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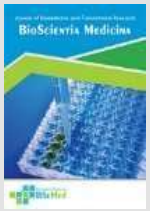

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Analysis of the Role of Vitamin C Hypovitaminosis in Scurvy on Bone Health: A Single Center Observational Study at Dr. Moewardi General Hospital, Surakarta, Indonesia

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A B S T R A C T

Background: Scurvy, vitamin C deficiency, is a rare condition but remains relevant in Indonesia. This study aims to analyze the role of vitamin C hypovitaminosis in the development of scurvy and its impact on bone health through an observational study at Dr. Moewardi General Hospital. Surakarta. **Methods:** A cross-sectional observational study was conducted on 30 patients diagnosed with scurvy at Dr. Moewardi General Hospital Surakarta during the 2020-2023 period. Demographic data, medical history, nutritional status, and severity of scurvy were collected. A radiological examination of the bone is performed to assess scurvy-related changes. Descriptive, comparative, and Spearman correlation statistical analyzes were used. **Results:** The majority of patients were men (66.7%) with a mean age of 45 years. A history of an unbalanced diet with low fruit and vegetable intake was found in the majority of patients (86.7%). Common symptoms include fatigue (86.7%), joint pain (73.3%), bleeding gums (60%), and skin bleeding (53.3%). The severity of scurvy varied, with 10 patients (33.3%) experiencing severe scurvy. Radiological examination shows significant changes in long bones, especially osteoporosis and thinning of the cortex, which is more obvious in patients with severe scurvy. Spearman correlation analysis showed a positive correlation between the severity of scurvy and the incidence of osteoporosis (rho = 0.495, p = 0.005) and cortical thinning (rho = 0.394, p = 0.031). **Conclusion:** Vitamin C hypovitaminosis plays a significant role in the development of scurvy and has a negative impact on bone health. Early screening and diagnosis of scurvy are important to prevent musculoskeletal complications. Nutritional education and dietary interventions to increase vitamin C intake need to be intensified, especially in high-risk groups.

1. Introduction

Scurvy, a disease caused by vitamin C (ascorbic acid) deficiency, is not a new disease. This disease has infected humans for centuries, especially sailors and explorers who made long journeys without access to fresh food. At that time, scurvy became a frightening specter because it could cause death from massive bleeding and infection. With the advancement of science and improved nutrition, the prevalence of scurvy has decreased significantly in developed countries. However, this disease is still a relevant health problem in various parts of the world, especially in developing countries with limited access to nutritious food. In Indonesia, scurvy is still found, especially in community groups with an unbalanced diet and low fruit and vegetable intake.[1,2]

Vitamin C, also known as ascorbic acid, is an essential nutrient that the human body cannot

produce itself. Therefore, vitamin C must be obtained from food, especially fresh fruits and vegetables. Vitamin C has various important roles in maintaining body health. Vitamin C is an important cofactor in the synthesis of collagen, the main structural protein in connective tissue. Collagen provides strength and elasticity to the skin, blood vessels, bones, teeth, and other organs. Vitamin C plays a role in strengthening the immune system by increasing the production of white blood cells and antibodies. Vitamin C functions as an antioxidant that protects body cells from damage caused by free radicals. Vitamin C helps the absorption of non-heme iron from plant foods. Vitamin C is involved in the production of carnitine, a molecule that is important for the transport of fatty acids into the mitochondria to produce energy. This research focuses on the impact of vitamin C hypovitaminosis, namely a condition of vitamin C deficiency, on bone health. Bone is a living tissue that continues to undergo a remodeling process, namely a balance between the formation of new bone by osteoblasts and bone resorption by osteoclasts. Vitamin C plays an important role in both of these processes, both directly and indirectly.[3,4]

