ID Design 2012/DOOEL Skopje, Republic of Macedonia
Open Access Macedonian Journal of Medical Sciences. 2017 Jun 15; 5(3):332-334.
https://doi.org/10.3889/oamjms.2017.066
eISSN: 1857-9655
Clinical Science

Correlation between Serum Homocysteine and Vitiligo Area Scoring Index

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Citation: Hasibuan DRU, Putra IB, Jusuf NK. Correlation between Serum Homocysteine and Vitiligo Area Scoring Index. Open Access Maced J Med Sci. 2017 Jun 15; 5(3):332-334. https://doi.org/10.3889/oamjms.2017.066

Keywords: Vitiligo; serum homocysteine; pathogenesis.

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Received: 02-Mar-2017; **Revised:** 11-Apr-2017; **Accepted:** 18-Apr-2017; **Online first:** 11-Jun-2017

Funding: This research did not receive any financial support.

Competing Interests: The authors have declared that no competing interests exist.

Abstract

BACKGROUND: Vitiligo is a chronic skin disorder. White macules caused by melanocyte destruction is a characteristic finding that cosmetically disturbing. Until recently, pathogenesis of vitiligo is still unclear. The role of homocysteine in vitiligo is mentioned in previous studies thus it is probable that it can be a biomarker to determine vitiligo severity.

AIM: To determine correlation between serum homocysteine and vitiligo area Scoring Index (VASI)

SUBJECT AND METHOD: This was a cross-sectional analytic study which involved 30 vitiligo patients that were diagnosed by clinical and Wood's lamp examinations then VASI score was determined and same numbers of control. We conducted blood sampling and measurement of serum homocysteine level to the patients.

RESULTS: There is no significant correlation between serum homocysteine and VASI score ($p = 0.133$, $r = 0.281$), family history ($p = 0.706$), and duration of vitiligo ($p = 0.993$, $r = 0.002$). There is no significant difference between serum homocysteine in vitiligo patients and controls ($p = 0.905$). There is a correlation between serum homocysteine with gender ($p = 0.001$) and age ($p = 0.036$; $r = 0.385$) in vitiligo patient.

CONCLUSION: There is no significant correlation between serum homocysteine and VASI score, family history, and duration of vitiligo. There is no significant difference between serum homocysteine in vitiligo patients and controls. There is a correlation between serum homocysteine with gender and age in vitiligo patient.

Introduction

Vitiligo is a skin depigmentation disorder with the characteristic as a white macule caused by melanocyte destruction. Aetiology of vitiligo is still unknown. But there are several hypotheses like genetic, autoimmune and biochemistry [1-3]. This hypothesis was thought to simultaneously work together and caused vitiligo. Genetic predisposition can trigger autoimmune process, and with the addition of oxidative stress, elevation can result in the destruction of melanocyte, therefore, inducing white macule in vitiligo subjects [4].

One compound thought to be involved in this hypothesis is homocysteine [5]. Homocysteine-mediated melanocyte destruction via production of interleukin-6 (IL-6), activating *nuclear factor-kappa* B (NF-κB) and increased oxidative stress [6].

Subjects and Methods

This was a cross-sectional analytic study involving 30 vitiligo patients and 30 controls who were 18 years old or above and submitted to the outpatient dermatology and venereology clinic in Haji Adam Malik General hospital, Medan, North Sumatera, Indonesia. This study conducted from June until October 2016. Each subject signed informed consent were included in this study. Exclusion criteria were consumption of vitamin B_6, B_{12}, and folic acid within the last 6 months, breastfeeding, pregnancy, and vitiligo treatment during the last 6 months. Ethical clearance was given by Health Research Ethical Committee, Faculty of Medicine, University of Sumatera Utara.

All subjects with vitiligo were diagnosed by clinical and Wood's lamp examinations. VASI score was determined by calculating body part involved and depigmentation severity. VASI was calculated using a

formula that includes contributions from all body regions (possible range, 0–100). VASI = ∑ 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. It is used as a guide to estimate the baseline percentage of vitiligo involvement in each body region. The body was divided into separate regions: upper extremities (excluding hands), hands, trunk, lower extremities (excluding feet), feet and head and neck. 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.

Fasting blood sample from subjects then processed into the serum. Homocysteine level was measured from serum by using ADVIA Centaur HCY®.

