Aetiology and Pathogenesis of Vitiligo

Subjects: Tropical Medicine

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Vitiligo is an acquired, chronic condition characterised by depigmentation of the epidermis or by destruction/loss of melanin. Skin cells (melanocytes) are responsible for producing melanin, the substance that gives pigmentation to the skin. Although there is no specific ethnic group, gender, or skin type that is more prone to vitiligo than others, it can affect anyone. Even though vitiligo is typically thought of as a cosmetic disorder, its effects on the physical and psychosocial health of sufferers cannot be ignored.

Keywords: vitiligo ; melanocyte ; pathogenesis ; autoimmune

1. Introduction

The skin loses colour due to a disorder called vitiligo (pronounced vit-il-EYE-go) [1]. In the Aushooryan era, roughly 2200 B.C., vitiligo was first mentioned in writing under the name Kilăsa. Further, the Egyptian Ebers Papyrus also has information on vitiligo that dates back to 1550 B.C. [2]. It is described as an autoimmune disease characterised by depigmented macules as well as patches of various shapes that are driven by the destruction of melanocytes or loss of their functioning in the skin [3]. As a result, several areas of the body, including the skin, hair, and mucous membranes, develop discoloured white marks. The lesion is known as a macule if the area of the skin losing colour is less than 1 centimetre wide and as a patch if it is greater than that [4]. Like all other skin disorders, patients with vitiligo are considered social outcasts in various societies, which has psychological and physical impacts [5]. Vitiligo has received very little investigation since most epidemiological studies either focus on highly chosen contexts, such as clinical populations, or on the prevalence of comorbidity in vitiligo patients without discussing the general population [6][7]. One study included more than 50 studies using a variety of methodologies and general demographic subgroups. Kruger et al. [8] found that the prevalence of vitiligo in the world's population overall ranges between 0.06% and 2.28% and between 0.0 and 2.16% in children and adolescent populations.

Geographically, prevalence rates vary and are frequently greater in Africa and India [9]. The incidence of vitiligo in the Indian subcontinent has the highest proportion at 9.98% [10], followed by Nigeria at 2.8% [11], and Romania at 2.28% [8]. According to various studies from India, vitiligo prevalence among dermatology outpatients ranges between 0.25 and 4%, with the states of Gujarat and Rajasthan having a maximum frequency of 8.8% [12]. These variations in the results might point to the existence of a single skin institute in India, or they might demonstrate the inclusion of cases involving toxic and chemical depigmentation, which could explain the high value in some areas [8][13].

Males and females are equally affected; however, few studies have indicated a female predominance, which may be related to women's higher tendency for autoimmune disorders or because women tend to be more concerned with their appearance when seeking advice and treatment [14][15]. Vitiligo typically begins before the age of 30, and most studies show that half of the patients begin to experience symptoms by age 20. When the disease has an early onset in children, it may be related to a family history [16]. Segmental and non-segmental vitiligo are both types of vitiligo. While non-segmental vitiligo can appear at any age, young people between the ages of 10 and 30 are the most frequently affected, and about 25% of vitiligo sufferers develop the illness before becoming 10 years old. On the other hand, segmental vitiligo develops earlier than non-segmental vitiligo and can occur in 41.3% of patients before the age of 10 years [17].

Thomas B. Fitzpatrick created Fitzpatrick skin phototypes in 1975 based on a person's skin tone and how they react to exposure to the sun in terms of burning and tanning [18]. The Fitzpatrick skin type has been most frequently employed in a prospective population-based and case-control research study to analyse sun sensitivity and the causes of skin cancer, including exposure to UV radiation, tanning, and protective activities [19]. Although many recent studies have revealed that people of all ethnicities and skin types (Fitzpatrick) are affected by vitiligo equally [20]. An online panel was used to recruit 35,694 people over the age of 18 from Europe, Japan, and the USA to participate in a survey about any skin conditions, including vitiligo, that they may have had in the past. The estimated prevalence of vitiligo overall was 1.3%. Europe has the highest prevalence (1.6%), followed by the USA (1.4%), and Japan came in third (0.5%). According to the Fitzpatrick

scale, the prevalence of vitiligo was highest among people with type III (light brown; 0.5%) and type IV (moderate brown; 0.4%) skin phototypes [21].

