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Correlation between *verruca vulgaris* and superoxide dismutase

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ABSTRACT

Background: *Verruca vulgaris* is a form of benign tumors that infected epidermal cells caused by Human papillomavirus (HPV). In several studies states that imbalances in oxidant and antioxidant systems play an important role in HPV infection. SOD is a potent protective enzyme that selectively cleanses radicals of antioxidants by catalyzing dismutation to hydrogen peroxide.

Aim: The study aimed to determine the correlation between SOD level and *verruca vulgaris*.

Methods: This was an analytic study with a cross sectional design involving 35 subjects with *verruca vulgaris* and 35 healthy controls. Diagnosis of *verruca vulgaris* was made based on history and clinical examination. The authors conducted blood sampling and measurement of plasma SOD level to the patients and controls.

Results: The study found that the mean of SOD levels in *verruca vulgaris* patients were higher (49.27 ± 100.47 U/L) than controls (35.12 ± 50.44 U/L), but it didn't find a correlation between *verruca vulgaris* and SOD with p = 0.511. The mean level of ≥ 6 months were higher (59.69 ± 140.85 U/L) than < 6 months (39.43 ± 36.09 U/L) with p = 0.369. The mean multiple lesion levels were higher (62.12 ± 140.76 U/L) than the SOD level of patients with a single lesion (37.14 ± 34.89 U/L) with p = 0.405. The mean of SOD levels of patients who had previously experienced *verruca vulgaris* was higher (72.79 ± 151.73 U/L) than those who had not it (31.63 ± 18.26 U/L) with p = 0.961.

Conclusion: We didn't found a correlation between *verruca vulgaris* and SOD.

Keywords: *verruca vulgaris*, HPV, SOD

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INTRODUCTION

Verruca is a benign proliferation of skin and mucous membranes caused by human papillomavirus (HPV).[1,2,3,4] *Verruca vulgaris* caused by cutaneous HPV type 1,2,3,4,27 and 57.[5] *Verruca vulgaris* is the most common type of verruca.[1,5,6] Can occur anywhere on the skin, especially on the fingers, soles of the feet and face.[1,7] HPV infections often occur, in general, every human has experienced this infection in his life.[8] *Verruca vulgaris* can be experienced at any age and the incidence increases at school age and peaks in adolescence and young adulthood.[9]

Infection with the type of HPV that causes *verruca vulgaris* often occurs through micro-injuries.[10] Transmission can occur directly from one individual to another or indirectly through contaminated objects or surfaces. Autoinoculation (through scratching) from one body location to another body location may also occur.[9,11]

This infection begins when the virus enters basal cell epithelial proliferation, possibly through a small wound because this cell layer is normally inaccessible to the virus.[10,12] Clinical features of verruca is determined by the type of virus, the location of the infection, and the immunity status of the host.[1,7] *Verruca vulgaris* appear in varied types with dense, hyperkeratotic, rough papules that can form broad masses with confluence.[7]

The skin has a complex system to protect itself from oxidative stress. This defense mechanism consists of enzymes and non-enzymes.[12] The main function of the immune system is to protect the host against infectious agents by phagocytosis and to reduce ROS (reactive oxygen species) mediated by phagocytes. In addition, the immune system has a variety of regulatory functions that depend on oxidant and antioxidant balance.[13] SOD is the central defense of superoxide radicals and the first defense mechanism against oxidative stress.[14] SOD is an antioxidant enzyme that catalyzes the dismutation of highly reactive superoxide anions into less reactive O_2 and H_2O_2.[15]

METHODS

This research was an analytic observational study with a cross-sectional design involving 35 *verruca vulgaris* patients and 35 controls submitted to the outpatient dermatology and venereology clinic in General Hospital of Sumatera Utara University Medan, Indonesia. The study had been committed according to a valid ethical clearance number 424/TGL/KEPK/ FK-USU-RSUP HAM/2017. Each subject signed informed consent were included in

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this study. Exclusion criteria were pregnant and nursing women, antioxidant, NSAID consumption within the last three months. Ethical clearance was declared by the Health Research Ethical Committee, Faculty of Medicine, University of Sumatera Utara. All subjects with *verruca vulgaris* were diagnosed by anamnesis, clinical examination, and blood collection to be examined for plasma SOD levels.