Vitamin C is required for the differentiation of precursor cells into mature and functional osteoblasts. Vitamin C also increases osteoblast activity in producing collagen and mineralizing bone matrix. Osteoblasts are highly susceptible to free radical damage, especially during the bone formation process. Vitamin C, as a powerful antioxidant, protects osteoblasts from oxidative damage, thereby ensuring optimal function in bone formation. Vitamin C increases calcium absorption in the intestine, ensuring sufficient calcium is available for bone mineralization. Vitamin C can suppress the production of parathyroid hormone, a hormone that stimulates bone resorption. By inhibiting parathyroid hormone, vitamin C helps maintain the balance between bone formation and resorption.[5,6]

Vitamin C deficiency disrupts the bone remodeling process, causing an imbalance between bone formation and resorption. This can result in various pathological changes in the bones. Vitamin C deficiency reduces collagen production and disrupts bone matrix mineralization, leading to decreased bone mineral density. This makes the bones brittle and susceptible to fractures. The dense outer layer of bone, called the cortex, becomes thin and weak due to vitamin C deficiency. This reduces bone strength and increases the risk of fracture. Vitamin C deficiency can disrupt bone microstructure, causing increased porosity and decreased overall bone quality.[7,8] Observational research at Dr. Moewardi General Hospital Surakarta aims to analyze in depth the impact of vitamin C hypovitaminosis on bone health in scurvy patients. This study identified the clinical and radiological characteristics of scurvy patients and evaluated the relationship between the severity of vitamin C deficiency and pathological changes in the bones. By better understanding the pathophysiology of scurvy and its impact on bone, it is hoped that more effective prevention and treatment strategies can be developed. Nutritional education, dietary interventions, and vitamin C supplementation can be important steps in preventing and treating scurvy, as well as protecting people's bone health.

2. Methods

This research adopted a cross-sectional observational design, which means that observations of research subjects were carried out at one specific point in time. This approach allows the simultaneous collection of data regarding the variables studied, namely the demographic and clinical characteristics of scurvy patients, as well as radiological changes in their bones. The selection of a cross-sectional design was based on several considerations. First, this design is relatively efficient in terms of time and resources, as it does not require long-term monitoring of research subjects. Second, this design allows to identify the prevalence and distribution of scurvy and associated bone changes in a specific population. Third, this design provides insight into the relationship between scurvy severity and bone changes at a single time point, which can provide a basis for further research.

The target population for this study was all patients diagnosed with scurvy at Dr. Moewardi General Hospital Surakarta during the 2020-2023 period. The selection of this hospital was based on the consideration that Dr. Moewardi General Hospital is one of the main referral hospitals in the Surakarta area and its surroundings, so it is hoped that it can capture a representative sample of scurvy patients. However, due to time and resource limitations, not all patients in the target population could be included in this study. Therefore, samples were selected that met the predetermined inclusion and exclusion criteria. The inclusion criteria aim to ensure that research subjects indeed suffer from scurvy and do not have other conditions that could affect the research results. The inclusion criteria for this study are a diagnosis of scurvy confirmed by a specialist doctor: This criterion ensures that the research subject really suffers from scurvy, not another condition that has similar symptoms. The diagnosis of scurvy is made based on a combination of clinical symptoms, such as fatigue, joint pain, bleeding gums, and skin bleeding, and laboratory examination results, such as low levels of vitamin C in the blood; Age 18 years and over: This criterion aims to limit the research subjects to adults because scurvy in children has different clinical and radiological characteristics; Willing to participate in research: This criterion ensures that research subjects give voluntary consent to participate in research after receiving a complete explanation of the aims, procedures, benefits, and risks of the research.

Meanwhile, the exclusion criteria are patients with chronic diseases that can affect bone metabolism: Conditions such as diabetes mellitus, chronic kidney disease, or hyperthyroidism can affect bone metabolism and cause radiological changes that are not related to scurvy. Therefore, patients with these conditions were not included in the study to avoid biasing the results; Patients on therapy that may affect bone metabolism: Therapies such as corticosteroids or hormone therapy may also affect bone metabolism. Exclusion of patients undergoing therapy was aimed at ensuring that the bone changes observed were the result of vitamin C deficiency, not a side effect of therapy; Patients who cannot provide informed consent: Informed consent is approval given by research subjects after receiving a complete explanation regarding the research. Patients who were unable to provide informed consent, such as patients with cognitive or psychiatric disorders, were excluded from the study to protect their rights and well-being. By applying strict inclusion and exclusion criteria, the research samples obtained can represent the target population and provide valid and reliable research results.

