ORIGINAL ARTICLE

Serum homocysteine and vitiligo

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ABSTRACT

Background: The etiopathogenesis of vitiligo is still not fully clear. A relationship between homocysteine (Hcy) level and activity of vitiligo has been suggested, however, this remains controversial.

Objective: The aim of this work was to estimate the serum level of Hcy in vitiligo patients to evaluate its possible role in the pathogenesis of the disease and its relation to disease activity.

Methods: Thirty patients complaining of vitiligo were enrolled in this study as group I. Thirty age and sex matched healthy controls served as group II, after eliminating factors affecting Hcy levels by suitable exclusion criteria. Estimation of Hcy level was done using ELISA technique. Vitiligo extent was measured according to the Vitiligo Area Scoring Index (VASI).

Results: There was no significant difference in the mean Hcy level between vitiligo patients and controls [11.35 +/- 3.14 versus 10.49 +/- 1.68 micromol/L ($p > 0.05$)]. There was no significant association between mean Hcy level and duration or onset of the illness ($p > 0.05$). There was no correlation between activity of vitiligo and mean level of Hcy ($p > 0.05$). There was a significant positive correlation between mean Hcy level and mean age of patients and controls ($p < 0.05$).

Conclusion: This study doesn't support the possibility that Hcy may be a precipitating factor for vitiligo. Mean Hcy was positively correlated with age of patients but not with activity of the disease.

KEYWORDS: Vitiligo, serum homocysteine, vitiligo severity, VASI.

INTRODUCTION

Vitiligo is an idiopathic disorder characterized by depigmented patches in skin due to loss of melanocytes. Death of pigmented cells may be caused by factors from inside and/or outside the cell.[1] Vitiligo occurs worldwide, with an incidence between 0.1% and 2%. The causes of the disease are uncertain but seem to be dependent on the interaction of genetic, immunological and neurological factors.[2] In general it shows multifactorial etiology and polygenic inheritance.[3]

Numerous studies and investigations from all over the world have attempted to determine the mechanisms behind this disease; however, the pathogenesis of vitiligo remains elusive.[4] Pigmentary dilution is observed in patients with homocystinuria. Therefore, it is possible that an increase of local homocysteine (Hcy) interferes with normal melanogenesis and plays a role in the pathogenesis of vitiligo.[5] Hcy may mediate melanocyte destruction via increased oxidative damage, interleukin 6 production and nuclear factor κB activation.[6] Also Hcy metabolism may be altered by mutations in catalase gene and low catalase activity is detected in vitiligo patients.[7]

It is thought that patients with vitiligo are more

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likely to have pernicious anaemia and vitamin B12 deficiency. Vitamin B12 and folic acid are major determinants of Hcy levels, and a nutritional deficiency in either of these two vitamins results in hyperhomocysteinaemia.[8] Hcy has an inhibitory action on the histidase and tyrosinase activity of the skin. Therefore, it is possible that an increase in Hcy may interfere with normal melanogenesis and play a role in the pathogenesis of vitiligo.[9]

Prior published studies of the association between vitiligo and Hcy found conflicting results. Silverberg and Silverberg[6] demonstrated an association between serum Hcy and extent of vitiligo, suggesting Hcy as a new biomarker of vitiligo extent. Balci et al,[10] performed a Turkish age/gender-matched case-control study, finding no association between Hcy and vitiligo. In this study we aimed to estimate the serum level of Hcy in vitiligo patients to evaluate its possible role in the pathogenesis of the disease and its relation to disease severity.

SUBJECTS AND METHODS

Thirty Egyptian patients complaining of vitiligo were enrolled in this study to estimate their serum level of Hcy (group I). Thirty age and sex matched healthy individuals were selected as controls (group II). Subjects taking any drug or suffering from diseases known to alter serum level of Hcy were excluded. Also subjects who were physically active (manual workers and athletes) were excluded as physical activity can lower plasma Hcy level.[11] Vitiligo extent was measured according to the Vitiligo Area Scoring Index.[12] Patients with vitiligo in head and neck area were excluded as VASI doesn't include head and neck region. Clinically, vitiligo was defined as localized, generalized, or universal. Whereas disease activity was identified as stable or progressive. For all subjects, Hcy level determination was done by enzyme linked immunosorbant assay (ELISA) technique.

The total body VASI was calculated using a formula that includes contributions from all body regions (possible range, 0–100).

VASI = $\sum$ Hand Units of all body sites ×Residual Depigmentation.

One hand unit, which encompasses the palm plus the volar surface of all the digits, is approximately 1% of the total body surface area.[13] It is used as a guide to estimate the baseline percentage of vitiligo involvement in each body region. The body was divided into five separate regions: upper extremities (excluding hands), hands, trunk, lower extremities (excluding feet), and feet.[12] The axillary region was included with the upper extremities while the buttocks and inguinal areas were included with the lower extremities.