Table 1 Distribution of research subjects based on gender

	Case		Control	
Gender	**n**	**%**	**n**	**%**
Male	23	65.7	20	57.1
Female	12	34.3	15	42.9
Total	35	100.0	35	100.0

Table 2 Distribution of research subjects based on age

Age	**Case**		**Control**	
(Years)	**n**	**%**	**n**	**%**
<18	2	5.7	2	5.7
18-25	14	40.0	15	42.8
26-35	5	14.3	6	17.2
36-45	8	22.8	9	25.7
46-55	4	11.4	2	5.7
56-65	1	2.9	1	2.9
>65	1	2.9	0	0
Total	35	100.0	35	100.0

Table 3 Distribution of verrucca vulgaris based on duration

Duration	**n**	**%**
< 6 months	18	51.4
≥ 6 months	17	49.6
Total	35	100.0

Table 4 Distribution of verruca vulgaris based on the number of *verruca vulgaris*

Number of	**n**	**%**
Single	17	49.6
Multiple	18	51.4
Total	35	100.0

Table 5 Distribution of verruca vulgaris based on the history of *verruca vulgaris*

History	**n**	**%**
Ever	15	42.8
Never	20	57.2
Total	35	100.0

As to analyze the correlation between SOD values and the incidence of *verruca vulgaris,* the study using the Mann-Whitney test where $p \leq 0.05$ is considered a significant result.

RESULTS

Most of the research subjects in this study were men, aged 18-25 years, had *verruca vulgaris* < 6 months, multiple and never had experienced *verruca vulgaris* before. The mean SOD level in *verruca vulgaris* subjects were higher (49.27 ± 100.47 U/L) than control plasma SOD level (35.12 ± 50.44 U/L); p = 0.511. The mean level of ≥ 6 months was higher (59.69 ± 140.85 U/L) than SOD < 6 months (39.43 ± 36.09 U/L); p = 0.369. The mean multiple lesion levels were higher (62.12 ± 140.76 U/L) than SOD level of patients with a single lesion (37.14 ± 34.89 U/L); p = 0.405. The mean SOD levels of patients who previously had experienced *verruca vulgaris* were higher (72.79 ± 151.73 U/L) than those who don't have it (31.63 ± 18.26 U/L); p = 0.961.

DISCUSSION

The study revealed that the mean SOD level in *verruca vulgaris* subjects was higher than control (p-value = 0.511). The research conducted by Sasmaz et al. found the mean serum SOD levels in the group of non-genital warts higher (3127 ± 1176 U/g Hb) than control (2178 ± 484 U/g Hb) with p-value < 0.001.[3] Increased antioxidant activity in patients compared to healthy patient controls may be a peripheral response from organisms to increase oxidative stress. It can also be said that an increase in antioxidant activity can reflect the introduction of cellular oxidative stress or as a compensation mechanism. Excessive production of superoxidase radicals and H_2O_2 will induce expression of the SOD enzyme.[3] SOD can act as a coordinator and balance system to protect tissue and body fluids from damage produced by ROS which can be produced physiologically or is a form of response to inflammation, infection or disease. In health, the balance between ROS and antioxidant defense increases slightly so that it can still fulfill their biological role.[16] In this study, even though it obtained the SOD level in *verruca vulgaris* was higher than control, but it was not statistically significant. This might be caused by several factors, such as smoking. ROS are produced by cellular metabolic activities and environmental factors, such as air pollutants or cigarette smoke.[17] However, in a study conducted by Arican et al. regarding oxidative stress cutaneous at plantar warts, the average SOD levels with lesions were lower (2.40 ± (1.80-3.20)