Data collection was carried out through a combination of qualitative and quantitative methods. Interviews are used to obtain information regarding demographic data, medical history, and patient dietary history. A physical examination is carried out to assess clinical symptoms of scurvy, such as bleeding gums, skin bleeding, and joint pain. Supporting examinations, namely X-rays of long bones, are carried out to assess radiological changes in the bones, such as osteoporosis and thinning of the cortex. Demographic data includes age, gender, occupation, and patient education level. This information is important to identify the patient's socioeconomic characteristics that may be associated with the risk of vitamin C deficiency. Medical history includes history of previous illnesses, history of medication consumption, and diet history. This information can help identify risk factors that contribute to the development of scurvy. The severity of scurvy was determined based on clinical and laboratory criteria in accordance with current guidelines. Clinical criteria include symptoms and signs of scurvy, while laboratory criteria include blood levels of vitamin C. Radiological examination of long bones (femur, tibia, humerus) using X-rays is carried out to assess bone mineral density, thinning of the cortex, and the presence of fractures. This examination provides objective evidence of the impact of scurvy on bone health.

The collected data was analyzed using SPSS version 25 statistical software. Descriptive analysis

was used to describe the patient's demographic and clinical characteristics, such as age distribution, gender, occupation, education level, dietary history, clinical symptoms, and severity of scurvy. Comparative analysis was used to compare differences in characteristics and radiological changes between groups of patients with different levels of scurvy severity. Spearman correlation analysis was used to assess the relationship between the severity of scurvy and the incidence of osteoporosis and cortical thinning. Spearman's correlation was chosen because the data on the severity of scurvy are ordinal, while the data on the incidence of osteoporosis and cortical thinning are binary. Spearman's correlation coefficient (rho) shows the direction and strength of the relationship between two variables, with values ranging from -1 (perfect negative correlation) to 1 (perfect positive correlation). The p-value shows the statistical significance of the correlation. The significance level used in this research is $p < 0.05$. This means that if the p-value is less than 0.05, then the relationship between two variables is considered statistically significant, which means it is unlikely to occur by chance.

3. Results

Table 1 presents an interesting picture of scurvy patients treated at Dr. Moewardi General Hospital Surakarta during the 2020-2023 period. It can be seen that scurvy predominantly attacks men (66.7%) with an average age of 45 years. This indicates that the productive age group and male gender have a higher susceptibility to vitamin C deficiency, possibly influenced by suboptimal diet or other risk factors that need further investigation. An unbalanced diet, especially low fruit and vegetable intake, is the main risk factor experienced by the majority of patients (86.7%). These findings underscore the importance of nutritional education and dietary interventions to prevent scurvy. The clinical symptoms most frequently complained of by patients were fatigue (86.7%), joint pain (73.3%), bleeding gums (60%), and skin bleeding (53.3%). These complaints are in line with the classic manifestations of scurvy due to impaired collagen synthesis, a crucial protein that plays a role in maintaining the integrity of the body's connective tissue.

Table 1. Demographic and clinical characteristics of scurvy patients at Dr. Moewardi General Hospital Surakarta.

Characteristics	Number of patients (n = 30)	Percentage (%)
Male	20	66.7
Female	10	33.3
Average age (years)	45	-
History of an imbalanced diet	26	86.7
Symptoms:		
Fatigue	26	86.7
Joint pain	22	73.3
Bleeding gums	18	60.0
Skin bleeding	16	53.3

Table 2 provides an overview of the distribution of the severity of scurvy in patients treated at Dr. Moewardi General Hospital Surakarta from a total of 30 patients, it appears that moderate scurvy cases dominate with a percentage of 50%, followed by severe scurvy (33.3%) and mild scurvy (16.7%).

