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#### CASE SERIES

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# The Forgotten Disease in the 21st Century: Scurvy Outbreak in Hawassa Central Prison, Hawassa, Sidama, Southern Ethiopia, 2023

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**Background:** Dietary deficiencies in vitamin C lead to scurvy, an uncommon disease of nutritional deficiency in contemporary clinical practice. The inability of humans to synthesize vitamin C necessitates the regular consumption of vitamin C containing fruits, vegetables, or tablets.

**Objective:** To report a series of cases that came to HUCSH from May 25th up to the 18th of July, 2023, and to describe clinical features of scurvy from an observational study of on-site prison investigation.

**Methods:** A descriptive analysis of a case series of ten patients admitted to HUCSH between May 25th and July 18th, 2023, and onsite observational study of 67 patients over one month. A structured questionnaire was used to collect data, and SPSS version 25 was used for analysis.

**Results:** From the case series, all of the ten patients had either unilateral or bilateral leg swelling or pain as common compliant and all of them were male prisoners with mean age of  $25.6\pm5.33$  years and following admission, the hemoglobin value increased to  $7.1\pm1.34$  g/dL with treatment from  $4.6\pm1.88$  g/dL. From observational study of the prison, 67 cases were identified based on unilateral or bilateral leg swelling and/or pain, which was the presenting feature in the cluster of cases seen at HUCSH. The mean age was  $23.57\pm6.4$  years, and each patient got therapeutic doses of ascorbic acid 500mg PO daily using directly observed therapy and follow-up visit was after two and four weeks of ascorbic acid initiation and all patients showed significant improvement.

**Conclusion:** For clinicians in modern medicine, there should be a high index of suspicion for scurvy as a possible differential diagnosis when a patient presents with leg swelling in high-risk population, such as prisoners. Health-care providers in prison clinics need to be alert to such forgotten yet life-costly disease in resource constrained prison clinics.

Keywords: anemia, prison, scurvy, vitamin C, vitamin deficiency

## Introduction

Scurvy is an ancient human disease caused by a vitamin C deficiency. It rarely occurs because of the adequate intake of ascorbic acid.<sup>1,2</sup> But it can still occur in specifically at-risk groups such as alcoholics with poor nutrition, isolated elderlies, institutionalized patients and patients with malabsorption.<sup>3</sup>

Scurvy develops in people who eat insufficient amounts of fresh fruits and vegetables for a variety of reasons, including limited food options, finances, and food access. Inadequate nutrition causes these imbalances, which lead to scurvy.

Asthenia, vascular purpura, bleeding, and gum abnormalities are the primary symptoms. In 80% of cases, the manifestations of scurvy include musculoskeletal symptoms such as arthralgia, myalgia, hemarthrosis, and muscular hematomas.<sup>4</sup> The spectrum of presentation varies, and it includes dental, dermatological, bone, and systemic manifestations and the common symptoms in adults include gum disease, tooth loosening, weakness, irritability, pain in the

muscles and joints of the leg.<sup>5</sup> Upon examination, many patients display follicular hyperkeratosis, swollen joints, swollen bleeding gums, and peripheral edema and shortness of breath may also occur and the skin can become dry and rough.<sup>6</sup>

Full clinical syndrome does not appear until the normal body pool has been depleted to less than 300 mg, and the main stay of treatment in emergencies and scurvy is the supplemental dose of vitamin C for all groups and therapeutic doses of vitamin C for those with clinically defined scurvy and left untreated, Scurvy in any age group can lead to death.<sup>5,6</sup>

High dietary sources of ascorbic acid are citrus fruits and some vegetables such as tomatoes, potatoes, broccoli, cabbage, cauliflower, spinach, and strawberries. Absorption from diet and supplements is similar and the dietary recommended daily allowance (RDA) for those; aged >18 years: males, 90 mg daily; females, 75 mg daily; pregnant females, 19 to 50 years:- 85 mg daily; lactating females, -19 to 50 years:- 120 mg daily; and for adult smokers, an additional 35 mg daily and upper limit of intake should not exceed 2000 mg daily.<sup>7</sup>

Previously from a double-blind controlled trial called MRC trial which was initiated in October 1944 and lasted until February 1946. The conclusion of this trial referred mostly to how 10-mg daily vitamin C intake prevents and treats the clinical appearance of scorbutic wounds - a sign of frank scurvy.<sup>8</sup> This narrative conclusion did not refer to scar strength data or histology, which, when analyzed recently, tell an opposite story: an average daily 10-mg vitamin C intake fails to prevent or treat collagen-related pathologies though it may indeed be sufficient to prevent frank scurvy but fails to maximize health, so a vitamin C dose of 10 mg daily effectiveness in preventing and treating scurvy has been proven wrong.<sup>9</sup>