Table 6 Plasma levels of SOD

	Plasma SOD levels (U/L)						
	n	Mean	Median	SD	Min	Max	p
Verruca vulgaris	35	49.27	27.60	100.47	5.9	604.0	0.511
Control	35	35.12	24.10	50.44	7.7	316.2	

**Mann-whitney*

Table 7 Correlations between SOD plasma and durations of *verruca vulgaris*

	Plasma SOD levels (U/L)						
Duration	n	Mean	Median	SD	Min	Max	p
< 6 months	18	39.43	29.55	36.088	7.6	165.6	0.369
≥ 6 months	17	59.69	26.30	140.85	5.9	604.0	

**Mann-whitney*

Table 8 Correlations between SOD plasma and number of *verruca vulgaris*

	Plasma SOD levels (U/L)						
Number	n	Mean	Median	SD	Min	Max	p
Single	18	37.14	30.45	34.89	7.6	165.5	0.405
Multiple	17	62.12	24.10	140.76	5.9	604.0	

**Mann-Whitney*

Table 9 Correlations between SOD plasma and history of *verruca vulgaris*

	Plasma SOD levels (U/L)						
History	n	Mean	Median	SD	Min	Max	p
Ever	15	72.79	29.80	151.73	7.6	604.0	0.961
Never	20	31.63	26.75	18.26	5.9	79.2	

** Mann-Whitney*

U/mg) than on the surface without lesions (5.30 ± (3.95-6.00) U/mg) with p value < 0.001.[18]

The mean value of plasma SOD levels of *verruca vulgaris* patients based on duration was found ≥ six months higher (59.69 ± 140.85 U/L) then SOD < 6 months (39.43 ± 36.09 U/L) with p = 0.369. According to research conducted by Sasmaz et al., where they found an increase of SOD enzyme activity but did not confirm a statistically significant correlation with the duration of non-genital warts.[3]

The mean value of plasma SOD levels of *verruca vulgaris* patients based on the number of multiple vulgaris warts lesions was found to be higher 62.12 ± 140.76 U/L than of single injuries 37.14 ± 34.89 U/L with p = 0.405. According to research conducted by Sazmaz et al., they found an increase of SOD enzyme activity but did not see a statistically significant correlation with the number of warts nongenital.[3]

The mean SOD levels of patients who had previously experienced *verruca vulgaris* were higher (72.79 ± 151.73 U/L) than SOD levels of patients who had not previously experienced *verruca vulgaris* (31.63 ± 18.26 U/L) with p = 0.961

The oxidative stress process in viral infections is a common occurrence during the inflammatory response to infection, due to the release of ROS from neutrophils and macrophages during an oxidative explosion. Active phagocytes release prooxidant cytokines. HPV is weak immunogenic and does not require induction of the inflammatory response. Interestingly, oxidative stress plays a significant role in the pathogenesis of viruses in this infection. Although the significant role of oxidative stress in the viral life cycle of this disease is unknown, significant biological effects in increasing oxidative stress have been found.[19] During the inflammatory process, and there will be excessive production of superoxidase radicals and H_2O_2 which will induce expression of the SOD enzyme.[20,21]

In the latest pathogenesis study, it was suggested that the effects of superoxide play an essential role in viral infections, and other diseases such as damage to reperfusion or autoimmune diseases. In all these

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conditions the increase in superoxide levels is due to the results of tissue damage, through increased purine metabolism.[21]

The balance between oxidants and antioxidants has an important role in the spontaneous regression of HPV infection. Furthermore, it stated that the antioxidant system has a relationship with immunity. If an increase in antioxidant activity also activates cellular immunity, we can expect rapid regression in this disease and a low risk of recurrence.[3]

CONCLUSION

There is no correlation between *verruca vulgaris* and plasma SOD levels.

CONFLICT OF INTEREST

None declared.

AUTHOR CONTRIBUTION

All authors have contributed to the design and implementation of the research, to the analysis of the results and to the writing of the manuscript.

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