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Correlation between malondialdehyde levels and disease activity in vitiligo



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ABSTRACT

Background: Vitiligo is an acquired depigmented skin disease that occurs due to the death of melanocytes. There are various presumed theories about the cause of melanocyte death in vitiligo; one of them is oxidative stress theory. Lipid peroxidation is the primary manifestation of oxidative stress, producing malondialdehyde (MDA) as its end product. Malondialdehyde is a stable marker to assess the occurrence of oxidative stress. This study aims to prove the differences in serum MDA levels in the active vitiligo, stable vitiligo, and normal control groups.

Method: This research is an analytical cross-sectional study involving 64 vitiligo patients with active and stable lesions and 20 normal controls. The study was conducted at Sanglah General

Hospital Denpasar in February - November 2019. Serum MDA levels were measured to assess oxidative stress. The measurement of MDA levels was carried out by a spectrophotometer instrument using Competitive-ELISA method.

Results: In this study, there were significant differences in MDA levels between active, stable vitiligo patients, and control group ($p=0.000$) with active vitiligo type have the highest MDA mean, followed by stable type and control group respectively.

Conclusion: Increased serum MDA levels are an indicator of oxidative stress in vitiligo, which leads to melanocyte death and manifests as increased vitiligo disease activity. The results of

Keywords: disease activity, malondialdehyde, vitiligo

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INTRODUCTION

Vitiligo is an acquired pigmentation disorder which is still become a problem in dermatology. Vitiligo causes significant psychological impact due to the appearance of uneven skin tone. To date, the outcome of vitiligo therapy has not been satisfying because the result is varied for each individual. The prevalence of vitiligo is estimated around 0.5-2% of the entire world population and can be found at all ages, but 50% of vitiligo cases occur before the age of 20 years old.¹

The etiopathogenesis of vitiligo is not certainly known, but there are several theories that can explain melanocyte death in vitiligo; one of them is oxidative stress theory.² This theory explains that in vitiligo there is reduction-oxidation (redox) status imbalance on the skin, which produces reactive oxygen species (ROS). The accumulation of ROS triggers lipid peroxidation, deoxyribonucleic acid (DNA) damage, increased production of pro-inflammatory and anti-melanogenic cytokines, and function loss in enzymes that play essential roles in melanogenesis. Melanocytes are the subject of oxidative stress due to ROS exposure

during melanin synthesis which involves oxidation reactions and superoxide anions (O_2^-) and hydrogen peroxide (H_2O_2) formation. Oxidative stress can disrupt melanocyte homeostasis and lead to melanocyte death.^{2,3} Malondialdehyde is the main metabolic product to evaluate the occurrence of lipid peroxidation which can be used as reliable biomarker of oxidative stress. The main metabolic product of this lipid peroxidation is also cytotoxic to melanocytes. Measurement of serum MDA levels is a useful method to predict oxidative stress levels.⁴⁻⁶ Therefore, this study aims to know the comparison between serum MDA levels as a biomarker of oxidative stress in active and stable vitiligo and also in normal controls.

METHOD

This research is an analytical cross-sectional study to compare malondialdehyde levels in active, stable, and normal control vitiligo patients. The research was conducted at Sanglah General Hospital Denpasar from February to November 2019. The degree of disease activity is determined based on the VIDA (Vitiligo Disease Severity) score. Active

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vitiligo patients were defined as patients with vitiligo skin lesions that had expanded or developed new lesions in the past one year [VIDA score (+1) to (+4)]. Stable vitiligo patients were defined as patients who did not have expanded or developed new lesions in the past one year [VIDA score (-1) and (0)]. Normal controls were patients without vitiligo or other inflammatory skin and systemic diseases. The inclusion criteria are all vitiligo patients who visited Dermatology and Venereology Polyclinic at Sanglah General Hospital Denpasar, Indonesian citizens, men and women aged 5 to 75 years, have good general condition, willing to be included in the study, and sign informed consent form. Factors controlled by exclusion in this study were smoking history, alcohol consumption, pregnancy, chronic renal failure, coronary heart disease, rheumatoid arthritis, systemic lupus erythematosus, diabetes mellitus, bronchial asthma, malignancy, hepatic cirrhosis, HIV infection, psoriasis, atopic dermatitis, not undergoing phototherapy, and not taking topical or systemic anti-inflammatory and antioxidant drugs. MDA level measurement was carried out by spectrophotometer using Competitive-ELISA method by taking 3 mL of venous blood measured in ng/mL.

RESULTS

This study was followed by 84 participants consisting of 64 participants with vitiligo and 20

healthy participants. The characteristics of the study participants shown in [Table 1](#).

The degree of vitiligo disease activity was calculated using the VIDA score in which six-point scale is used to assess the stability and progression of vitiligo from time to time. In this study, there were no study participants with spontaneous repigmentation (score (-1)). Active vitiligo is vitiligo with VIDA score (+1) to (+4), while stable vitiligo is vitiligo with VIDA score (-1) and (0), from total 84 study participants, 46.4% were active vitiligo, 29.8% were stable vitiligo and 23.8% were non-vitiligo groups ([Figure 1](#)).

Because the data were not homogeneous and not normal, a non-parametric test was performed using the Kruskal Wallis test. Based on the analysis, it was found that there were significant differences in MDA levels between active, stable vitiligo patients, and the control group ($p=0.000$). It was also found that the active type of vitiligo had the highest MDA mean, followed by stable type and control group, respectively ([Table 2](#)).

To see differences between groups, a post-hoc test was performed using the Mann-Whitney test. From this test, it was found that there were significant differences in MDA levels between active and stable ($p=0.001$), active and control ($p=0.000$), and also stable and control vitiligo groups ($p=0.000$).

