorder ranges between 0.5% and 1% of the population worldwide [4]. The disease has no ethnic, racial or socioeconomic predilection. It can also affect all age groups, with almost half of the affected people developed the disease before the age of 20 [1,2] with no gender differences [2].

The exact pathogenesis of vitiligo is not known. However, the multifactorial background is generally accepted, with the autoimmune hypothesis is the major leading one [1], where it explains the destruction of melanocytes and subsequent loss of pigmentation by an alteration in humoral and cellular immunity. Based on this autoimmune assumption of origin, it can be accordingly expected an association between vitiligo and other autoimmune disorders. Examples are observed in autoimmune thyroid disease, whether clinically presented with hyperthyroidism or hypothyroidism, Addison's disease, systemic lupus erythematosus, type 1 diabetes mellitus, rheumatoid arthritis and pernicious anaemia. Of note, it was found that around 30% of vitiligo patients will be affected by at least one or more other autoimmune diseases [1,4]. Genetic factors are also implicated in the occurrence of the disease, and it was demonstrated that 20%–30% of patients with vitiligo have a positive family of vitiligo [1].

The histopathology of vitiligo is characterized by typical features including the dermal-epidermal junction, residual melanocytes and also, a few granules of melanin may be still demonstrated at borders of the white macules while the rest of the lesion is devoid of any melanocytes as well as melanin granules. In some instances, the outer active part of the lesion may contain a lymphoid infiltrate. Isolated areas of vacuolizations and mononuclear cells at the dermal-epidermal junction may be present at the healthy skin near the hypopigmented macule [7]. Diagnosis of vitiligo rests mainly on the characteristic clinical features, with no particular tests for identifying the disease. The differential diagnosis list of the disease includes some other hypopigmented disorders: pityriasis versicolor, pityriasis alba, leprosy, sarcoidosis, lichen sclerosus, et atrophica [7].

4. Effect of pregnancy on the evolution and prognosis of vitiligo

Pregnancy is a physiological process characterized by special modifications in endocrine, immune, metabolic and vascular functions of the body systems required for the development and survival of the foetus. However, these changes may deviate from the norm resulting in either specific or ill-defined disorders affecting the different body systems and functions, including the skin. These cutaneous manifestations associated with the pregnancy process may be categorized into three groups: physiological skin changes related to pregnancy, specific cutaneous lesions developed with pregnancy, and flaring up or exacerbations of the already present dermatomes [8]. A little is known about the clinical course and evolution of these conditions in pregnant women as there is a lack of data from the literature dealing with them. Moreover, some cutaneous disorders may typically improve during pregnancy [8]. A descriptive transversal questionnaire study conducted on 86 women with vitiligo revealed that 28 patients (43.07%) of the women studied had a diagnosis of vitiligo coinciding with pregnancy, totalling 57 pregnancies (33.92%) with vitiligo. Regarding the influence of pregnancy on vitiligo, it was found that only 17.54% of the cases had worsening of the disease during the pregnancy—no difference or stability of the condition in 66.66% with improvement in 12.8%.

As for the situation during the six months at the postpartum period,

28.07% of patients experienced a condition worsening, 63.15% remained the same, and 5.26% improved while in 3.50% the patient failed to provide accurate information about the behaviour of the disease during that period, the study concluded that in most cases, vitiligo course showed no change during pregnancy and for six months post-delivery [2]. Another survey study conducted on 24 patients to assess the activity of the disease during pregnancy demonstrated that 15 women (63%) experienced stability or even improvement during pregnancy, 5 women (21%) reported a worsening of their condition, 3 women (12%) reported a definitive improvement. In contrast, only 1 patient (4%) claimed onset of the disease with pregnancy [9]. In line with the previously mentioned one, the study concluded that most patients included in this study showed either stabilization or even improvement of vitiligo activity during pregnancy. Accordingly, a protective effect exerted by pregnancy against the process of melanocyte destruction and subsequent skin depigmentation was postulated 9. Increased cortisol and IL10, which normally occurred in pregnancy, could explain the associated disease improvement [8].

A similar descriptive study from Singapore was carried out in 2016. It included women with vitiligo acquired either before or during pregnancy (20 patients) through a standardized questionnaire to assess the clinical features of the disease throughout pregnancy and for six months after delivery. The results delivered from the study showed that (70%) of the participating patients claimed either worsening of their condition (40%) or onset of vitiligo, for the first time, during pregnancy (30%). Of note, all patients who experienced the disease during pregnancy were primigravidae. For the six months postdelivery assessment, about (36%) of patients reported disease worsening, while improvement of the disease was observed in (10%) of them [10].

5. Effect of vitiligo on pregnancy outcomes

It was established that many of the autoimmune diseases are associated with adverse pregnancy and neonatal outcomes, including recurrent spontaneous miscarriages, premature delivery and perinatal mortality. It is also known that systemic lupus erythematosus is associated with significantly higher prenatal morbidity and mortality risks. Psoriasis is also associated with definitive increased risks of recurrent miscarriages, chronic hypertension, and higher caesarean deliveries [1]. A recent retrospective cohort study from Taiwan indicated that women with vitiligo had a higher risk of miscarriages. However, it showed no increased risk of other perinatal complications such as prematurity, gestational diabetes mellitus, intrauterine growth retardation, stillbirth and pre-eclampsia/eclampsia [11].

