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Exploring the link between pernicious anemia and vitiligo: Digging Deeper

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Vitiligo is a skin condition characterized by loss of pigmentation in areas of the skin, which leads to presence of white patches on the skin. This occurs as a result of the melanocytes being destroyed. The true cause of vitiligo is not yet known, however, the hypothesis that vitiligo is an autoimmune disorder is most widely accepted. [1] According to various studies the prevalence of vitiligo is estimated to be from less than 0.1% to more than 8%. In 2011, there was an international consensus which divided vitiligo into 2 major types, Non-Segmental Vitiligo (NSV) and Segmental Vitiligo (SV). In NSV the white patches usually appear on both sides of the body and the disease is prone to reactivation even after being stable for several years. Whereas, SV is characterized by loss of melanocytes primarily on one side of the body and it becomes inactive after being stable for around 2 years. [2] Vitiligo is characterized by the destruction of melanocytes. There are many theories proposed for this destruction, including genetic, autoimmune, melanocyte detachment mechanism and oxidative stress. However, in the recent times, there has been a consensus on the autoimmune theory. Earlier it was believed that both NSV and SV had different pathogenesis but in recent times it was observed that the pathogenesis for both might be overlapping. [3] The treatment for vitiligo still remains one of the hardest challenges in in dermatology. When seeking treatment for vitiligo, people are usually prescribed topical corticosteroids, calcineurin inhibitor, phototherapy and immunosuppressants that may help in halting the disease or repigmentation of the white areas.[4] Pernicious Anemia is the most common macrocytic anemia which is caused by Vitamin B1 or cobalamin deficiency. It is autoimmune in origin and usually caused by the deficiency of intrinsic factor in the stomach. Often people who suffer from pernicious anemia may not be are of it unless a full blood count is done, this causes some problems with the treatment. It is a relatively rare condition with a prevalence of up to 2% worldwide.[5] The primary pathophysiology includes the reduced absorption of B12 due to the decreased intrinsic factor in the body, however other factors such as dietary problems, surgical removal of part of the stomach and certain medicines may be involved. Patients who suffer from pernicious anemia but are not diagnosed with any obvious dietary or malabsorptive disorder are tested for other autoimmune disorders. The most common treatment for pernicious anemia includes cobalamin replacement therapy. [6]

Various studies have examined the relationship between pernicious anemia and vitiligo. For instance, in one study, 300 patients with vitiligo were examined for the presence of pernicious anemia. Patients admitted to the Toronto Western Hospital Phototherapy Unit were reviewed retrospectively and the parameters including patient characteristics, associated diseases in the family and admission bloodwork were recorded and analyzed using the Fisher exact test wherever applicable. It was found that there was a 1.3% significant increase in the prevalence of pernicious anemia in the population and a 12% of the patient shad hypothyroidism. The study concluded that there is a significantly higher prevalence of pernicious anemia and hypothyroidism in patients with vitiligo. [7] On the other hand, a study was conducted on 200 patients in India to study the common disorders including the autoimmune diseases associated with vitiligo. It was observed that autoimmune disorders were present in 18.5% of the patients and this included the thyroid disorders in about 5% of the patients, alopecia areata in 1.5%, rheumatoid arthritis in 1%, diabetes mellitus in 2% and atopy in 2%. However, pernicious anemia was not detected in any patients. This study concluded that at least 30% of the patients had one other autoimmune disease in relation to vitiligo and the link between pernicious anemia and vitiligo as stated in earlier studies was not significant in this population. [8]

Furthermore, a cross- sectional study that was conducted for 1873 patients that presented to the Henry Ford Health System in Detroit, MI with vitiligo between January 2002 and October 2012 revealed that approximately 20% had at least one other comorbid autoimmune disease. It was also found that compared to the general US population there was a higher prevalence of pernicious anemia by 0.5%, alopecia areata by 3.8% and thyroid disease by 12.9%. The study concluded that there is a higher prevalence of comorbid autoimmune diseases in patients with vitiligo and it also reports several new associations. [9] In the year 2013, 300 patients were randomly selected from a total of 3280 patients carrying the diagnosis of vitiligo and were used to check and identify the prevalence of comorbid autoimmune diseases. It was found that 23% of the patients presented with one of the following comorbidities; 11.7% presented with thyroid disorders, 7.6% presented with psoriasis, 2.9% presented with rheumatoid arthritis, and so on. However, no cases of pernicious anemia were recorded. The study concluded that thyroid disorders and psoriasis were the most common comorbidities and that screening for these conditions most importantly the thyroid disorders should be considered in patients with vitiligo. [10]

A case control study was conducted in Saudi Arabia for the confirmed cases of vitiligo between the time period of July 2014 to December

2015. The control group and the vitiligo cases had their blood samples collected and evaluated for vitamin B12 level, hemoglobin level, TSH and fasting blood glucose. There were a total of 115 subjects and it was found that 1% of the subjects had macrocytic anemia compared to 2% of the control group, vitamin B12 deficiency was found in 16% of the subjects as compared to only 2% of the control group and hypothyroidism also had a higher prevalence in the subjects as compared to the control group. The study concluded that hypothyroidism and vitamin B12 Deficiency was more prevalent in Saudi Arab vitiligo patients, and it also warranted the need to screen the vitiligo patients for these diseases. [11] Another case control study that was carried out in 2020 to check the Vitamin B12 and folate serum levels in vitiligo patients and the control group disclosed that the serum MCV level was significantly lower in the vitiligo patients as compared to the control group. It was also found that the vitamin B12 and folate serum levels were significantly decreased in patients suffering from vitiligo. [12]

The etiology of vitiligo is not completely understood, which makes it difficult to find a cure. The most accepted theory is that vitiligo is an autoimmune disorder. It was reported that 30% of the patients diagnosed with vitiligo have at least one other autoimmune disorder including pernicious anemia, alopecia areata, thyroid disorders etc. It has been suggested that folic acid and vitamin B12 are necessary for many biological processes including playing a significant role in melanin synthesis. [12] Several studies have shown the significance of vitamin B12 and folic acid in the pathogenesis of vitiligo but the findings are still limited. These studies showed that vitamin B12 and folic acid levels were lower in patients as compared to the normal population [11,13], although another study that was conducted in Turkish patients did not show any difference in the vitamin B12 and folic acid levels between the patients and general population.[14] It was also reported in a study conducted by Liza Gill BS et. al, that older age, later age of onset and longer duration of the disease could mean that there is more incidence of development of comorbid autoimmune diseases and although not statistically significant, those with NSV were twice as likely to have an associated comorbid autoimmune disease. [9]

To sum up, the link between pernicious anemia and vitiligo is based on the hypotheses that vitiligo is an autoimmune disorder. This link has been studied in the past but the results were not clear. Supplementation with vitamin B12 showed improvement in vitiligo in some patients but had no effect on the other patients. This relation needs to be studied more extensively to get a clear understanding.

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