Adults with scurvy are usually treated with 300-1000 mg per day for one month; dose and duration of therapy should be individualized and improving the vitamin C content of the diet, either by supplementation, fortification, or consumption of a vitamin C-rich diet.<sup>10,11</sup>

#### Statement of the Problem

Since late May 2023, we observed a cluster of unusual cases of young male patients from the central prison of Hawassa. We have seen male patients in their 20s and 30s who came to our hospital medical OPD as well as the emergency department with a major complaint of painful leg swelling involving single or both extremities with associated easy fatigue, malaise, and intermittent dry cough. On physical examination, the extremities were swollen, shiny, hot to touch, and tender to palpation. Some patients had knee joint involvement with an associated restriction of active and passive movements. On further physical examination, consistent findings were pale conjunctivas, gum hypertrophy, and generalized skin hyperpigmentation.

Patients were investigated using basic laboratory studies and had severe anemia with normal or low MCV. Imaging studies is done and it revealed normal radiographs and ultrasonography showed increased soft tissue echogenicity, indicating cellulitis. Some patients were admitted to the adult emergency room for cellulitis management and severe anemia workup. Peripheral blood morphological studies were performed by pathologists and internists that showed normocytic and normochromic anemia. Iron therapy and antibiotics were initiated to patients admitted to adult emergency unit. One patient is admitted to the medical ward with bilateral leg swelling, with a superinfected wound over the leg and pancytopenia, and was on treatment for cellulitis and neutropenic fever, but died in the medical ward despite repeated transfusion and broad-spectrum antibiotic administration.

Based on the nutritional history of prisoners, vegetables and fruits were excluded from their diet because of the occurrence of acute watery diarrhea in the prison. Based on the above clusters of clinical presentations and literature reviews, we have considered scurvy as the top differential diagnosis as the cause of leg swelling and severe anemia.

According to the WHO,1999 "Scurvy and its prevention and control in major emergencies" report: Even a single case of clinical scurvy seen in a population reflects a public health problem and calls for a full nutritional assessment using biochemical methods to assess the vitamin C deficiency in the population. It is difficult to clinically define scurvy, and very few people in the field have been adequately trained to recognize scurvy correctly.<sup>6</sup>

In addition to being a public health problem, even with a single case of clinical scurvy, it is infrequently taught in contemporary clinical practice as a potential differential diagnosis in clinical year training programs for healthcare professionals.

#### Literature Review

The clinical manifestations of scurvy include bleeding into the tissue; purpura and ecchymoses are observed in the skin, whereas dusky subcutaneous discoloration and induration in the legs reflect an underlying hematoma and painful and swollen joints resulting from hemarthroses. In the developed world, scurvy is a relatively rare condition that is most commonly observed in malnourished and chronic alcoholics. Classically, affected patients present with bleeding gums, loose teeth, and petechial hemorrhage. Scurvy can also be linked to underlying anemia or other metabolic abnormalities.

Iron absorption is normal in scurvy, despite bleeding into the tissues, and hemorrhagic gingivitis that occurs in scorbutics, gastrointestinal bleeding is not a feature of scurvy.<sup>12,13</sup>

Early recognition of scurvy can be difficult because the symptoms may appear non-specific and mimic more common conditions. In any patient with a spontaneous hematoma and purpura scurvy should be systematically considered in cases of nutritional disorders. As this disease can lead to severe complications, such as bone pain, heart failure, or gastro-intestinal symptoms, vitamin C supplementation should not be delayed, which is a simple and rapidly effective treatment. Vitamin C deficiency with clinical manifestations that is scurvy, was a fairly common disorder in the 18th century, but is virtually unseen in today's medicine. Modern clinicians should have a low threshold for suspecting this diagnosis in high-risk populations (elderly, mentally ill, smokers, alcoholics, and those with low socioeconomic status), especially in those with the correct clinical presentation.<sup>14,15</sup>

A total of 118 probable instances of scurvy with unilateral or bilateral swelling and no known etiology were found from a total of 2790 prisoners during an outbreak investigation as an epidemic of scurvy in a southwest Ethiopian prison in 2016. Seven of the eight probable cases had clinical symptoms that were compatible with scurvy after being thoroughly evaluated. Three of them had serum vitamin C levels that were undetectable. In the study, the prison's attack rate was 4.2%, and 11 deaths were reported, resulting in a 9.3% case fatality rate. Clinical cases of scurvy showed evidence of follicular hyperkeratosis, petechiae, peripheral edema, and mouth lesions, in addition to symptoms of weariness, arthralgia, and myalgia. The hemoglobin level in each clinical case was less than 6 g/dl, indicating severe anemia. Fruits and vegetables are not a part of the jail diet. Vitamin C supplementation was initiated immediately, as scurvy was the cause of the outbreak. Over the course of a 4-week active surveillance period, all symptomatic detainees improved, and no new cases were found.<sup>1</sup>