DISCUSSION

The significant difference between active and stable vitiligo and normal controls in this study is in line with the results of the study by Dammak et al. and Yaldrim et al. in which it was found that MDA levels are higher in vitiligo than normal controls. Higher MDA levels were also found in active vitiligo compared to stable vitiligo group.^{7,8} Higher MDA levels in vitiligo subjects compared to non-vitiligo subjects reflecting that increased lipid peroxidation was occurred, which was classified as the main manifestation of oxidative stress in subjects with vitiligo. Increased MDA level in vitiligo subjects illustrates that higher level of oxidative stress was occurred to vitiligo subjects compared to non-vitiligo subjects.^{9,10} Depigmented lesions in vitiligo occur due to the death of epidermal melanocytes. Melanocyte mortality in vitiligo is related to the increased sensitivity of melanocytes toward oxidative stress. Oxidative stress is a state of imbalance between the production of ROS and the ability of the biological system to detoxify reactive intermediates or repair the damage caused by the production of ROS. The disruption in this balance then cause toxic effect on cells through the production of free radicals that harm all cell components such as lipids, proteins, and DNA.¹¹

Table 1. Characteristics of study participants

Characteristics	Vitiligo (n= 64)	Non-Vitiligo (n=20)
Sex		
Male	36 (56.25%)	4 (20%)
Female	28 (43.75%)	16 (80%)
Age (years old)		
5 – 15	7 (10.94%)	0 (0%)
16 – 25	6 (9.37%)	0 (0%)
26 – 35	8 (12.50%)	18 (90%)
36 – 45	7 (10.94%)	2 (10%)
46 – 55	20 (31.25%)	0 (0%)
56 – 65	11 (17.19%)	0 (0%)
66 – 75	5 (7.81%)	0 (0%)
Onset		
Early-onset	22 (34.38%)	-
Late-onset	42 (65.62%)	-
Family History		
Yes	9 (14.06%)	-
No	55 (85.94%)	-
Vitiligo Diagnosis		
Non-Segmental	47 (73.4%)	
Segmental	5 (7.8%)	
Unclassified	12 (18.8%)	

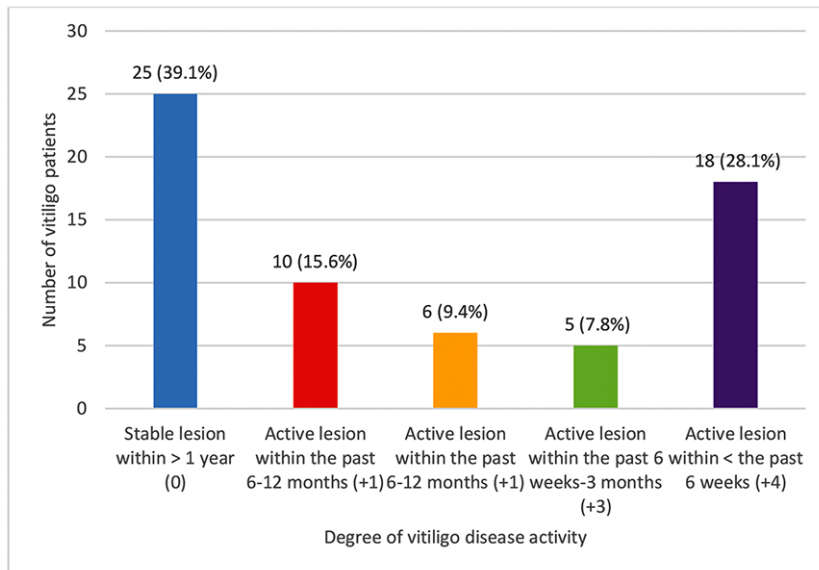


Figure 1. Degree of vitiligo disease activity

Table 2. Analysis of MDA Levels in Active, Stable and Normal Control Vitiligo Group

		n	Mean of Serum MDA Levels (ng/mL)	p-Value
Activity	Active	39	58.65	0.000
Disease	Stable	25	42.90	
Vitiligo	Normal Control	20	10.50	

Malondialdehyde is the main product to evaluate the occurrence of lipid peroxidation which can be used as a marker of cell injury.^{6,12,13} Increased serum MDA levels are known to have toxic effects on melanocytes and lead to melanocyte death which subsequently generates vitiligo.⁶

CONCLUSION

Vitiligo is an acquired pigmentation disorder that is still become a problem in dermatology because it causes significant psychological impact due to the appearance of uneven skin tone, the pathogenesis is not certainly known, and the therapy is still varied. This study aims to determine the correlation between serum malondialdehyde (MDA) levels, a marker of oxidative stress that is presumed to play a role in the incidence of vitiligo on vitiligo patients with stable, active disease activity, and also normal control. In this research, it was found that there were significant differences in MDA levels between active, stable vitiligo patients and control groups with active vitiligo type having the highest MDA mean, followed by stable type and control group,

respectively. In this study, it was also found that MDA levels differed significantly based on the type of vitiligo and the onset of vitiligo events, in which non-segmental vitiligo and late-onset vitiligo tend to have higher MDA levels. These findings further demonstrate the role of oxidative stress in vitiligo pathogenesis and indicators of oxidative stress like serum MDA levels can be used as biomarkers in evaluating vitiligo disease activity.

CONFLICT OF INTEREST

The author declares there is no conflict of interest regarding publication of this article.

ETHICAL CONSIDERATION

Current study has been approved by Ethical Committee Faculty of Medicine, Universitas Udayana/Sanglah General Hospital, all procedures in accordance to Helsinki declaration of human rights.

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