This distribution indicates that the majority of patients come to the hospital with scurvy conditions that have progressed quite significantly, requiring more intensive medical treatment. The proportion of

patients with severe scurvy (33.3%) is also quite worrying, indicating a delay in diagnosis or lack of public awareness of the early symptoms of scurvy. These findings underscore the importance of screening efforts and early detection of scurvy, especially in high-risk groups such as individuals with an unbalanced diet or certain medical conditions that affect vitamin C absorption. Early intervention can prevent the progression of scurvy to a more severe stage and reduce the risk of long-term complications. In addition, the high proportion of moderate and severe cases of scurvy may also reflect the presence of other factors that contribute to disease severity, such as overall nutritional status, the presence of comorbidities, or genetic factors.

Table 2. Scurvy severity spectrum in patients at Dr. Moewardi General Hospital Surakarta.

Severity level	Number of patients (n = 30)	Percentage (%)
Severe	10	33.3
Moderate	15	50.0
Mild	5	16.7

Table 3 highlights the close relationship between the severity of scurvy and structural changes in the bones, especially in the long bones. Osteoporosis, a condition of brittle bones due to decreased mineral density, and thinning of the cortex, the dense outer layer of bones, are clear evidence of the impact of prolonged vitamin C deficiency. In patients with mild scurvy, bone changes remain relatively minimal, with only a small proportion showing signs of osteoporosis or thinning of the cortex. However, as the severity of the scurvy increases, these changes become more pronounced and widespread. In the severe scurvy group, almost all patients experienced osteoporosis and cortical thinning, confirming that severe vitamin C deficiency can significantly damage bone integrity. These findings provide strong evidence that vitamin C is not only an important nutrient for the immune system and wound healing, but also plays a vital role in maintaining bone health. Collagen, the main protein in bone tissue, relies heavily on vitamin C for its synthesis and maintenance. Vitamin C deficiency inhibits collagen production, causing bones to become brittle and susceptible to damage. In addition, this table also shows that radiological examination can be a useful tool to evaluate the severity of scurvy and monitor disease progression. Bone changes detected through X-rays or CT scans can help doctors determine appropriate treatment strategies and predict the risk of long-term complications, such as fractures. Overall, table 3 provides a clear and interesting picture of how scurvy, an often underestimated disease, can slowly but surely damage bones. These findings are an important reminder of the importance of adequate vitamin C intake to maintain bone health and prevent complications that can reduce quality of life.

Table 3. Radiological bone changes in scurvy patients based on severity level.

Severity level	Osteoporosis (n)	Cortical thinning (n)
Mild	1	2
Moderate	8	10
Severe	9	9

Table 4 reveals an interesting and significant association between the severity of scurvy and two serious bone health problems: osteoporosis and cortical thinning. Spearman correlation analysis showed that there was a fairly strong positive correlation between the severity of scurvy and the incidence of osteoporosis (rho = 0.495) and cortical thinning (rho = 0.394). The very small p-value ($p < 0.05$) indicates that this relationship is very unlikely to occur by chance. These findings provide strong evidence that scurvy, a vitamin C deficiency that is often taken for granted, can have a detrimental impact on bone health. The more severe the degree of scurvy, the greater the patient's risk of developing osteoporosis, a brittle bone condition that increases the risk of fractures, and thinning of the cortex, which makes bones more susceptible to damage

Table 4. Results of the Spearman correlation test between the severity of scurvy and the occurrence of osteoporosis and cortical thinning.

Correlation	Spearman's rho	p-value
Severity of scurvy vs. Osteoporosis	0.495	0.005
Severity of scurvy vs. Thinning of the cortex	0.394	0.031

The strongest correlation was seen between the severity of scurvy and osteoporosis (0.495), indicating that severe vitamin C deficiency can significantly increase the risk of osteoporosis, a condition of brittle bones that is prone to fractures. Although the correlation between scurvy severity and cortical thinning (0.394) was slightly lower, it was still statistically significant. This suggests that scurvy can also cause thinning of the dense outer layer of bone, which impacts overall bone strength and integrity. The upward-sloping regression line on the graph confirms the positive relationship between the severity of scurvy and both indicators of bone health. This means that the more severe the degree of scurvy, the greater the patient's likelihood of experiencing osteoporosis and cortical thinning (Figure 1).

