Zagazig University Medical Journal
www.zumj.journals.ekb.eg
https://dx.doi.org/10.21608/zumj.2020.50275.2018 Volume 29, Issue 1, - January 2023, Page (235-239) Supplement Issue

Manuscript ID ZUMJ-2011-2018 (R3)
DOI **10.21608/zumj.2020.50275.2018**

ORIGINAL ARTICLE

Evaluation of malondialdehyde in vitiligo patients as a marker of lipid peroxidation.

Mahmoud Yousry Abd Elmowla[1], Somia Hasan Abd Allah[1], Shrook Abd Elshafy Khashaba [1]and Noha Saad Elsayed[2]

1Dermatology, Venereology and Andrology department, Faculty of Medicine ,Zagazig University, Egypt.
2Dermatology, Venereology and Andrology department, Mitghamer hospital,Aldqhlia, Egypt

Corresponding author
noha saad elsayed
E-mail:
nsaad13@yahoo.com

Submit Date 2020-11-19
Revise Date 2020-11-26
Accept Date 2020-12-06

ABSTRACT

Background : Vitiligo is a chronic depigmented skin disorder with melanocytes depletion. The pathogenesis of melanocyte damage in vitiligo is still unclear. However, there were some in vivo and in vitro studies that indicate the role of oxidative stress in pathophysiology of vitiligo. Vitiligo is characterized by a blunt increase of ROS and inflammatory mediators, such as cytokines and nitric oxide (NO), contributing to melanocyte dysfunction and/or destruction. Oxidative stress may be a good model for vitiligo pathogenesis . Lipid peroxidation in the cellular membrane of melanocyte may play an important role in depigmentation of vitiligo.

Subject and Methods: The study was conducted on 50 participants: 25 patients with vitiligo and 25 aged matched healthy controls. Malondialdehyde (MDA) was measured spectrophotometerically.

Results: There was highly statistical significant difference between studied groups regarding MDA level ($p \leq 0.001$).

Conclusions: Oxidative stress may play an important role in the pathogenesis of vitiligo**.**

Keywords: Vitiligo, Oxidative stress, Malondialdehyde.

INTRODUCTION

Vitiligo is the most common depigmentation disorder with an overall estimated worldwide prevalence of 0.5 to 2%, characterized by white macules on the skin caused as a result of the systematic destruction of functional melanocytes. **[1]**

The pathophysiology of vitiligo is thought to start by a trigger event that instigate stress responses in the skin , eliciting an autoimmune response in genetically susceptible individuals that ultimately targets the melanocytes known to have an inherited fragility, predisposing individuals to develop vitiligo. **[2,3]**

Oxidative stress supposed to be one of the triggering events in melanocyte degeneration in vitiligo. Melanogenesis produces significant levels of reactive oxygen species (ROS). ROS along with other radicals can induce oxidative stress. **[4]**

Malondialdehyde (MDA) arising from the free radical degradation of polyunsaturated fatty acids, can cause cross-linking in lipids, proteins and nucleic acids. Lipid peroxidation in melanocyte cell membrane may play an important role in depigmentation of vitiligo. **[5]**

AIM OF THE WORK

The aim of study is to evaluate serum levels of MDA in vitligo patients compared to healthy controls.

SUBJECTS AND METHODS

Patients:

Twenty five patients with vitiligo were included in this case control study. Along with twenty five age and sex matched healthy subjects were taken as controls. The study was conducted in Dermatology outpatient clinics and Biochemistry department, Faculty of Medicine, Zagazig University Hospitals, spanning period from April 2018 to October 2018.

Written informed consents obtained from the patients participating in the study. The study had approval of the Institutional Review Board (IRB) in Faculty of Medicine, Zagazig University (ZU-IRB#4531/6-4-2018).

Patients with vitiligo of any type or extent , any age ,both sexes are included in the study. Exclusion criteria included Pregnant and lactating females.

Methods:

All participants were subjected to complete history taking, general and dermatological examination to detect type and sites of vitiligo. Vitiligo European Task Force assessment (VETFa) was calculated to assess the three dimensions of the disease (extent (area), staging and spreading). Area is divided into head and neck (0-9%), trunk (0-36%), lower limbs (0-36%), upper limbs (0-18%) , hand and feet are included in evaluation of extent in upper and lower limbs. Staging is divided into stage 0: normal pigmentation, stage 1: incomplete depigmentation, stage 2: complete depigmentation, may include hair whitening in a minority of hairs <30%, stage3: complete depigmentation with significant hair whitening >30% and Stage 4: complete hair whitening. Spreading is divided into +1 progressive, 0 stationary and -1 regressive. Total area is the summation of all areas, total staging is the summation of staging of all areas and total spreading is the summation of spreading of all areas. **[6]**

Specimen collection and storage:

Three ml of venous blood were taken from each participant in the morning without fasting under complete aseptic condition then put in a sterile, dry, clean separator gel tube for serum isolation and left to clot. After clotting, the samples were centrifuged for 10 minutes at 5000 rpm. Serum was separated and stored at -20˚C in blood bank to detect MDA.

