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Original article

Association of vitiligo with anemia, vitamin B12 deficiency, diabetes mellitus, and thyroid dysfunction in Saudi Arab patients: A case control study

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Abstract

Objectives: To assess the association of vitiligo with thyroid dysfunction, vitamin B12 deficiency, diabetes mellitus and anemia; among Saudi Arab individuals using laboratory data in a controlled fashion. *Methods:* A case control study was conducted among Saudi nationals with a confirmed diagnosis of vitiligo presenting between July 2014 and December 2015. Sex- and age-matched randomly selected subjects were included as controls. Blood samples from both vitiligo patients and controls were collected and assayed for hemoglobin level, mean corpuscular volume, thyroid stimulating hormone level, free thyroxine level, vitamin B12, and fasting blood glucose.
Results: Of the 115 vitiligo subjects, 15% had microcytic anemia compared to 7% of control ($p = 0.072$). Macrocytic anemia was diagnosed in 1% of vitiligo subjects and in 2% of control ($p = 0.404$). Vitiligo group had significantly higher prevalence (5%) of primary hypothyroidism compared to control (0%) ($p = 0.030$). Vitamin B12 deficiency was significantly more prevalent in vitiligo group (16%) compared to control (2%) ($p = 0.001$). The prevalence of diabetes mellitus was higher in vitiligo group (8%) as compared to control (4%) ($p = 0.334$).
Conclusion: Primary hypothyroidism and vitamin B12 deficiency are significantly more prevalent in Saudi Arab vitiligo patients. Screening vitiligo patients for thyroid dysfunction and vitamin B12 deficiency may be warranted.

Keywords: Vitiligo; Arab; Saudi; Hyperthyroidism; Hypothyroidism; Anemia

1. Introduction

Vitiligo is an acquired depigmenting cutaneous disorder characterized by the loss of melanocytes from the epidermis. It affects approximately 0.5% of the population worldwide, although it may be higher (Taieb et al., 2013). The mechanism by which melanocytes are lost is not fully understood. There are three major hypotheses for the pathogenesis of vitiligo (Alkhateeb et al., 2003; Nunes and Esser, 2011). The first and most acceptable hypothesis

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considers vitiligo as an autoimmune disease. The second is the neural hypothesis which suggests that accumulation of a neurochemical substance decreases melanin production. Finally, the biochemical hypothesis implies auto-destruction of melanocytes as a result of cytotoxic by-products of melanin synthesis.

Vitiligo has been reported in association with several autoimmune diseases including thyroid diseases (Nunes and Esser, 2011), diabetes mellitus (DM) (Gopal et al., 2014; Gould et al., 1985), and pernicious anemia (Sawicki et al., 2012; Alissa et al., 2011). However, there is a paucity of data on the true prevalence of these associations in the Saudi Arabian population. A survey-based epidemiological study was previously performed by our group and addressed coexistence of autoimmune diseases in Saudi patients with vitiligo (Alissa et al., 2011). The aim of the current study was to assess the association of vitiligo with other autoimmune disorders among Saudi Arab individuals using laboratory data in a controlled fashion.

2. Methods and materials

This is a case control study that was conducted at the National Center of Psoriasis and Vitiligo (Light Clinic) in Riyadh, Saudi Arabia between July 2014 and December 2015. All new cases of various types of vitiligo (115 cases) attending the center were included. A total of 89 age and sex-matched randomly selected subjects, presenting with other common, non-immune mediated, skin conditions were included as controls. Pregnant women and individuals below 18 years of age were excluded. Vitiligo was diagnosed clinically. A written informed consent was obtained from all subjects prior to the study. The study has been performed according to the Declaration of Helsinki principles and was approved by the institution's ethics committee.

Blood samples from both patients and controls were collected and assayed for hemoglobin (Hb) level, mean corpuscular volume (MCV), thyroid stimulating hormone (TSH) level, free thyroxine (FT4) level, vitamin B12, and fasting blood glucose (FBS).

The normal reference ranges of all blood tests are summarized in Table 1. A diagnosis of anemia was made when Hb was low. The anemia is considered microcytic when MCV was also low and macrocytic anemia when MCV was additionally high. Primary Hypothyroidism was diagnosed if thyroid function test showed low level of FT4 with raised level of TSH and a diagnosis of primary hyperthyroidism was made when TSH serum level was low and FT4 was high. Vitamin B12 deficiency was diagnosed when vitamin B12 level was low. The subject was considered diabetic if FBS was higher than 6.40 mmol/L.

Statistical analysis was performed using Statistical Package for the Social Sciences (SPSS) version 19 software (SPSS Inc., Chicago, IL, USA). Mean, standard deviation, standard error, and median range for all quantitative variables (i.e. Hb, MCV, MCH, TSH, FT4, vitamin B12, and FBS) were all calculated. The Kolmogorov-Smirnov test was used to examine the distribution of variables which revealed non-normal distribution. Consequently, the Mann-Whitney *U* test was used to compare the mean values of quantitative variables between patients and control groups. We assumed there was a statistically significant when *p*-value was less than 0.05.

Table 1
Normal laboratory reference ranges of different laboratory tests used in the current study.

	Normal values
Hb	Male: 13.5–17.5 g/dl Female: 11.5–15.5 g/dl
MCV	80–95 fl
TSH	0.47–5.01 uIU/ml
Free T4	0.71–1.58 ng/dl
Vitamin B_{12}	141–698 pmol/L
FBS	3.00–6.40 mmol/L

Hb = hemoglobin; MCV = mean corpuscular volume; TSH = thyroid stimulating hormone; FT4 = free thyroxine; FBS = fasting blood sugar.

3. Results

The mean age (Table 2) and gender distribution (Table 3) were similar in cases and controls with no statistically significant difference. The Hb level was low in 30 (26%) vitiligo patients as compared to 22 (25%) control subjects with no statistically significant difference ($p = 0.824$). Although not statistically significant, vitiligo patients were 2.4 times more likely to have microcytic anemia (Table 3) with a significantly lower mean MCV value when compared to controls ($p = 0.001$). More female patients (20%) were found to have microcytic anemia than males (8%) ($p = 0.061$) as shown in Fig. 1. On the other hand, macrocytic anemia was diagnosed in 1% and in 2% of vitiligo and control groups, respectively ($p = 0.404$). Surprisingly, none of the latter had vitamin B12 deficiency.

Thyroid functional abnormalities were generally found more in vitiligo patients. Although statistically non-significant, vitiligo patients were approximately 1.6 times

Table 2
Mean absolute values of various variables in the vitiligo and control groups.

	Vitiligo ($n = 115$) Mean ± SD	Control ($n = 89$) Mean + SD	*p*-value
Age	29.53 ± 9.22	30.73 ± 10.56	0.515
Hemoglobin	13.43 ± 1.69	13.56 ± 1.79	0.924
MCV	83.88 ± 8.01	86.58 ± 8.86	0.001*
TSH	3.42 ± 5.71	2.35 ± 1.77	0.067
Free T4	1.41 ± 1.46	1.36 ± 1.09	0.046*
Vitamin B_{12}	289.49 ± 187.93	359.68 ± 191.56	0.002*
FBS	5.41 ± 1.58	5.10 ± 0.96	0.106

SD = standard deviation; Hb = hemoglobin; MCV = mean corpuscular volume; TSH = thyroid stimulating hormone; FT4 = free thyroxine; FBS = fasting blood sugar.
* Indicates statistically significant difference.

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