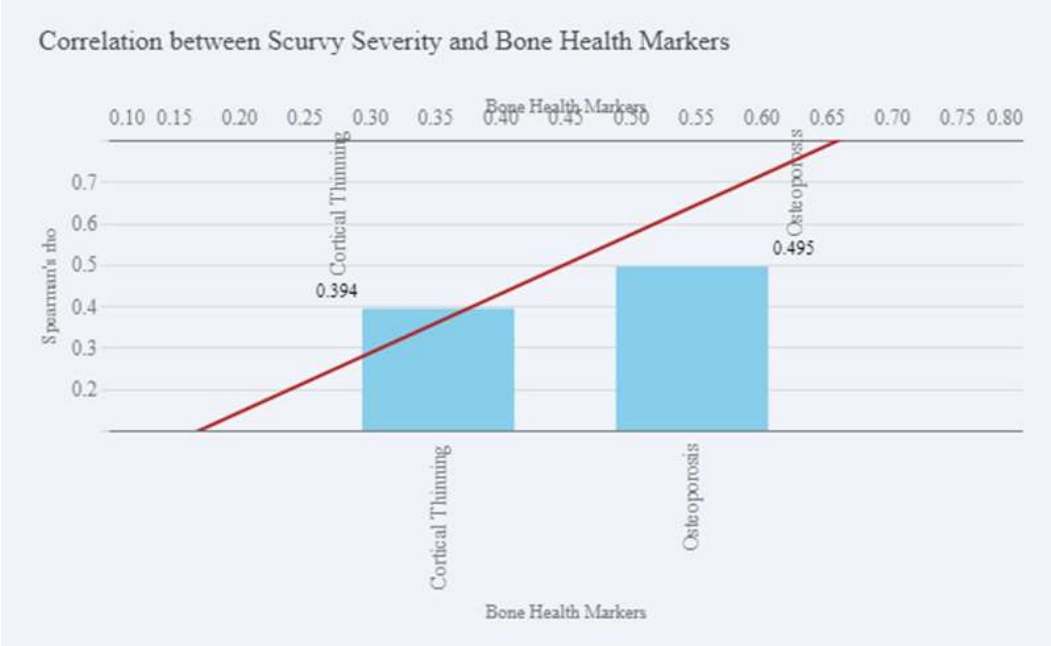

Figure 1. Correlation of scurvy severity and bone health.

4. Discussion

The results of this study reveal that scurvy, although rare, is still a relevant health problem in Indonesia. The majority of patients diagnosed with scurvy at Dr. Moewardi General Hospital Surakarta are male (66.7%) with an average age of 45 years. These findings indicate that the productive age group, especially men, have a higher susceptibility to vitamin C deficiency. This can be associated with several factors, including unbalanced diet, lifestyle, and socio-economic factors. An unbalanced diet, characterized by low fruit and vegetable intake, was found in the majority of patients (86.7%). Fruit and vegetables are the main sources of vitamin C in food. Insufficient consumption can cause a gradual vitamin C deficiency, ultimately leading to the development of scurvy. Lifestyles, such as smoking and excessive alcohol consumption, can also increase the need for vitamin C and interfere with its absorption in the body. Socioeconomic factors may also play a role in susceptibility to scurvy. Individuals with low levels of education and income may have limited access to nutritious foods, including fresh fruit and vegetables. In addition, insufficient knowledge about the importance of vitamin C and its food sources can contribute to unhealthy eating patterns.[9-11]

The clinical symptoms most frequently reported by scurvy patients in this study were fatigue, joint pain, bleeding gums, and skin bleeding. These symptoms correspond to the classic manifestations of scurvy that have been described in the medical literature. Fatigue is a common symptom of vitamin C deficiency because this vitamin plays an important role in energy production and iron metabolism. Joint pain can be caused by bleeding in the joint due to the fragility of the blood vessels. Bleeding gums and skin bleeding are also typical signs of scurvy due to impaired synthesis of collagen, the main structural protein in connective tissue.[12,13]

