ORIGINAL ARTICLE

Bali Medical Journal (*Bali MedJ*) 2021, Volume 10, Number 1: 296-299
P-ISSN.2089-1180, E-ISSN: 2302-2914

Bali Medical Journal
www.BaliMedicalJournal.org
Published by Bali Medical Journal

Analysis of Malondialdehyde (MDA) levels in skin tags patients

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Received: 2021-01-26
Accepted: 2021-04-22
Published: 2021-04-30

ABSTRACT

Background: Skin tags (known as acrochordon) are the most common benign skin tumors, usually skin-colored or hyperpigmented, found in the natural folds of the skin. They have been associated with various clinical conditions. A few studies results have been reported regarding the oxidative stress are strongly associated with skin tumor. Malondialdehyde (MDA) is an end product of lipid peroxidation by free radicals in the body. MDA assay is widely used as a biomarker to evaluate systemic oxidative stress in biomedical fields. This study evaluated the difference in serum MDA level in skin tags patients and control.

Methods: This study is an analytic observational study with a cross-sectional design, including 40 patients with skin tags and 40 healthy volunteer controls, based on inclusion and exclusion criteria. Age, sex, and family history of skin tags were estimated on the patients. Diagnosis of skin tags was made based on history and clinical examination. Measurement of MDA level by enzyme-linked immunosorbent assay (ELISA) to the patients and controls. Mann- Whitney test is used to determine the differences in serum MDA levels. The results were significant, with a p-value<0.05.

Results: Mean MDA level of skin tags patients was highest at age 50– 59 years (27,01 ± 10,87 nmol/ml). The mean MDA level of male skin tag patients (15,99 ± 8,23 nmol/ml) was higher than females (15,23 ± 8,17 nmol/ml). The mean MDA level of skin tag patients with a family history (19,77± 7,92 nmol/ml) was higher compared to patients without a family history (11,82 ± 8,48 nmol/ml). The mean of MDA level was significantly higher in the skin tags group (15,81 ± 8,23 nmol/ml) than the control group (8,86± 7,02ng/ml) with p = 0.032.

Conclusion: There were higher significant differences in serum MDA levels in the skin tags patients than in control.

Keywords: skin tags, malondialdehyde, oxidative stress.
Cite This Article: Ridlo, M., Putra, I.B., Jusuf, N.K. 2021. Analysis of Malondialdehyde (MDA) levels in skin tags patients. *Bali Medical Journal* 10(1): 296-299. DOI: 10.15562/bmj.v10i1.2214

INTRODUCTION

Acrochordon, softwart, or soft fibroma, commonly known as skin tags, are pedunculated bumps or tumors most commonly located on the neck, eyelids, axillae, and groin.[1] Skin tags are usually asymptomatic but can become painful when irritation occurs.[2]

The incidence increases with age, and it was to be more prevalent in women than men. It is estimated that almost half of adults have at least one skin tag. These lesions are commonly found in the adult population over 40 years of age.[2,3]

The etiology of skin tags is still unknown. Some of the factors associated are skin rubbing, obesity, metabolic syndrome, and hormonal imbalance.[4] These lesions are associated with conditions like pregnancy, intestinal polyps, growth disorders, metabolic syndromes. Until now, there have been many theories explaining the pathogenesis of skin tags, including the process of repeated scratching or friction on the skin, hereditary factors in the family, hormonal factors, and obesity.[5] Histologically, fibroblast proliferation and epidermal hyperplasia are the primary pathologic abnormalities seen in all skin tag types. The human mast cells can stimulate fibroblast proliferation, and oxidative stress was shown to induce mast cell degranulation. The mast cells are increased in many skin diseases, including many benign or malignant tumors.[6] Skin tags are benign skin tumors of fibrous tissue that are thought to be affected by oxidative stress in the body, but the research is still minimal.[7,8,9]

Oxidative stress refers to elevated levels of reactive oxygen species (ROS) that cause damage to proteins, lipids, and DNA, which can cause damage to cell structure and function.[8,10] ROS are believed to activate proliferative and cell survival signaling that can alter apoptotic pathways that may be involved in the pathogenesis of several skin disorders.[10]

Several markers of oxidative stress in the body are currently available. One of the most important was malondialdehyde (MDA), low-molecular-weight aldehydes derived from lipid peroxidation processes. MDA has been used as a marker of lipid peroxidation. MDA is more chemically stable than another biological marker of oxidative stress.[11,12]

However, research on the occurrence of oxidative stress, especially in patients with benign skin tumors, is still limited. Therefore, the present study aimed to determine the differences between serum

MDA levels in skin tag patients and controls.

