Correlation between serum α-MSH and vitamin D levels in vitiligo patients

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Background: Vitiligo is a skin disease caused by the destruction of melanocytes of the epidermis, leading to well-defined white patches that are often distributed symmetrically. The present study aimed to determine the correlation relationship between the α-MSH and vitamin D serum levels among Iraqi vitiligo patients.

Materials and Methods: This study was done on outpatients who attended the Dermatology and Venereology Consulting Clinic of Salah-Al Deen General Hospital from November 2017 to March 2018. One hundred and ninety individuals were stratified into 110 cases of vitiligo and 80 healthy controls. Serum assays for α-MSH and vitamin D levels were sent for all subjects.

Results: Vitiligo patients had significantly lower α-MSH levels and vitamin D levels than the controls (P ≤ 0.01). There was a significant, positive correlation between α-MSH and vitamin D levels in vitiligo patients overall (r = 0.236; P ≤ 0.01), though this correlation was negative within the male and female subgroups (r = -0.392 and -0.661, respectively; P ≤ 0.01).

Conclusion: Compared to normal controls, vitiligo patients had significantly lower levels of α-MSH and vitamin D. These findings may back the normalization of both α-MSH and vitamin D levels in vitiligo patients as an important step toward disease recovery.

Keywords: vitiligo, vitamin D, α-MSH

INTRODUCTION

Vitiligo may be derived from *vitelius*, a Latin word that refers to a calf, because the white patches of the disease resemble those of a calf. Other researchers believe that vitiligo (leukoderma) might have evolved from the term *vitium*, meaning a defect. Vitiligo is a skin disease caused by the destruction of melanocytes of the epidermis, leading to well-defined white patches that are often distributed symmetrically. It occurs with a prevalence rate of 0.5-4%, with equal frequency among males and females. It affects people of all races and ethnicities [1,2].

Vitiligo is not contagious and the precise reason behind it is not well-understood; it may be due to a mixture of genetic and environmental factors. Some authors have reported triggers like emotional distress or sunburns. Vitiligo is not painful, but its social and psychological effects are well-documented [3].

Alpha-MSH is a peptide that is secreted into the blood and is responsible for skin pigmentation; however, it may play a role in regulating reproductive function, immunomodulation/inflammation, and energy homeostasis [4]. It acts on the melanin pigment of the skin by its direct effect on keratinocytes of the epidermis and less commonly on melanocytes or Langerhans cells to minimize skin damage induced by UV radiation [5,6].

Calcitriol isthe active form of vitamin D and may be considered as a hormone [7].

Since both α-MSH and vitamin D play a role in the occurrence and configuration of vitiligo the present study aimed to find out the relationship between the serum levels of α-MSH and vitamin D among Iraqi vitiligo patients.

MATERIALS AND METHODS

This case-control study was done on outpatients who attended the Dermatology and Venereology Consulting Clinic of Salah-Al Deen General Hospital in Tikrit, Iraq, from November 2017 to March 2018; these months were selected for sampling to avoid summer solstice. The total number of subjects was 190 male and female individuals, stratified into 110 vitiligo cases and 80 healthy individuals (control group). The adult age range of 18-55 years was targeted to avoid childhood or old age hormonal and enzymatic changes that may influence the data of the study. Serum assays for α-MSH and vitamin D were conducted using ELISA Kits (Sunlong Biotech Company) for all participants, taking into consideration that normal values may have international and national variations.

Patients who presented with different types of vitiligo and had not taken any medications in the preceding three months were included in the study. Exclusion criteria included patients with chronic systemic illness, autoimmune diseases, or inflammatory bowel disease; use of medications like anticonvulsants drugs, glucocorticoids, and supplementary vitamins, as well as drugs that interfere with skin pigmentation like hormonal therapy including oral contraceptive pills; pregnant and lactating females; and heavy smokers, alcoholic, or immunocompromised patients.

An ethical agreement statement was obtained from each subject according to the World Medical Association Declaration of Helsinki, revised in 2000, Edinburgh. The authors declare no conflicts of interest related to the present study since it is academic research under the supervision of the Ministry of Higher Education and Scientific Research.