The findings of this study indicate a close relationship between scurvy and pathological changes in bone, especially osteoporosis and thinning of the cortex. This relationship is supported by strong scientific evidence, both in terms of theory and biological plausibility. Vitamin C plays an important role in the synthesis of collagen, the main structural protein in connective tissue, including bones. Collagen provides strength and elasticity to bones, so vitamin C deficiency can interfere with the formation and maintenance of collagen, causing bones to become brittle and susceptible to damage. Apart from that, vitamin C also plays a role in the differentiation and function of osteoblasts, bone-forming cells. Vitamin C is required for the activation of the enzymes prolyl hydroxylase and lysyl hydroxylase, which play a role in the hydroxylation of proline and lysine residues in procollagen, a collagen precursor. This hydroxylation is important for the formation of cross-links between collagen molecules, which provide strength and stability to the bone matrix. Vitamin C deficiency can also interfere with bone mineralization, namely the process of deposition of calcium and phosphate minerals into the bone matrix. Vitamin C plays a role in the regulation of acid-base balance in the bone microenvironment, which is important for optimal mineral deposition.[14-16]

Evidence of biological plausibility regarding the impact of scurvy on bone health can be seen from various studies on animals and humans. Studies in animal models of scurvy show a decrease in bone mineral density, thinning of the cortex, and an increased risk of fracture. In humans, observational studies and clinical cases have also reported radiological changes in the bones of scurvy patients, such as osteoporosis and thinning of the cortex. In addition, studies at the cellular and molecular level show that vitamin C deficiency impairs osteoblast proliferation, differentiation, and function. This leads to decreased collagen production and impaired bone mineralization, which contributes to decreased bone quality and strength.[17,18]

Several studies have reported an association between vitamin C deficiency reduced bone mineral density and increased risk of fracture. A meta-analysis involving more than 10,000 participants found that low vitamin C intake was associated with an increased

risk of hip fracture. Other research shows that vitamin C supplementation can increase bone mineral density in postmenopausal women. Studies in animal models of scurvy also provide strong evidence regarding the impact of vitamin C deficiency on bone health. Mice fed a diet low in vitamin C showed reduced bone mineral density, thinning of the cortex, and increased risk of fracture. In addition, studies on cultured osteoblast cells show that vitamin C deficiency impairs osteoblast proliferation, differentiation, and function, leading to decreased collagen production and impaired bone mineralization.[18,19]

The findings of this study have important clinical implications. Early screening and diagnosis of scurvy is essential to prevent long-term complications, including osteoporosis and fracture. Patients at high risk of vitamin C deficiency, such as individuals with poor diets, smokers, heavy alcohol drinkers, or patients with certain medical conditions, need special attention. Nutritional education and dietary interventions to increase vitamin C intake need to be intensified, especially in high-risk groups. Vitamin C supplementation may also be considered to prevent and treat vitamin C deficiency, especially in patients with clinical symptoms or significant radiological changes. Further studies with prospective designs and larger sample sizes are needed to confirm the causal relationship between vitamin C hypovitaminosis and bone changes, as well as evaluate the effectiveness of therapeutic interventions and preventive strategies. Research also needs to be carried out to identify specific risk factors that contribute to the high prevalence of scurvy among men of reproductive age in Indonesia.[19,20]

5. Conclusion

Vitamin C hypovitaminosis plays a significant role in the development of scurvy and has a negative impact on bone health. The research results showed that the majority of scurvy patients were men of productive age with a history of an unbalanced diet. The most frequently reported clinical symptoms are fatigue, joint pain, bleeding gums, and skin bleeding. Radiological examination reveals significant changes in long bones, especially osteoporosis and thinning of the cortex, which are more pronounced in patients with severe scurvy. Spearman correlation analysis confirmed a positive relationship between the severity of scurvy and the incidence of osteoporosis and cortical thinning.

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