



# Serum Vitamin B12 and Folic Acid in Vitiligo Patients: A Case Control Study

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**Abstract:** Background: Vitiligo is an autoimmune disease characterized by the destruction of melanocytes by immune mechanisms. The role of vitamin B12 and folate in melanin synthesis has been well recognized. Aim of the study: To evaluate the serum levels of vitamin B12 and folate in Libyan patients with vitiligo vulgaris. Patients and Methods: Blood samples for haemoglobin (Hb) level, mean corpuscular volume (MCV), serum levels of Vitamin B12 and folate were obtained from 50 patients with vitiligo vulgaris and 50 age and sex-matched healthy controls at Dermatology Department of Eljumhuria Hospital in Benghazi, Libya. Results: 50 patients with vitiligo vulgaris, with mean of age  $34 \pm 6$  years, 34% had active disease. Blood Hb level was non-significantly lower in 26% vitiligo patients as compared to 16% control subjects ( $P=0.064$ ). A significant difference was observed regarding the MCV level which was lower in vitiligo patients in comparison to that of control subjects ( $P=0.03$ ). 38% of vitiligo patients have microcytic anemia ( $P=0.142$ ). None of the patients has macrocytic anemia. Female patients were found to have significantly lower Hb and lower MCV than males ( $P=.000$ ). Serum vitamin B12 and folate were lower in patients than control subjects and this difference was statistically significant ( $P=.05$ ,  $P=0.001$ ). There was no significant correlation between serum levels of vitamin B12 and folate with sex, age, family history, duration and activity of the disease ( $P > 0.05$ ). Conclusions: Decreased levels of serum vitamin B12 and folate are significantly prevalent in vitiligo patients, and screening vitiligo patients for vitamin B12 and folate deficiency may be warranted.

**Keywords:** Vitiligo, Serum, Vitamin B12, Folate

## 1. Introduction

Vitiligo is an acquired disorder characterized by depigmented macules and patches that result from the destruction of melanocytes [1]. The precise aetiology of vitiligo is still unknown, but the major hypotheses state that stress, accumulation of toxic compounds, infection, autoimmunity and mutations can all contribute to its etiopathogenesis [1, 2]. Increased frequencies of autoimmune disorders, such as autoimmune thyroid disease, pernicious anaemia, and Addison disease have been detected in patients with vitiligo [3]. Vitamin B12 and folate both are important in melanin synthesis through many enzymatic pathway activations. Studies on the blood levels of vitamin B12 and

folate in vitiligo have been reported, though results are still conflicting [4]. The aim of the present study to assess whether there were significantly higher frequencies of Hb, iron, vitamin B12, and folic acid deficiencies in vitiligo patients.

## 2. Methods

### 2.1. Patients and Control Subjects

Fifty vitiligo patients and 50 age and sex-matched healthy subjects attending OPD of Dermatology Department, El-Jumhuria Teaching Hospital, in Benghazi, Libya participated in the present study. All patients had vitiligo vulgaris, based on clinical and wood lamp examination. Exclusion criteria included pregnancy or lactation, taking mineral supplements or

receiving any medication, metabolic or systemic disorders and skin problems other than vitiligo. A complete history was taken from each patient, which included the demographic data, medical and drug history, duration of vitiligo, and familial history of vitiligo. Laboratory tests were recommended from both patients and control subjects, which comprised complete blood count, Folate and Vitamin B12 levels. Vitiligo patients were divided into two groups as active and stable according to the progression of the disease in the last three months. Signed consent was obtained from all patients and subjects after explaining the nature of the study to them and the manuscript is according to the declaration of Helsinki.

## 2.2. Statistical Analysis

All statistical analyses were performed using SPSS software for Windows (Version 16.0). Results are presented as mean and standard deviations for continuous variables and as a number (%) for categorical variables. Comparisons between the patients and the control group were done by t-test. P values <0.05 were considered significant.

## 3. Results

A total of 50 vitiligo patients and 50 age and sex-matched healthy subjects were enrolled in this study. Table 1 show the demographic data of the patients and control subjects under study. Serum vitamin B12 and folate were lower in patients than control subjects and this difference was statistically significant. A significant difference was observed regarding the mean of MCV level in vitiligo patients in comparison to that of control subjects (Table 2). Blood haemoglobin level was non significantly lower in 26% vitiligo patients as compared to 16% control subjects (P=.064). 38% of vitiligo patients have microcytic anemia (P=0.142). Female patients were found to have lower haemoglobin and lower mean MCV than males and this difference statistically significant. No significant difference between male and female patients regarding folate and vitamin B12 serum levels (Table 3).

There was no significant correlation between blood Hb and the serum levels of folate and vitamin B12 with the activity of the disease (Table 4). Blood haemoglobin, MCV, vitamin B12 and Folate levels did not show significant difference according to age, family history and duration of vitiligo.

**Table 1.** The demographic data of vitiligo patients under study.

Demographic data	Vitiligo patients	Control subjects	P value
Age mean±SD yrs	34 ±6 yrs	32.2±9 yrs	.235
Sex			
Female	26 (52%)	27 (54%)	.902
Male	24 (48%)	23 (46%)	
Duration yrs ±SD †	10.5±9 yrs	NA*	
Activity of disease			
Active	17 (34%)	NA*	
Stable	33 (66%)		

\*NA: None applicable †SD: standard deviation.