SPSS (Statistical Package For Social Sciences) was used for statistical analysis to measure the mean and standard deviation (SD). Pearson correlation coefficient test was used to find the correlation coefficient (r) between α-MSH and vitamin D levels. The level of statistical significance was considered at $P \leq 0.05$.

RESULTS

Level of α-MSH in vitiligo patients and controls

In the present study the α-MSH level (mean ± SD) in the vitiligo patients and controls was 236.89 ± 80.81 and 332.56 ± 64.2 pg/ml, respectively, ranging between 92.4-402.3 and 220.8-452 pg/ml, respectively. The mean age in the vitiligo and control groups was 32.63 ± 8.1 and 30.23 ± 7.12 years, respectively, with a range of 18-55 years in both groups. These results show that the vitiligo patients had significantly lower α-MSH levels than the controls ($P \leq 0.01$).

On the other hand, theα-MSH level in male vitiligo patients and male controls was 272.5 ± 42.66 (range: 208.9-338.6) and 374.12 ± 39.01 (range: 324-452) pg/ml, respectively, with a mean age of 32.82 ± 8.06 and 30.0 ± 6.43 years, respectively. Statistical analysis revealed a highly significant difference ($P \leq 0.01$) in α-MSH levels between male vitiligo patients and male controls. A similar finding was found among female vitiligo patients, whose mean α-MSH level (190.33 ± 95.97 pg/ml; range: 92.4-402.3 pg/ml) was lower than female controls (282.34 ± 39.21 pg/ml; range: 220.8-352.4 pg/ml). The mean age of the female participants was 32.38 ± 7.73 and 30.46 ± 7.97 years among the patients and controls, respectively. Again, there was a significant difference ($P \leq 0.05$) in α-MSH levels between female vitiligo patients and female controls. These results are summarized in Table 1.

Another finding of this study was a significant difference ($P \leq 0.05$) in α-MSH levels between male and female vitiligo patients, besides a highly significant difference ($P \leq 0.01$) in α-MSH levels between healthy males and females (controls).

Level of vitamin D in vitiligo patients and controls

In the current study, the vitamin D level (mean ± SD) in vitiligo patients and controls was 14.55 ± 6.24 and 19.86 ± 2.09 ng/ml respectively, with ranges of 6.0-28.3 and 14.8-28.7 ng/ml,

Table 1. Level of α-MSH in vitiligo patients compared with control group.

		Vitiligo Patients			Control Group		
		Total	Male	Female	Total	Male	Female
Number of subjects		30	17	13	30	15	15
Age (years)	Mean ± SD	32.63 ± 8.1	32.82 ± 8.06	32.38 ± 7.73	30.23 ± 7.12	30.0 ± 6.43	30.46 ± 7.97
	Range	20-45	23-45	20-45	20-45	20-40	20-45
α-MSH (pg/ml)	Mean ± SD	236.89 ± 80.81	272.5 ± 42.66	190.33 ± 95.97	332.56 ± 64.2	374.12 ± 39.01	282.34 ± 39.21
	Range	92.4-402.3	208.9-338.6	92.4-402.3	220.8- 452	324-452	220.8-352.4

respectively. The mean age of individuals in these groups was 32.63 ± 8.1 and 30.23 ± 7.12 years, respectively. These results show that the vitiligo patients had significantly lower vitamin D levels than the controls (P ≤ 0.01).

Moreover, the mean vitamin D level in male vitiligo patients and male controls was 18.94 ± 4.54 and 20.63 ± 3.48 ng/ml, respectively, with ranges of 10.1-28.3 and 14.8-28.7 ng/ml, respectively. The mean age of individuals in these groups was 32.82 ± 8.6 and 30.0 ± 6.43 years, respectively, with an overall range of 18-40 years. Statistical analysis revealed no significant difference (P ≥ 0.05) in vitamin D levels between male vitiligo patients and male controls. On the other hand, female vitiligo patients had significantly lower vitamin D levels (8.81 ± 1.91 ng/ml) than female controls (18.59 ± 2.86 ng/ml; P ≤ 0.01). These results are presented in detail in Table 2.