Measurement of Malondialdehyde spectrophotometerically.

Malondialdehyde in serum sample was calculated by the following equation.

MDA in Serum sample = $\frac{\text{sample}}{\text{standard}} \times 10$ nmol. **[7]**

Statistical analysis:

Data analysis was performed using the software SPSS version 20. Quantitative variables were described using their means and standard deviations. Categorical variables were described using their absolute frequencies. Chi square test and Fisher test were used to compare the proportion of categorical data. Kolmogorov-Smirnov (distribution-type) and Levene (homogeneity of variances) tests were used to verify assumptions for use in parametric tests. Non-parametric test (Mann Whitney) was used to compare means in two groups. To compare means of more than two groups, Kruskal wallis test was used. To find the correlation between two continuous variables which are normally distributed, Spearman correlation coefficients was used according to type of data. The level statistical significance was set at $P<0.05$. Highly significant difference was present if $p\leq0.001$.

RESULTS

Twenty five patient with vitiligo was included in the study,their age ranged from 13-56 years with a mean ± SD of 39.88 ± 16.15, male to female ratio 1.5: 1, along twenty five age and sex healthy controls, their age ranged from 16-55 years with a mean ± SD of 33.16 ± 11.68, male to female ratio 1.5: 1. There was no statistical significant differences between the two studied groups in age or sex distribution.

Regarding clinical data of patients group, 44% showed generalized vitiligo, 24% focal, 16% acrofacial, 12% segmental and 4% mucosal. Family history was +ve in 44% of cases. 96% of cases showed progressive course. Duration of disease ranged from 0.17-22 months with a mean ± SD of 7.23 ± 7.26. Patients have previous ttt in the form of phototherapy (56%), topical corticosteroid (48%) and calcineurin inhibitors (20%). Regarding VETFa, 36% was stage 4, 32% stage 2, 24% stage 10, 4% stage 3 and 4% stage 1. 40% was spread 2, 32% spread 1, 24% spread 5 and 4% spread 0. Percentage area involved ranged from 2-76% with a mean ± SD of 20.82 ± 22.92. As shown in **table (1) , figure (1).**

Serum malondialdehyde level in vitiligo patients ranged from 3.4-18.9 with a mean ± SD of 10.7 ± 4.4. MDA level of control group ranged from 2.1-7.7 with a mean ± SD of 4.56 ± 1.11. There was highly statistical significant difference between studied groups regarding MDA level ($p\leq0.001$). As shown in **table (2) , figure (2).**

There was a negative correlation between disease duration and malondialdehyde ($p>0.05$). As shown in **table (3).**

There was a negative correlation between malondialdehyde with spreading and staging scores, while there was a positive correlation between malondialdehyde and percentage area ($p>0.05$). As shown in **table (4)**.

Table (1): Disease specific characteristics in patients with vitiligo group:

Variable	N	%
Course		
Progressive	24	96
Stationary	1	4
Duration (years):		
Mean ± SD	7.23 ± 7.26	

Variable	N	%
Range	0.17 - 22	
Treatment:		
Topical corticosteroids	12	48
Phototherapy	14	56
Calcineurin inhibitors	5	20
Family history:		
Irrelevant	14	56
Relevant	11	44
Clinical types:		
mucosal	1	4
Acrofacial	4	16
generalized	11	44
focal	6	24
segmental	3	12
Vitiligo European Task Force assessment (VETFa)		
Staging:		
1	1	4
2	8	32
3	1	4
4	9	36
10	6	24
Spreading:		
0	1	4
1	8	32
2	10	40
5	6	24
Percentage area:		
Mean ± SD	20.82 ± 22.92	
Range	2 – 76	

Table (2): Serum malondialdehyde levels in studied groups:

Variable	Vitiligo group (n=25)	Control group (n=25)	Test	P
MDA:(nmol)				
Mean ± SD	10.7 ± 4.4	4.56 ± 1.11	-5.037	<0.001**
Range	3.4 - 18.9	2.1 -7.7		

SD : standard deviation **highly significant (p≤0.001)**

Table (3): Correlation between MDA and duration:

Variable	r	p
Duration		
MDA (nmol)	-0.175	0.404 NS

r:Spearmans correlation coefficient **NS: Non significant (P> 0.05)**

Table (4): Correlation between VETF and MDA :

Variable	MDA (nmol)	
	r	P
VETF:		
Area	0.210	0.348 NS
Spreading	-0.129	0.539 NS
Staging	-0.136	0.517 NS

r:Spearmans correlation coefficient **NS: Non significant (P > 0.05)**

Figure (1): pie chart showing clinical types of vitiligo among studied patients.