The destruction of melanocytes and the development of white patches in vitiligo have been linked to a variety of different mechanisms. They include neural, genetic, autoimmune, oxidative stress, production of inflammatory mediators, and other mechanisms for melanocyte separation [22].

2. Autoimmune Theory

Autoimmune mediation is the most common and well-established theory that suggests a disruption in the response causes melanocytes to be destroyed by autoimmune effector mechanisms, either memory cytotoxic T cells or autoantibodies targeted to melanocyte surface antigens. It is well recognised that vitiligo and autoimmune disorders are related; for example, vitiligo is usually associated with thyroid disorders including Hashimoto's thyroiditis and Graves' disease, as well as other endocrinopathies like Addison's disease and diabetes mellitus. There has to be additional research on the relevance of some of these conditions, including autoimmune polyglandular syndrome, alopecia areata, systemic lupus erythematosus, inflammatory bowel disease, rheumatoid arthritis, psoriasis, and pernicious anaemia [23][24].

3. Genetic Theory

Familial clustering is observed in vitiligo. According to numerous studies, the prevalence of vitiligo among first-degree relatives ranges from 0.14% to 20%. The information clearly shows a genetic component; however, just 23% of monozygotic twins showed concordance, indicating that there may be a considerable non-genetic factor in the pathophysiology of vitiligo. On the other hand, since vitiligo is a polygenic condition, several candidate genes have been identified, including the major histocompatibility complex (MHC), angiotensin-converting enzyme (ACE), catalase (CAT), cytotoxic T lymphocyte antigen-4 (CTLA-4), protein tyrosine phosphatase, human leukocyte antigen (HLA), and interleukin-2 receptor A (IL2RA). All of these involved in the control of immunity have been tested for genetic association with generalised vitiligo [3][23][25].

4. Oxidative Stress Theory

According to the oxidative stress theory, the intra-epidermal buildup of reactive oxygen species, the most well-known of which is hydrogen peroxide (H_2O_2), whose concentration can reach up to one millimole, is the primary factor in the pathogenesis of vitiligo. H_2O_2 causes alterations in the mitochondria at this concentration, which causes the melanocytes to apoptose and die. Patients with vitiligo frequently exhibit changes in redox status indicators. Malondialdehyde (MDA), selenium, vitamins C and E, glutathione peroxidase (GPx), superoxide dismutase (SOD), and catalase (CAT) are significant markers of interest. MDA is a by-product of lipid peroxidation and a sign of oxidative stress. Selenium, a key antioxidant found in erythrocytes, is necessary for GPx action. Superoxide radicals are neutralised by SOD, which lessens their toxicity, and are converted to oxygen (O_2) and water (H_2O) by CAT. Patients with vitiligo have significantly greater amounts of SOD, decreased erythrocyte GPx activity, low levels of the enzyme CAT, and low levels of the vitamins C and E in both their epidermis and serum [23][24][25].

5. Neural Theory

The neural theory postulates that nerve endings release neurochemical substances that can reduce melanin production or damage melanocytes. It also proposes that the pathogenesis of vitiligo is connected to the catalase gene. The peroxisome enzyme catalase is present in almost all living things. It stimulates the hydrolysis of hydrogen peroxide into water and oxygen, which protects cells from highly reactive oxygen radicals. Catalase enzyme activity is decreased in both lesional and nonlesional skin of vitiligo patients [22][26].

6. Biochemical Theory

The biochemical theory suggests that the accumulation of toxic intermediate metabolites of melanin synthesis and inadequate free radical defence lead to excessive amounts of hydrogen peroxide (H_2O_2), which is a cause of melanocyte destruction. Some theories include that the genetic factor, flaws in melanocyte structure and function, and a lack of melanocyte development factors all contribute to the depigmentation process [22][26][27]. The overall contribution of each of these mechanisms is still subject to debate, even though there is now general agreement that vitiligo is an autoimmune

disease. None of these suggested hypotheses is sufficient to explain the many vitiligo phenotypes. However, the development of manifest diseases depends on environmental factors [28].

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