The results were analysed with SPSS version 19. Quantitative data were analysed using mean and SD. The Student t-test was used to compare the means of different groups. Spearman test was used to determine relationships. P values less than 0.05 were considered significant.

Results

There is no significant correlation between serum homocysteine and VASI score (p = 0.133, r = 0.281), family history (p = 0.706), and duration of vitiligo (p = 0.993, r = 0.002).

Table 1: Serum homocysteine level in vitiligo subjects and controls

Subjects	Serum homocysteine level		
	Mean (μmol/L)	Standard Deviation (μmol/L)	p
Vitiligo	10.66	2.89	0.905
Control	10.58	2.01	
Male	13.02	1.48	0.001
Female	9.81	2.81	
Positive family history	11.07	2.16	0.706
Negative family history	10.56	3.08	

There is a correlation between serum homocysteine with gender (p = 0.001) and age (p = 0.036; r = 0.385) in vitiligo patient. There is no significant difference between serum homocysteine in vitiligo patients and controls (p = 0.905).

Table 2: Correlation between the serum homocysteine with VASI score and other variables

	p	r
Serum homocysteine with VASI score	0.133	0.281
Serum homocysteine with age of vitiligo subjects	0.036	0.385
Serum homocysteine serum with duration of disease	0.993	0.002

Discussion

In this study we didn't find any significant correlation between serum homocysteine level and VASI score (p > 0.05; r = 0.281). This is in agreement with another study in Dr M. Djamil Padang, which conducted a study with 17 samples (r = 0.061; p > 0.05) [7].

A similar finding by Zaki et al. in Egypt also didn't find any significant relation between serum homocysteine level and VASI score (p > 0.05). Zaki et al. reveal this study used VASI score instead of rules of nine like in other studies. VASI score evaluates vitiligo lesion both quantitatively and qualitatively [8].

This result was in disagreement with El-Dawela and Abou-elf touch who conducted a study with 70 samples and found a correlation between VASI score and homocysteine serum (r = 0.835, p = 0.001) with mean VASI score was 9.5 ± 19.5 [9]. Similar findings found by Agarwal et al in India with 50 vitiligo subjects (r = 0.567; p = 0.000). In this study VASI score ≥ 30 significantly higher than VASI score <30 (p = 0.001) [6]. Sabry et al. in an outpatient clinic in Benha University Hospital, Egypt with 35 subjects found serum homocysteine level and the extent of vitiligo (p = 0.001; r = 0.559). In this study vitiligo extent assessed using rules of nine [10].

Until now, it is still unclear about the underlying pathogenesis of vitiligo. Homocysteine was one compound thought to be involved in vitiligo. Homocysteine can induce oxidative damage, producing IL-6 and activating NF-κB which results in melanocyte destruction. IL-6 can increase the expression of intercellular adhesion molecule-1 that will stimulate adhesion melanocyte to leucocyte, inducing activation of polyclonal B cell and increasing production of autoantibody [11]. Activation of NF-ΚB by homocysteine then modulate expression of pro-apoptotic p53 in vitiligo lesion [12]. All of these could damage melanocyte [11, 12].

Other than that homocysteine also can produce oxidative stress, accumulate melanocytotoxic compound and inhibit natural detoxification which contributing in melanocyte destruction. Homocysteine can also affect tyrosinase in melanin synthesis at enzyme's active location. Free homocysteine also can react nonenzymatically with sulfhydryl and thiolation

can also occur. Both of which can affect the function of enzyme and protein [10, 13, 14].

In this study, there is no significant difference of serum homocysteine in vitiligo and control (p = 0.905). Factors affecting homocysteine are genetic, blood vitamin, sex, age, life style, drugs, hyperproliferating disease, renal failure, heart failure and diabetes mellitus [5, 15]. A similar finding was found by Zaki et al. who didn't find any difference between vitiligo subjects and control (p = 0.191) [8].

In disagreement, Singh et al at Sir Sunderhal Hospital, Varanasi, India with 200 vitiligo subjects and 75 controls found homocysteine level was significantly higher than control [16]. El-Dawela, Abou-elfetouh, Sabry and Agarwal found similar results [6, 9].

In conclusion, there is no significant correlation between serum homocysteine and VASI score, family history, and duration of vitiligo. There is no significant difference between serum homocysteine in vitiligo patients and controls. There is a correlation between serum homocysteine with gender and age in vitiligo patient. Further study needed to determine the pathogenesis of vitiligo and whether homocysteine had an influence on that.

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