METHODS

This research was an analytic observational study with a cross-sectional design involving 40 skin tag patients and 40 controls aged 20-60 years in Dermatology and Venereology outpatient clinic in Universitas Sumatera Utara Hospital Medan. Each subject of the study who had signed the informed consent was included in this study. Exclusion criteria are pregnant and lactating women and a history of using oral antioxidant supplements. Patients with vitiligo, leprosy, basal cell carcinoma, psoriasis, and systemic lupus erythematosus will be excluded.

Ethical permission is given by the Health Research Ethics Committee, Faculty of Medicine, Sumatera Utara University, and Sumatera Utara Hospital Medan. The history was taken for all study subjects, clinical examination, and blood sampling test to examine serum MDA levels.

MDA levels were measured by human MDA Enzyme-Linked Immunosorbent Assay (ELISA) kit, determining the optical density of MDA using a spectrophotometer (Multiskan Thermo Scientific™).

The results were analyzed in descriptive analysis, Kolmogorov-Smirnov normality test, and Mann-Whitney test to determine differences between the two subject groups of the study where $p<0.05$ was considered a significant result.

RESULTS

In this study, the demographic characteristics of skin tags patients were highest in the age range of 50-59

years (35%), female sex (75%), and 20 subjects (50%) had a family history of skin tags. Sociodemographic characteristics that include gender, age, education level, occupation, and family history are presented in table 1.

In this study, it was found that the highest serum MDA levels in patients aged 50-60 years (27.01±24.51) (Table 3), male (15.99±19,4) (Table 2), and have a family history of skin tags (19.77±22.55) (Table 4). Statistically, there were higher significant differences in serum MDA levels in the skin tags patients (15.81±17.67) compared to the control (8.86±7.26) ($p = 0.032$) (Table 5).

Table 1. Overview of characteristics of research subjects

Characteristics	Skin tag patients		Control	
	n	%	n	%
Gender				
Male	10	25	11	27.5
Female	30	75	29	72.5
Age (years)				
20 - 29	2	5	14	35
30 - 39	13	32,5	16	40
40 - 49	11	27,5	10	10
50 - 60	14	35	0	0
Education				
Elementary School	20	50	14	35
Junior High School	5	12.5	5	12.5
Senior High School	11	27.5	11	27.5
College	4	10	10	25
Occupation				
Farmer	1	2.5	0	0
Government employee	1	2.5	5	12.5
Entrepreneur	17	42.5	15	37.5
Unemployment	21	52.5	20	50
Family History of skin tags				
Present	20	50	0	0
None	20	50	0	0

Table 2. Serum MDA levels based on gender in skin tags patients

Gender	Mean (nmol/ml)	Median (nmol/ml)	SD (nmol/ml)	Min-Max (nmol/ml)
Male	15,99	8,23	19,40	(5,8 – 68,9)
Female	15,23	8,17	17.39	(4,47 – 64,67)

Table 3. Serum MDA levels based on age in skin tags patients

Age (years)	Mean (nmol/ml)	Median (nmol/ml)	SD (nmol/ml)	Min-Max (nmol/ml)
20 - 29	7,61	7,61	2,13	6,10 – 9,12
30 - 39	8,39	7,68	4,38	4,57 – 13,40
40 - 49	17,07	8,60	17,53	4,47 – 64,67
50 - 60	27,01	10,87	24,51	4,89 – 68,90

Table 4. Serum MDA levels based on the family history of skin tags

Family history of skin tags	Mean (nmol/ml)	Median (nmol/ml)	SD (nmol/ml)	Min-Max (nmol/ml)
Present	19,77	7,92	22,55	4,57 – 68,9
None	11,82	8,48	9,92	4,47 – 43,33

DISCUSSION

The condition of skin tags patients is prevalent in adulthood to middle age, and the incidence increases with age. It is estimated that 46% - 50% of all

Table 5. Serum MDA levels between skin tags patients and control

Group	Mean (nmol/ml)	Median (nmol/ml)	SD (nmol/ml)	Min – Max (nmol/ml)	p-value
Skin tags	15,81	8,23	17,67	4,47 – 68,90	0,032
Comtrol	8,86	7,02	7,26	3,87 – 46,05	

individuals have at least one skin-tagged lesion, and about 50% of them develop by age 69.[13-15] The incidence of skin tags is not different in men and women. Several studies have stated that skin tags appear more frequently in middle-aged and older women, which usually appear together with seborrheic keratosis.[13] This study illustrates that skin tags' incidence is higher in women (75%) than men (25%). This study's results are consistent with Jusuf et al. that skin tags mainly occurred in female patients (68.7%).[3] Nurhayati et al. found in their research that skin tags were more dominant in women (81.8%) compared to men.[14] Skin tags are considered to be associated with hormonal mechanisms, especially in obese women. Estrogen is the predominant hormone that plays a role in females and affects body organs' function, including the skin, which is the largest estrogen target for non-reproductive organs. This reason is why skin tags are more appear women than men.[13]