The extent of residual depigmentation was expressed by the following percentages: 0, 10%, 25%, 50%, 75%, 90%, or 100%. At 100% depigmentation; no pigment was present, at 90%; specks of pigment were present, at 75%; the depigmented area exceeded the pigmented area, at 50%; the depigmented and pigmented areas were equal, at 25%; the pigmented area exceeded the depigmented area, at 10%; only specks of depigmentation were present.[12]

STATISTICAL ANALYSIS

The SPSS version 16 was used. Quantitative data were analyzed using mean and SD. The Student t-test was used to compare the means of different groups. Pearson correlation was used to determine relationships. P values less than 0.05 were considered significant.

RESULTS

The present study was conducted on 30 patients with vitiligo [their ages ranged from 16 to 46 years (mean ± SD 29.63 ± 9.91 yrs)] and 30 age and sex matched healthy controls [their ages ranged from 17 to 45 years (mean ± SD 29.37 ± 9.35 yrs)] to estimate their serum level of Hcy.

There was no significant difference in the mean Hcy level between vitiligo patients and controls [(11.35 +/- 3.14 versus 10.49 +/- 1.68 micromol/L ($p > 0.05$)] (Table 1). There was no significant association between serum mean Hcy level and duration or onset of the illness ($p > 0.05$). There was no correlation between course of vitiligo and mean serum level of Hcy ($P > 0.05$). Comparison of patients with stable or progressive vitiligo did not reveal any significant difference (Fig. 1, Table 2). There was a significant positive correlation between mean Hcy level and mean age of patients and controls ($p < 0.05$) (Fig. 2, Table 3).

Regarding indoor/outdoor activities, 16 (53.33%) patients were working indoor and 14 (46.67%) were working outdoors. In controls, 10 (33.33%) persons were working indoor and 20 (66.67%) were working outdoors. There was insignificant difference among both groups ($p > 0.05$). Family history of vitiligo was positive in only 2 patients (6.7%) and negative in 28 patients (93.3%). It was negative in all control subjects; a difference that was not statistically significant ($p > 0.05$). Rel-

Table 1 Mean Hcy level among both groups

Groups	Hcy level (µmol/L)		T test	
	Range	Mean±SD	*t*	*P* value
Group I	7.6 - 20.3	11.35 ± 3.14	1.32	0.191
Group II	7.1 - 14.4	10.49 ± 1.68		

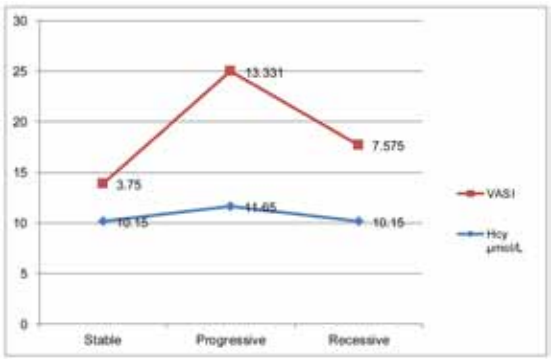

Fig. 1 Correlation between Hcy level, VASI and course of the disease.

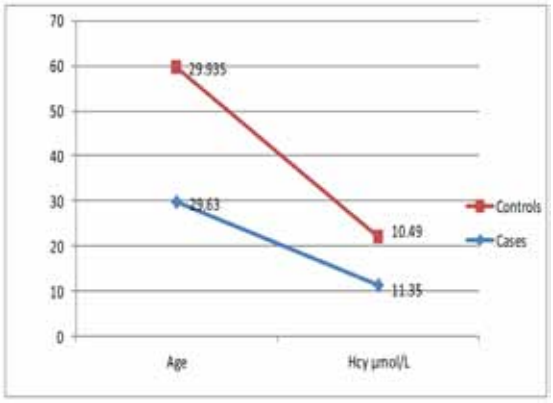

Fig. 2 Correlation between Hcy level and age of patients and controls.

Table 3 correlation between Hcy level and age of patients and controls

	Age Mean ± SD	Hcy µmol/L Mean ± SD	T test	*P* value
Cases	29.63 ± 9.91	11.35 ± 3.14	1.200	0.043
Controls	29.73 ± 9.35	10.49 ± 1.68	1.000	0.010

Table 2 Correlation between Hcy level, VASI and course of the disease

	Stable (2 cases)		Progressive (24 cases)		Regressive (4 cases)		F test	*P* value
Hcy (µmol/L)	Mean	SD	Mean	SD	Mean	SD	0.529	0.595
	10.150	7.070	11.650	3.396	10.150	1.826		
VASI	3.750	1.060	13.331	7.479	7.575	3.868	2.601	0.093

evant medical history showed that only 1 patient (3.3%) was anaemic and 2 patients (6.7%) were hypertensive. The medical history of controls was irrelevant. The relevance of medical history among both groups was insignificant ($p > 0.05$).