**Table 2.** Mean of serum levels of hemoglobin, MCV, vitamin B12 and folate in vitiligo patients and control subjects.

Serum level	Vitiligo patients Mean ± SD	Control subjects Mean ± SD	P value
Hemoglobin (g/dl)	12 ±2	12.7±2	.064
MCV† (fl)	34.9±6.4	37.9±7	.030*
Folate (ng/ml)	7.3±4	9.5±5	.019*
Vitamin B12 (pg/ml)	284±100	370±136	.001*

\*P value <0.05 significant, †MCV mean corpuscular volume.

**Table 3.** Correlation between the gender of the patients and other variables.

	Gender: Mean ±SD		P value
Hemoglobin (g/dl)	M: 13.5±1.4	F: 10.7±.7	.000*
MCV (fl)	M: 39.2±6	F: 30.6±4	.000*
Folate (ng/ml)	M: 7.5±4	F: 7±4	.614
Vitamin B12 (pg/ml)	M: 261±86	F: 306±109	.105

\*P value <0.05 significant.

**Table 4.** Correlation between the activity of the disease and other variables.

Serum level	Active disease	Non-active disease	P value
Hemoglobin (g/dl)	11.7±1.5	12.2±2	.365
Folate (ng/ml)	8.5±4	6.7±4	.137
Vitamin B12 (pg/ml)	283±100	285±102	.960

## 4. Discussion

Vitiligo is an acquired, idiopathic, and in the majority of cases, a progressive, unpredictable skin disease [2]. Its aetiology is still unclear, however, several hypotheses have been proposed these include; the autoimmunity; auto-destruction of melanocytes and the neural hypothesis [3].

The autoimmune aetiology of vitiligo is the most widely accepted, Alkhateeb et al. reported at least 30% of patients with vitiligo to be affected with at least one additional autoimmune disorder like; thyroid diseases, Pernicious anaemia, Addison's disease and alopecia areata [5]. Folic acid and vitamin B12 require each other in biological reactions. Vitamin B12 is needed for the reduction of folic acid to tetrahydrofolic acid which is prerequisite for participation of folic acid in enzymatic reactions [6]. Vitamin B12 acts as a coenzyme in the folate-dependent synthesis of pyrimidines and purines [7]. Moreover, it has also been suggested that folate may play a role in the melanin synthesis through the enzymatic hydroxylation of phenylalanine to tyrosine, and through the activity of its components; pteridine, para-aminobenzoic acid, and also through vitamin B12-dependent formation of methionine [7, 8].

Although statistically insignificant, a quarter of the patients under study had microcytic anaemia, in the agreement of previous studies [9, 10], however, Gonul et al reported a lower prevalence (9.9%) of anaemia in vitiligo patients [11]. Vitiligo patients have been reported to be more susceptible to develop celiac disease, an autoimmune disorder known to be associated with iron deficiency [12].

Female patients with vitiligo under study were found to have microcytic anaemia than males and this difference statistically significant. It is well-known that hypochromic microcytic anaemia is more common in premenopausal females because they lose blood with each menstrual cycle or during delivery [13].

Recent studies on the role of vitamin B12 and folate in the etiopathogenesis of vitiligo have shown controversial findings and are still limited. The present study showed that vitamin B12 and folate levels were lower in patients than in control subjects, in agreement with previous studies [4, 7, 9], however, the studies of Kim et al and Gonul et al did not show any difference in vitamin B12 and folate levels between vitiligo and control groups [6, 13]. Although, the incidence rate of pernicious anaemia in patients with vitiligo is thirty times higher than that observed in the general population [3, 6]. Alissa et al. reported a 0.1% prevalence of pernicious anaemia in Saudi vitiligo patients [14]. In the present study, haemoglobin was low in 29.4% of patients with low vitamin B12, none of the patients had macrocytic anaemia and this result was in agreement with previous studies which didn't report pernicious anaemia among patients with vitiligo [6, 9, 13].

It is well known that vitamin B12 and folic acid are major determinants of homocysteine, and a reduced level of either these two vitamins results in hyperhomocysteinaemia [4]. Homocysteine inhibits tyrosinase and leads to the release of reactive oxygen species that can inhibit melanin synthesis and destructs melanocytes [15]. It has been suggested that folate and vitamin B12 supplementation may have indirect effects on vitiligo and homocysteinuria [7]. Previous studies reported conflicting results regarding the use of vitamin B12 and folic acid for the treatment of vitiligo. Tjioe et al and Juhlin et al studies reported an improvement and repigmentation of vitiliginous skin in patients who received folate and vitamin B12 orally with exposure to UVB or sunlight, however, the authors suggested that vitamin B12 and folate might not be the main etiological factors in vitiligo [8, 16].

## 5. Conclusions and Recommendations

Decreased levels of serum vitamin B12 and folate are significantly prevalent in vitiligo patients under study. Screening vitiligo patients for vitamin B12 and folate deficiency may be warranted. Moreover, dermatologist should consider requesting a complete blood count as patients might have microcytic anaemia. More studies are required to clarify the importance of these findings in etiopathogenesis and treatment of vitiligo.

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