The study also showed that preconceptional adequate control of the disease with systemic treatments could improve the pregnancy outcomes. Another retrospective cohort study from Korea published few years before the previously mentioned one concluded that there is an increased risk of spontaneous miscarriages and lower live birth rates in women with vitiligo in this 10-years, nationwide, retrospective cohort study. There was no significant difference in other perinatal events as intrauterine growth restriction, gestational diabetes mellitus, pre-eclampsia/eclampsia. Also, caesarean sections rates showed no significant difference in patients with vitiligo. Of the individual indicators, only the rate of preterm deliveries was significantly low associated with vitiligo [4].

6. Management strategies for vitiligo during pregnancy

The target of vitiligo treatment is to achieve stabilized progressive depigmentation, continue repigmentation of already present lesions, and confirm the persistence of repigmentation once completed. A significant challenge in the process of vitiligo treatment is to maintain the survival and homeostasis of the successfully repigmented melanocytes, taken into account that depigmentation recurs in 40% of cases following complete therapeutic repigmentation [12].

The treatment of vitiligo varies between different countries, and choices mainly depend on the disease activity, patient's skin type, location of lesions, body surface area affected, motivation for treatment, risk-benefit ratio and also the availability of different treatment options as well as the health resources and facilities [12,13]. Unlike most of the diseases of autoimmune background, vitiligo is known to be fully reversible [14].

Limited treatment interventions for vitiligo in pregnancy are available for the time being. They may include topical corticosteroids and phototherapies. Folic acid supplementation is particularly advised for women in conjunction with phototherapy [8]. The best evidence for vitiligo treatment, including during pregnancy, is for a combination of steroids and ultraviolet light [15]. Topical corticosteroid use is mainly known to be complicated by skin atrophy which can be detected microscopically as degenerative skin changes as early as two weeks from treatment institution. The degree of these atrophic changes is influenced by the patient's age, site of the lesion on the body, potency of the corticosteroid used and presence of occlusion.

Other corticosteroid-associated side effects may include local irritation at the application site, genital hypertrichosis, and cutaneous infections may also be encountered. However, these adverse effects can be significantly reduced using a low potency corticosteroid for shorter periods, tapering policy of drug use from high potency to milder forms, advise an alternate day or weekend approach for drug use, avoid occlusions, and stop treatment once healing is achieved. In all cases, corticosteroids use should not exceed a total of 3 months duration. However, a more extended treatment period may be required in most cases, especially for extensive vitiligo. Therefore, a protocol of several weeks of corticosteroids with steroid holidays may be an acceptable compromise [3].

We have to emphasize that most of the systemically used drugs for the treatment of vitiligo are classified as category C pregnancy drugs, and it is continuing use with pregnancy is only subjected to the disparaging risk-benefit ratio of these drugs: oral corticosteroids, calcineurin inhibitors (even topical forms), vitamin D analogues as calcipotriol and tacalcitolare. Prostaglandin F2 alpha analogues, Psoralens, Minocycline, Cyclophosphamide and Azathioprine, are category D pregnancy drugs that should be avoided in pregnancy and lactation. Other like Basic Fibroblast Growth Factor (bFGF) derived peptide; the pregnancy category status is unknown. While no contraindication for administration of intravenous immunoglobulin (IVIG) and zinc with pregnancy 3. The retrospective cohort study from Taiwan studied the effect of pre-conceptional systemic treatment of vitiligo on pregnancy outcome by assessing the medical history of pregnant women one year before conception. It found that vitiligo patients who are treated systemically before conception had a lower risk of miscarriage [11].

Phototherapy entails exposing the affected skin areas of the body to UVB from UVB lamps, which is the simplest and most commonly prescribed treatment for vitiligo [15]. This treatment can be undertaken at home using the standard UVB lamp or in a specialized clinic. The exposure time should be controlled to avoid skin burn. Treatment duration may be in a few weeks if the lesions are just spots on the face and neck, especially if the period of the disease is less than three years. Longer treatment durations may be in the range of few months, will be required if the lesions are located on the hands or arms and lasting more than three years, duration [15]. Home treatment may be more effective than clinic one as it can be undertaken more frequently, even once/day. However, a lesion affecting a large body area should fully warrant body treatment in a hospital or specialist clinic. Both broadband and narrowband UVB lamps can be used with equivalent results [15].

7. Conclusion

There were mixed findings on the disease's adverse effects on pregnancy outcomes and the influence of pregnancy itself on the clinical evolution and prognosis of vitiligo.

In general, it can be concluded that women with vitiligo had a higher risk of miscarriages. However, vitiligo showed either stabilization or even improvement of during pregnancy. Like other autoimmune diseases, a lot still needs to be investigated about vitiligo, including the exact aetiology, pathogenesis, and behaviour during pregnancy.

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Consent

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Author contributions

Mohsen MA Abdelhafez and Karim AM Ahmed were responsible for conceptualizing the study and reviewing the literature. Nicholas Tze Ping Pang, Fairrul Kadir, Firdaus Hayati were involved in data collection, interpretation of studies, and manuscript drafting. Dg Marshita Pg Baharuddin, Win Win Than and Mohammad Saffree Jeffree were critically analyzing literature and expert input in synthesizing knowledge and finalizing the manuscript's content. All authors have seen and approved the final manuscript.

Trial registry number

1. Name of the registry:
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Declaration of competing interest

The authors report no conflict of interest nor proprietary or commercial interest in any product mentioned or concept discussed in this article.

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