Another finding of this study was a highly significant difference (P ≤ 0.01) in vitamin D levels between male and female vitiligo patients. This is while there was no significant difference (P ≥ 0.05) in vitamin D levels between male and female controls.
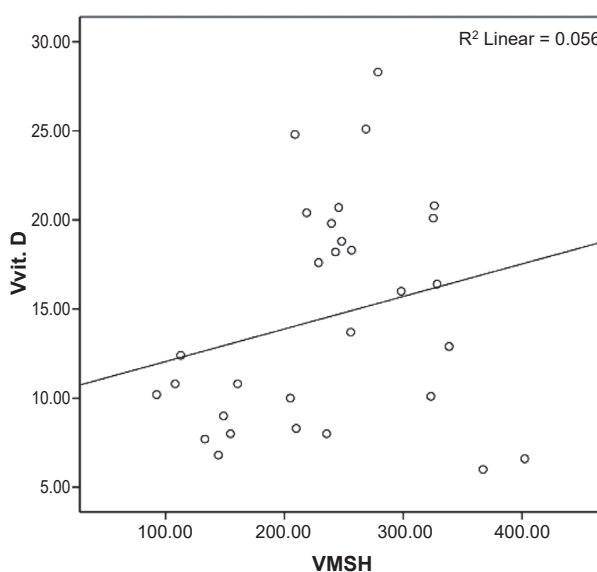
Correlation between α-MSH and vitamin D levels in vitiligo patients

The correlation coefficient (r) between the levels of α-MSH and vitamin D in vitiligo patients showed that there was a highly significant, positive correlation between α-MSH and vitamin D levels among the vitiligo patients (r = 0.236; P ≤ 0.01), as depicted in Table 3 and Figure 1. However, there were negative correlations between α-MSH

Table 3. Correlation between the level of α-MSH and vitamin D in vitiligo patients.

| Patients	α-MSH (pg/ml) (mean ± SD)	Vit.D (ng/ml) (mean ± SD)	r	P-value
Total	236.89 ± 80.81	14.55 ± 6.24	0.236	≤ 0.01
Male	272.5 ± 42.66	18.94 ± 4.54	-0.392	≤ 0.01
Female	190.33 ± 95.97	8.81 ± 1.91	-0.661	≤ 0.01

Figure 1. Correlation between the level of α-MSH and vitamin D in all vitiligo patients.
(VVit.D = vitamin D serum level of vitiligo patients; VMSH = α-MSH serum level of vitiligo patients)

Table 2. Level of vitamin D in vitiligo patients compared with control in total, male, and female subjects.

		Vitiligo Group			Control Group		
		Total	Male	Female	Total	Male	Female
Number of subjects		110	49	61	80	40	40
Age (years)	Mean ± SD	32.63 ± 8.1	32.82 ± 8.06	32.38 ± 7.73	30.23 ± 7.12	30.0 ± 6.43	30.46 ± 7.97
	Range	18-55	18-55	18-55	18-55	18-55	18-55
Vit. D (ng/ml)	Mean ± SD	14.55 ± 6.24	18.94 ± 4.54	8.81 ± 1.91	19.86 ± 2.09	20.63 ± 3.48	18.59 ± 2.86
	Range	6.0-28.3	10.1-28.3	6.0-12.4	14.8-28.7	14.8-28.7	14.0-24.5

and vitamin D levels within the male and female subgroups of vitiligo patients (r = -0.392 and -0.661, respectively) with strong statistical significance (P ≤ 0.01), as conveyed in Figures 2 and 3.
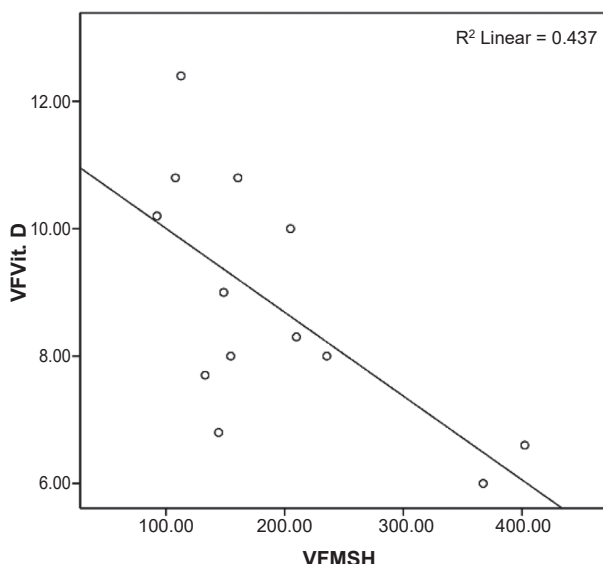
DISCUSSION

