Quality of Life, Burden of Disease, Co-morbidities, and Systemic Effects in Vitiligo Patients

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KEYWORDS

• Vitiligo • Comorbidities • Autoimmune diseases • Systemic • Quality of life • Burden • Depression

KEY POINTS

- Vitiligo is a disfiguring systemic disease with a complex and multifactorial pathogenesis.
- Vitiligo is associated with many autoimmune (AI) and autoinflammatory conditions that may be owing to shared AI and genetic susceptibilities.
- Vitiligo has a major impact on quality of life and self-esteem.
- Depression, anxiety, and other psychiatric comorbidities are common in vitiligo patients.
- Increased awareness of quality of life issues will help to ensure that vitiligo is no longer dismissed as a cosmetic or insignificant disease.

Vitiligo is an acquired chronic autoimmune (AI) pigmentation disorder resulting in patchy, white, nonscaly macules and patches. The worldwide prevalence of the disease is estimated to be around 1%.[1] Vitiligo is also a disfiguring disease that, despite its profound impact on quality of life and its frequent association with other comorbid AI diseases, is still considered a cosmetic condition.[2]

COMORBIDITIES AND SYSTEMIC EFFECTS

The etiology and pathogenesis of vitiligo is complex and multifactorial, including theories of AI, genetic, neural, cytotoxic, biochemical, oxidative, melanocyte, inflammatory, and hormonal origin.[3–7] Multiple susceptibility genes and various environmental triggers have also been associated with having a role in the pathogenesis of vitiligo.[8] Studies have also shown that vitiligo patients, including those with an AI or autoinflammatory disease, are more likely to have a family member with an AI disease, supporting the theory of a genetic AI susceptibility.[1,3,9] The AI origin of vitiligo, which includes cellular and humoral immunity, has been widely supported through the presence of circulating antibodies against melanocyte antigens whose levels correlate with disease activity, the immune-mediated destruction of melanocytes from vitiliginous skin, and the increased prevalence of associated AI disorders.[3,9,10]

Multiple studies have shown that individuals with vitiligo have an increased incidence (up to 25%) of other AI and inflammatory conditions.[10–12] These include AI thyroid disease (AITD), type I diabetes mellitus, pernicious anemia (PA), rheumatoid arthritis (RA), alopecia areata (AA), atopic dermatitis (AD), Addison's disease, psoriasis, dermatitis herpetiformis, celiac disease, systemic lupus erythematous (SLE), Sjögren syndrome

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(SS), myasthenia gravis, inflammatory bowel disease, and, more generally, auditory, neurologic, and ocular abnormalities (**Table 1**).[12–16] Vitiligo has also been observed in association with these latter abnormalities in several rare syndromes, including AI polyglandular disease (APG), Alezzandrini syndrome, and Vogt-Koynagi-Harada disease (VKH).[3] Isolated case reports also exist describing patients who have vitiligo with other conditions, including mucous membrane pemphigoid and mycosis fungoides.[17,18]

One reason suggested to account for these associations is a shared underlying genetic susceptibility between vitiligo and the AI diseases associated with it.[19] Genome-wide association studies and candidate gene association studies have been performed in patients with generalized vitiligo and many of the associated genes found in these patients encode immunoregulatory proteins, which were also associated with other AI diseases.[20,21] Many of these AI associations have been studied across varied populations from different regions of the world. The frequencies of AI diseases associated with vitiligo vary, but for several conditions have been found in higher frequencies than those found in the general population.[19] Studies show that these frequencies vary by geographic region and may be influenced by genetic and environmental differences within these regions.[6,20] A retrospective 10-year study by Sheth and colleagues[16] in a US population found that 23% of vitiligo patients had associated comorbid AI conditions. A cross-sectional study by Gill and colleagues[13] also in a US population, found that nearly 20% of vitiligo patients had at least 1 comorbid disease. In this study, older age, later age of onset, and longer duration of vitiligo all seemed to play a role in the development of AI disease. A Turkish study by Akay and colleagues[5] found that up to 55% of vitiligo patients having an associated AI disease, and another Japanese study by Narita and colleagues[19] found that it affected 20.3% of vitiligo patients. Chen and colleagues[22] evaluated comorbidity in a Taiwanese nationwide population-based study and found that 14.4% of the patients had 1 or more associated AI or atopic diseases, with AA being the most commonly associated AI disease.

The frequencies of AI diseases associated with vitiligo can also be affected by other demographic factors, such as race, age, and gender.[3,16,22] Several studies have found that women with vitiligo, compared with men, tend more frequently to have an associated AI disease, particularly thyroid disease.[3,16] A Taiwanese study found that female vitiligo patients were more likely to have thyroid disease, AD, RA, SLE, and SS, whereas male vitiligo patients were more likely to have psoriasis.[22] This study also stratified the data by age and found that older vitiligo patients were more likely to have SLE, SS, and RA, whereas younger vitiligo patients were more likely to have myasthenia gravis.[22] Some studies that have stratified their results by race have found the most common associations with vitiligo in Caucasian and Hispanics to be hypothyroidism and psoriasis, whereas in blacks, it has been RA and lupus, and in Asians, psoriasis.[16] Another study found that AA was less frequent in white patients and psoriasis was less frequent in black patients.[13]

In many of these studies, 15% to 26% of patients also had a positive family history of AI

Table 1
Comorbidities associated with vitiligo

More Common Associations	Less Common Associations
Thyroid disease Hashimoto's thyroiditis Graves' disease Hypothyroidism Hyperthyroidism	HIV/AIDS
Alopecia areata	Lichen sclerosus et atrophicus
Type I diabetes mellitus	Mucous membrane pemphigoid
Pernicious anemia	Mycosis fungoides
Atopic dermatitis	Spondyloarthritis
Rheumatoid arthritis	Scleroderma (including morphea)
Systemic lupus erythematosus	Pemphigus vulgaris
Sjögren syndrome	Rheumatic fever
Myasthenia gravis	Multiple sclerosis
Inflammatory bowel disease	Guillan-Barre syndrome
Psoriasis	Type 2 diabetes mellitus
Halo nevus	Addison's disease
Uveitis[a]	Dermatitis herpetiformis
	Celiac disease
	Sarcoidosis
	Multiple sclerosis
	Discoid lupus
	HIV/AIDS

Abbreviation: HIV, human immunodeficiency virus.
[a] Associated with Vogt-Kayanagi-Harada and Alezzandrini syndrome.