



Comparison of Serum Vitamin C Levels Between Pulmonary Tuberculosis and Healthy Controls in Medan

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Abstract

Background: Pulmonary tuberculosis infection is a high burden, especially in developing country. Vitamin C is a water-soluble micronutrient that contributes to immune defense by supporting a variety of innate and adaptive immunity. Vitamin C protects the host from reactive oxygen and reactive nitrogen intermediates generated during Mycobacterial infection. Pulmonary tuberculosis patients have lower vitamin C levels because Mycobacterium tuberculosis infection produces reactive oxygen species for replication as well as metabolism and also because of reduced nutrient intake. Vitamin C as an antioxidant also plays a role in killing *Mycobacterium tuberculosis* by encouraging Fenton reaction.

Methods: This is a case control study of serum vitamin C levels in pulmonary tuberculosis patients and healthy controls. Vitamin C levels were measured by ELISA (Enzyme Linked Immunosorbent Assay).

Results: The number of subjects was 40 people, divided into 20 subjects of pulmonary tuberculosis as cases and 20 healthy controls, aged between 18–65 years old. Vitamin C levels according to age group were 99.03±38.60 ng/ml and 80.53±27.38 ng/ml for 18–30 years, 84.85±49.69 ng/ml and 82.70±14.93 ng/ml for 31–40 years, 61.34±25.36 ng/ml and 79.93±22.81 ng/ml for 41–50 years, 71.43±18.36 ng/ml and 78.69±54.21 ng/ml for 51–65 years. Vitamin C levels of male subjects based on case and control groups were 88.11±42.07 ng/ml and 78.36±28.95 ng/ml while for the female were 73.20±11.56 ng/ml and 83.16±23.77 ng/ml. Mean vitamin C level in pulmonary tuberculosis patients was 83.64±35.99 ng/ml and in healthy controls was 80.22±26.44 ng/ml.

Conclusion: There was no significant difference in vitamin C levels between pulmonary tuberculosis patient and healthy people.

Keywords: healthy controls, pulmonary tuberculosis, vitamin C

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INTRODUCTION

Tuberculosis (TB) is an infectious disease caused by *Mycobacterium tuberculosis* (MTb) which can affect various organs, particularly the lungs. Although the DOTS strategy is very effective for TB control, the burden of TB disease in the community is still very high. In 2020 there were 10 million new cases of TB, and 1.5 million people died from this disease worldwide.¹ TB disease in Indonesia is the number one killer among infectious diseases and is the third leading cause of death after heart disease and acute respiratory disease for all ages.

The success of TB case control strategies is relatively high, and the presence of TB in various parts of the world indicates the need to identify various factors which increase the risk of TB,

including age, gender, and immunity.² Vitamin C is a water-soluble vitamin which has antioxidant effects on body tissues. Human body cannot produce vitamin C, so it requires intake from food sources. Levels of vitamin C as an antioxidant will continue to decline due to various factors such as age, gender, lifestyle, and chronic diseases, including pulmonary TB infection.³

Mycobacterium tuberculosis produces free radicals in activities at cellular level such as respiration, metabolism, and replication. Reddy et al. stated that glutathione, vitamin C, and vitamin E are antioxidants that are often found to be low in pulmonary TB patients.⁴

Study by John Kennedy et al. pointed out that levels of vitamin C and vitamin E in TB patients were low. This decline in antioxidant levels will cause a

decrease in total serum antioxidant levels in TB patients. Low antioxidants can be caused by a lack of intake and an increase in free radicals during phagocytosis process of *Mycobacterium tuberculosis*.⁵ Administration of antioxidants in TB patients could improve T-cell function and reduce levels of prostaglandin E2 as well as suppress free radicals. Susanto et al. observed an accelerated conversion based on sputum smear culture in pulmonary TB patients who received vitamin C supplementation.^{6,7}

METHODS

This was a case control study conducted at several public health centers and special pulmonary hospitals in Medan City from November to December 2018. The subjects of this study were new cases of pulmonary TB patients who met the inclusion and exclusion criteria. The inclusion criteria were men and women aged 18–65 years, new established TB cases based on clinical, radiological and positive AFB (Acid-Fast Bacillus) smear results, signed an informed consent and were willing to participate in the study.

Exclusion criteria were diagnosed as HIV positive, extra pulmonary TB, Diabetes Mellitus (DM), liver and kidney disease based on medical records, currently taking immunosuppressive drugs and currently taking vitamin C. Inclusion criteria in the control group were men and women aged 18–65 years old, no clinical signs of active TB based on history, chest x-ray within normal limits, not diagnosed as DM and other diseases, were willing to participate in the study.

The number of study subjects were 20 pulmonary TB patients and 20 controls (no pulmonary TB). Blood sample was taken from the median cubital vein in the study subjects. Vitamin C levels were examined using the ELISA (Enzyme Linked Immunosorbent Assay) method. Data were collected and analyzed using the Kruskal Wallis and Kolmogorov Smirnov test.

RESULTS

The study subjects were 40 people divided as 20 people in the pulmonary TB group as cases and 20 healthy people as controls. It was observed among the case group that the youngest age was 21 years while the oldest was 65 years, consisted of 14 men (70%) and 6 women (30%). In the control group, the youngest age was 18 years and the oldest was 65 years with 12 men (60%) and 8 women (40%).