DISCUSSION

The exact cause of vitiligo is not fully identified and many studies have tried to investigate this skin disorder from many aspects. Prior published studies of the association between vitiligo and Hcy found conflicting results. Some studies postulate a role of Hcy in the pathogenesis of vitiligo. Therefore, it is possible that increased Hcy plays a role in the destruction of melanocytes.[5,6] In this study we aimed to measure Hcy in serum of patients suffering from vitiligo in a trial to evaluate its possible role in the pathogenesis of the disease and its relation to the disease activity.

In this study, there was no statistically significant difference between vitiligo patients and controls regarding mean serum Hcy level ($p > 0.05$). This finding was in agreement with other studies.[10,14,15] Our result was not in agreement with previous studies which reported that serum Hcy level was significantly elevated in patients with vitiligo than in controls.[5,6,16-19]

The present study showed no association between serum Hcy and extent of vitiligo. This result was in agreement with Shaker and EI-Tahlawi[5] who reported that no correlation was found between serum Hcy levels and extent of vitiligo. In contrast, Silverberg and Silverberg[6] and Singh et al,[17] reported an association between serum Hcy and extent of vitiligo.

This difference may be due to methods of patient selection and sample of patients studied. Shaker and El-Tahlawi[5] selected patients with more severe disease and excluded patients with vitiligo extent less than 30% of body surface area but our study included vitiligo patients with less than and more than 30%, so we studied wider range of disease extent. Silverberg and Silverberg6 and Singh et al,[17] performed a study on 56 and 200 vitiligo patients respectively. They measured serum level of Hcy, vitamine B12 and folic acid and reported a significant association between Hcy level and extent of vitiligo. The difference between these studies and the present study may be due to the method of vitiligo scoring as we used VASI which is a qualitative and quantitative method that can record vitiligo extent and severity in the same equation for every patient. They recorded only extent of the disease not the severity of depigmentation by the rule of nine.

There was a significant correlation between mean Hcy level and mean age of patients and controls as Hcy level increases with age. This finding was in agreement with other reports.[20-23] On the other hand, this was contrary to Shaker and El- Tahlawy[5] and Sabry et al,[19] who reported that there was no correlation between Hcy level and age of subjects. This difference can be explained partly by sample of patients studied and partly by physiological and genetic factors.

Hu et al,[22] explained the age dependent increase of Hcy by attributing this to the deterioration of renal function and weak renal excretion of Hcy and impaired folate status. Wilcken and Gupta[20] and Kang et al,[21] also explained the increase in Hcy levels with advancing age in both sexes and decrease in children by 30% by a mechanism that suggest the well-known deterioration of renal function with age and the correlation between age and serum creatinine, which seems to be a strong determinant of Hcy concentration.

It was estimated that tubular cells normally have to take up and metabolize about 0.5 µmol of Hcy every 24 hours. Impairment of this important metabolic mechanism might explain the increase of Hcy in elder people.[20]

There was no correlation between course of vitiligo and serum level of Hcy, this was in agreement with Karadag et al,[18] who found that comparison of patients with stable or progressive vitiligo did not reveal any significant difference. Hyperhomocysteinemia and deficiency of vitamin B12 and folic acid were not significant risk factors for progressive vitiligo. Shaker and El-Tahlawi,[5] Singh et al,[17] and Sabry et al,[19] disagree with this result as they found that mean Hcy level was increased in active vitiligo patients than those with stable disease. The oxidation of Hcy produces toxic reactive oxygen species[24] which together with other biochemical abnormalities in vitiligo, lead to oxidative stress, accumulation of melanocytotoxic compounds and an inhibition of natural detoxifying processes that may contribute to the destruction of melanocytes in vitiligo skin.[25]

Also our study found no significant correlation between duration of vitiligo and serum level of Hcy. This finding was in agreement with Shaker and El-Tahlawi[5] and Sabry et al.[19]

This study showed no significant correlation between gender of patients or controls with serum level of Hcy. This was in agreement with Silverberg and Silverberg[6] and disagree with others.[5,17-19] They reported that Hcy level was significantly higher in men than in women among patients and controls. Males may have higher Hcy level than females due to greater muscle mass and more active life style, also it may be due to the effect of female sex hormones on Hcy metabolism.

CONCLUSION

Our study doesn't support the assumption that Hcy may be a precipitating factor for vitiligo in the predisposed individuals. It has been found that elevated serum Hcy level was related to age of the patients but not to activity of the disease or gender of patients. It is recommended that similar studies be done on larger number of subjects to confirm or contradict these results.

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