The findings of the present study showed lower
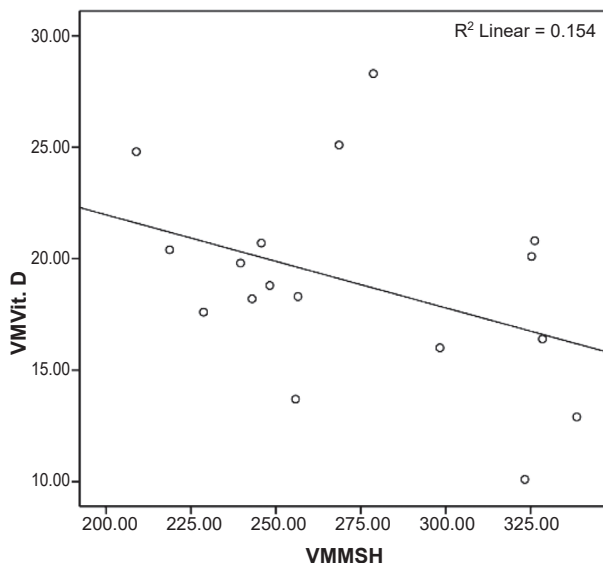
Figure 2. Correlation between the level of α-MSH and vitamin D in male vitiligo patients.
(VMVit.D = vitamin D serum level of vitiligo male patients;
VMMSH = α-MSH serum level of vitiligo male patients)

Figure 3. Correlation between the level of α-MSH and vitamin D in vitiligo female patients.
(VFVit.D = vitamin D serum level of vitiligo female patients;
VFMSH = α-MSH serum level of vitiligo female patients)

systemic levels of α-MSH in vitiligo patients. It is not clear whether this plasma α-MSH immunoreactivity originates in the pituitary gland or other tissues like the skin.

A study by Ramalingam *et al.* in 2018 [8] revealed that plasma α-MSH levels of patients with vitiligo were similar to those of controls and there were no significant differences between active vitiligo patients and normal subjects or between stable vitiligo patients and control subjects. These findings are in disagreement with those of the present study.

A study by Lips in 2010 [9] concluded that vitamin D deficiency and insufficiency are still very common globally, which may explain the results of the current study, which revealed that there was a highly significant difference(P ≤ 0.01) in vitamin D levels between vitiligo patients and healthy controls. This was also in agreement with other studies [10-14].

On the other hand, regarding gender, the vitamin D level was significantly lower in female vitiligo patients than males. This result is in agreement with the study done by Xu *et al.* in 2012 [12] but disagrees with the findings of Khurrum *et al.* [14], who reported lower vitamin D levels in males than females. On the other hand, studies conducted by Ramalingam *et al.* [8], Silverberg *et al.* [11], and Beheshti *et al.* [13] revealed no significant difference between female and male vitiligo patients in vitamin D levels.

Other studies have also identified similar as well as additional variables affecting serum vitamin D levels in vitiligo patients, such as outdoor jobs [13], a younger age [16], family history [14], presence of other autoimmune diseases [11,12], in addition to low dietary intake [11].

Various factors have been implicated in the etiopathogenesis of vitiligo including the role of calcium imbalance [17]; vitamin D receptor Apa-1 polymorphism [18]; and low levels of circulating vitamin D [11]. This last factor is in agreement with the present study findings, as mentioned above.

The data for each gender group is done separately under a special equation that yields a different polarity for each gender away from that of the total patients, which means it does not follow the normal statistical sum; this may explain the discrepancy between positivity of the correlation coefficient between vitamin D and α-MSH levels in all patients with vitiligo and the negativity of this

correlation when each gender was considered alone.

CONCLUSION

The α-MSH and vitamin D levels in vitiligo patients were significantly lower than those of controls. Furthermore, there was a significant, positive correlation between α-MSH and vitamin D levels in vitiligo patients overall, though this correlation was negative within the male and female subgroups, which might be due to hormonal differences. These findings may back the normalization of both α-MSH and vitamin D levels in vitiligo patients as an important step toward disease recovery.

Acknowledgments

Conflict of Interest: None declared.

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