Table 1. Characteristics of study subjects by age and gender

Characteristic		Pulmonary TB (Case)	Healthy People (Control)
Age	18–30 years	8 (40%)	4(20%)
	31–40 years	4 (20%)	3 (15%)
	41–50 years	3 (15%)	10 (50%)
	51–65 years	5(25%)	3 (15%)
Gender	Male	14 (70%)	12 (60%)
	Female	6 (30%)	8 (40%)

In table 1, it is observed that the most common age group in the case group was 18–30 years, with a total of 8 people (40%), most of whom were male for as many as 14 people (70%) of the total sample of 20 people (100%). Subjects in the control group were mainly in the age group of 41–50 years for as many as 10 people (50%) with 12 male subjects (60%).

Table 2. Mean levels of vitamin C in pulmonary TB patients (cases) and healthy people (controls)

Parameter	Pulmonary TB (Case) (Mean±SD)	Healthy People (Control) (Mean±SD)	P
Vitamin C (ng/ml)	83.64±35.99	80.22±26.44	0.284

Table 3. Vitamin C levels in pulmonary TB and healthy people by age and gender

Characteristic	Vitamin C (Mean±SD)	
	Pulmonary TB (Case)	Healthy People (Control)
Age		
18–30 years	99.03±38.60	80.53±27.38
31–40 years	84.85±49.69	82.70±14.93
41–50 years	61.34±25.36	79.93±22.81
51–65 years	71.43±18.36	78.69±54.21
Gender		
Male	88.11± 42.07	78.36±28.95
Female	73.20±11.56	83.16±23.77

Table 2 shows that vitamin C levels in the pulmonary TB group were higher than in the control group, but this difference was not significant ($P>0.05$). Table 3 denotes that vitamin C levels decreased with age in both cases and controls.

DISCUSSION

Vitamin C (ascorbic acid) is a water-soluble vitamin and is included in antioxidant vitamins which could counteract various extracellular free radicals. It was discovered in 1928 and was first used to prevent canker sores. Subsequent studies obtained that vitamin C had the effect of maintaining and increasing immunity against infection.³

Vitamin C is an antioxidant that neutralizes free radicals, able to work inside as well as outside the cells, and also able to protect DNA damage from free radicals and mutagens in humans. Vitamin C is not produced by the body and its level depends on dietary intake. The role of vitamin C as an antioxidant controls the Fenton reaction, where *Mycobacterium tuberculosis* releases reactive oxygen species (ROS), namely superoxide, hydroxyl peroxide, and hydroxyl radical.⁸

In addition to smoking, infection, alcohol and lack of nutritional intake in pulmonary TB patients can reduce serum antioxidant levels. A study by Reddy et al. mentioned that low levels of antioxidants were glutathione, vitamin C, and tocopherol (vitamin E), so a suitable antioxidant therapy may prove beneficial and nutritional antioxidant supplementation may represent a novel approach to fast recovery. Increased levels of ROS will lessen serum antioxidant levels as a consequence of phagocytosis during *Mycobacterium tuberculosis* infection, where at the time of infection, the body will respond in inflammation as a protection against tissue damage.²

This study observed that vitamin C levels in men were lower than in women, both in the pulmonary TB patient group and healthy controls. This might be because men had habits of smoking and consuming alcohol. Smoking provides the formation of free radicals in the body, resulting in cell damage. Vitamin C as an antioxidant and the body's defense mechanism will prevent it by donating electrons to free radicals to make it stable. This situation causes antioxidant levels to drop. Smoking habits can increase the failure of sputum smear conversion in patients with pulmonary TB, as

mentioned in a previous study by Wahyuni et al.⁹

Alcohol consumption induces low vitamin C levels due to the acetaldehyde in alcohol metabolism and an increase in the ratio of NADPH and NAD, reducing iron absorption.¹⁰ A study from Sinaga in Medan pointed out that smoking and alcohol increased the risk of pulmonary TB.¹¹ Smoking and alcohol consumption habits lead to damage of pulmonary cilia function, so that it will facilitate the occurrence of infections in the respiratory tract. Rosemary et al. obtained that vitamin C levels in men were lower than in women due to different lifestyle and activity.¹²

In this study, there was a tendency for vitamin C levels to decrease with age. In the elderly, vitamin C levels decrease due to the influence of the body's absorption ability, escalated oxidative stress due to age, and muscle weakness (decreased adipose tissue).¹³ Another study on vitamin C levels in a population aged over 60 years conducted in India by Ravilla D. Ravindran et al. found that vitamin C levels were influenced by age and were lower in men than women.¹⁴

LIMITATION

This study did not mention about the daily food intake of the subjects which could affect the vitamin C levels.

CONCLUSION

Vitamin C levels were higher in pulmonary TB patients compared to the control group, although the difference was not significant. Based on gender, men had lower levels of vitamin C than women. Vitamin C levels tended to decrease with age. The results of this study are expected to be used as a reference in further research with more in-depth interviews regarding food intake, smoking habits, and alcohol consumption.

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CONFLICT OF INTEREST

None.

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