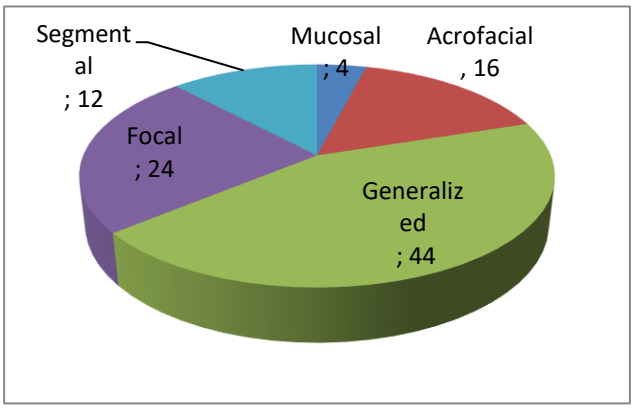
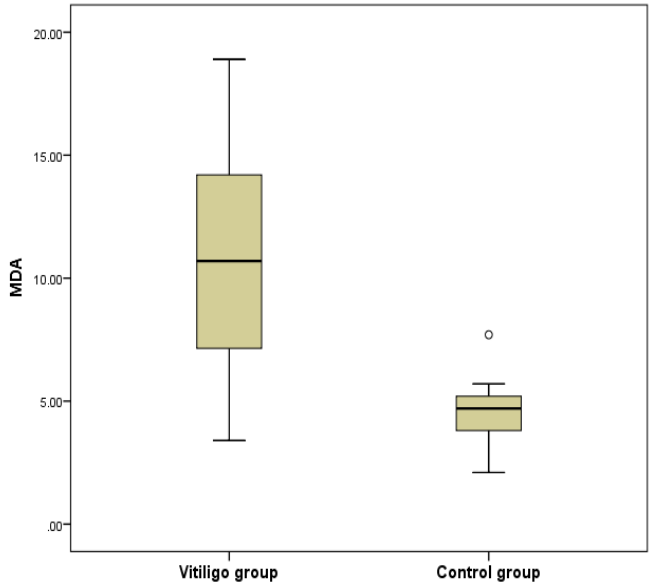


Figure (2): Bloxplot showing MDA of studied groups.



DISCUSSION

Vitiligo is manifested by depigmentation of the epidermis because of melanocytes destruction. Multiple theories have been proposed to explain pathomechanism of vitiligo but none of them could explain the exact pathomechanism of vitiligo. **[8]**

The current study was conducted to measure serum MDA level in vitiligo patients and healthy controls. There was highly statistical significance increase in MDA level among cases compared to control.

This result is in agreement with **El-Refaei et al. [9] ,** who found that MDA level showed a significant increase in 20 vitiligo patients compared to 10 healthy controls and there was also no relation between MDA and type of vitiligo. They have also analyzed the role of MDA in genetic predisposition of vitiligo, by comparing its level in patients with positive family history with those with negative family history and no significant difference was observed in MDA level of these two groups. Further, there was no significant difference between MDA level and the age of vitiligo patient.

Khan et al. [10] suggested that a defective antioxidant defense leads to unhindered cytotoxic action of ROS which can start a chain reaction and bring about lipid peroxidation producing lipid peroxides and lipoxides, whose further decomposition yields a variety of end products, including MDA. These end products can cause damage to cell membrane or DNA leading to cytotoxicity, mutagenecity and cell death. They are also cytotoxic to melanocytes and can inhibit tyrosinase enzyme.

In contrast to the present study, **Picardo et al. [11]** who studied 62 vitiligo patients with (acrofacial, segmental and generalized types) compared to 60 healthy controls. They found that serum levels of MDA were not significantly different between patients and control due to abnormal release of catecholamines from autonomic nerve endings.

Overproduction of reactive oxygen metabolites and/or limited production of antioxidants may trigger melanocyte destruction. Oxidative stress-induced accumulation of toxic free radicals may have a pathophysiological role in the initiation and progression of vitiligo. **[12]**

CONCLUSION

From this study, we can conclude that oxidative stress may play an important role in the pathogenesis of vitiligo.

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How to cite

Elsayed, N., Mahmoud, Y., Abd ALLAH, S., Khashaba, S. Evaluation of malondialdehyde in vitiligo patients as a marker of lipid peroxidation. Zagazig University Medical Journal, 2020; (): -. doi: 10.21608/zumj.2020.50275.2018