This study found that the mean serum MDA level in skin tags was higher in men (15.99 nmol/ml) than in women (15,23 nmol/ml). This result is consistent with Ozkan et al. in their study. Their study found that MDA levels in women with lung cancer are lower than in men.[16] Various factors can influence tissue damage due to oxidative stress, and men are more exposed to risk factors resulting from life, such as smoking, diet, and work. The results of other studies suggest that it can also be influenced by several things such as exposure to ultraviolet rays and obesity. This result indicates that men have a higher risk of oxidative stress than women. Pinchuk et al., in their research, found lower levels of MDA in women than men. However, in women aged 50-55 years, MDA levels are higher than men. It is suspected that there is a role in metabolic and hormonal changes in women who are menopausal.[17,18]

Based on table 1, the results show that 95% (38 people) of skin tag subjects were more than 30 years old, and the most common was 50 -60 years 35% (14 people). This study's results are consistent with Tamega et al. that the risk of developing skin tags increases with age and is more common at the age of 30 to 70 years.[19] This result is consistent with Jusuf et al. that found subjects with skin tags were more in women (68.7%) than men, and most were found in the age group 40-49 years (46.8%).[3] The incidence of skin tags with increasing age is thought to be the result of hormonal changes in individuals with metabolic diseases. However, Tosson et al. found no significant relationship between the occurrence of skin tags and age.[20]

This study found that the highest mean value of MDA levels in skin tags subjects aged 50 - 60 was 27.01nmol/ml. Waller et al., in their research that the contribution of free radicals occurred since the beginning of life, which increased with age. Free radicals are responsible for age-related damage to cellular and tissue levels. The level of free radicals that occurs with increasing age, apart from being caused by hormonal changes, is also thought to be associated with the presence of extrinsic factors such as; lifestyle, dietary patterns, radiation, disease, and medication.[8,9,21]

Based on table 1, it is known that of the 40 subjects who had skin tags, 50% had a family history of skin tags in their family. This result is consistent with Erkek et al. that of the 58 skin tag patients, 38 (65.5%) patients had a family history.[22] Similar results were obtained in a study by Jusuf et al. 16 (50%) patients with skin tags had a family history of them from their father and mother.[3] Nurhayati et al. In his study, 66.7% of his study patients had a family history, and most of them were inherited from their mother.[14] Family history related to the presence of inherited protooncogene genetic mutations will result in impaired signal transduction and mitogenic growth. Thus affecting the keratinocyte proliferation system and fibroblast growth that can lead to skin tags.[20,23]

Oxidative stress can not only affect the condition of one disease but can also affect other diseases such as hepatitis, diabetes mellitus, infections, tumors, malignancies, and HIV/AIDS. These free radicals are involved in the etiopathogenesis of various dermatoses, skin aging processes, and tumors or neoplasms on the skin. Superoxide ions generated in various diseases are a critical factor in endothelial proliferation and dysfunction, so that oxidative stress is a significant cause of disease in humans.[7,24] Although the role relationship between ROS and antioxidants in tumor/cancer is still controversial, several studies showed an increased level of intracellular ROS, which plays a role in carcinogenesis. ROS can affect various signaling pathways, including growth factors and mitogenic pathways, and control various cellular processes, including cell proliferation and stimulating uncontrolled cell growth that promotes tumor development and initiation of the carcinogenesis process. Kim et al., in their research, mentioned the role of ROS in stimulating cell proliferation and suppression of apoptosis. H2O2-induced oxidative stress can stimulate angiogenesis and tumor progression by changing the gene expression of CXC chemokine ligand 14 (CXCL14) and IL-8 via the epidermal growth factor receptor (EGFR) / mitogen-activated protein kinase (MAPK) signal pathway.[8,25]

Research on the measurement of oxidative stress markers, especially MDA, on tumor disorders or skin tumors is still limited. Hakan et al. found a significant increase in MDA levels in patients with breast tumors than controls.[26] The exact cause of skin tags is not clear, but many factors can influence skin tag lesions' appearance. According to Mangai et al., skin tags are benign skin tumors of fibrous tissue that are thought to be influenced by oxidative stress in the body.[27,28]

CONCLUSION

There were higher significant differences in serum MDA levels in the skin tags patients than in control.

ACKNOWLEDGMENTS

We want to express thanks gratitude to the Head of the Department of Dermatology and Venereology of Faculty of Medicine

Universitas Sumatera Utara and Universitas Sumatera Utara Hospital.

AUTHOR CONTRIBUTION

All authors have contributed to this research process, including preparation, data gathering, analysis, drafting, and approval to publish this manuscript.

ETHICAL STATEMENT

Universitas Sumatera Utara Hospital Ethics Commission has approved this research with letter number 2719/UN5.4.1.1.1/KPM/2020.

FUNDING

The authors are responsible for all of the study funding without a grant or any external funding source.

CONFLICT OF INTEREST

The authors declare no conflict of interest regarding the publication of this article.

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