Another observational study, which included 38 convicts, was conducted in 2010 at Yirgalem Hospital. All 38 patients reported limb edema, and 35 experienced numbness, tingling, and burning in the distal limbs. Patients' leg edema, hematuria, coughing, and gum bleeding entirely disappeared after five days of vitamin C administration, and their hemoglobin value increased during treatment from  $(10.3\pm3.31)$  to  $(12.7\pm2.26)$ . According to their nutritional history, they did not consume any fruits, vegetables, or animals. On average, eight to forty-nine months were spent behind the bars for each participant.<sup>2</sup>

Another investigation of an outbreak known as the Outbreak of Scurvy in Tana River County, Kenya, in 2016, revealed that over the course of a five-month period, clinicians noticed an increase in the number of patients visiting medical facilities with a common set of symptoms, including fever, joint pain, and gum hypertrophy. The patients were empirically started on ascorbic acid for putative scurvy after the initial investigation, and the treatment procedures failed to yield a diagnosis. Within two weeks, this approach caused the symptoms in 65 patients to disappear quickly.<sup>3</sup> Another outbreak investigation conducted at Kakuma Refugee Camp, Kenya, 2017–2018 for the Scurvy Outbreak Among South Sudanese Adolescents and Young Men revealed similar findings of clinical presentation, including lower limb pain and swelling (in some cases involving joints), lethargy, fatigue, gingival swelling and pain, hyperkeratotic skin changes, and chest pain. In this study, all patients who received vitamin C treatment showed symptom improvement within less than a week.<sup>16</sup>

#### Objective

The objective of this study was to analyze a cluster of cases that presented to our medical OPD and emergency department with bilateral or unilateral leg swelling.

To identify cases of scurvy in Hawassa prison by physical examination findings of scurvy and initiate therapeutic doses of ascorbic acid.

Early intervention measures for the possible outbreak of scurvy by initiating therapeutic and prophylactic doses of vitamin C.

Study of dietary content in prison and provide recommendations based on these findings.

## Significance of the Study

Undiagnosed and untreated scurvy is a serious medical illness and patients can succumb to death due to complications and the morbidity is significant which negatively affects patient's quality of life. Effective and curative treatment can be initiated early if timely diagnosis and intervention are made, further cases can be effectively prevented.

Identifying the risk factors for the occurrence of clinical cases in prison and modifying the risk factors can limit the number of further cases.

## **Methods and Materials**

The study has three parts.

The first part involved a descriptive analysis of the clusters of cases presented to our university hospital. Patients medical record number was recorded since we started to see the clusters and after getting IRB approval the medical records was evaluated for demographic, clinical presentation, laboratory studies and imaging studies and descriptive statistics used to describe the clinical findings.

The next step in this study was to conduct a field study in prison. After obtaining IRB approval from HUCSH, and a letter of cooperation, we communicated with the prison personnel to obtain permission to conduct the field study. To identify cases similar to the clusters which came to our hospital, we used a check list tool for screening of scurvy including the chief complaint of the clusters which was "unilateral or bilateral leg swelling." After obtaining a written consent, we obtained a brief history from the prisoners to identify complaints of leg swelling, leg pain, or joint pain. For prisoners who claimed to have the case definition, further history was obtained, physical examination was performed and the findings were recorded using a structured questionnaire and analyses were performed using SPSS version 25. Individuals who were considered to have a consistent history and physical findings of scurvy by the examining physicians were started on an ascorbic acid therapeutic dose of ascorbic acid 500mg PO daily. The reason why we decided to start empirical treatment of scurvy without determining the serum vitamin C level was due to the unavailability of the test in the country. Those patients who were started on ascorbic acid therapy were given a specific follow-up number and were evaluated two and four weeks later, after ascorbic acid initiation for the clinical outcomes of the treatment.

The third part was an environmental and dietary study of the prison. The living conditions, and dietary constituents of the food offered in prison were evaluated through interviews with the prison personnel.

## Results

#### Case Series of Scurvy Outbreak in Hawassa Central Prison

Starting from May 25th up to July 18th of 2023, our university hospital started to have patients from the Hawassa central prison and there were ten patients in total and all of them were initially treated in the prison clinic by different types of analgesics with a working diagnosis of arthritis and up on presentation to our hospital all of the ten patients had either a unilateral leg swelling, bilateral leg swelling or leg pain as a common compliant and all of them were male prisoners with mean age of  $25.6\pm 5.33$  years and with mean hemoglobin level of  $4.6\pm 1.88$  g/dL and ranges between 2.8 g/dL up to 7.5 g/dL, except one all had a hemoglobin level below 7 g/dL.

Up on discharge their hemoglobin level ranges from 5.1 g/dL up to 9.3 g/dL and the mean hemoglobin level was 7.1  $\pm$ 1.34 g/dL. The average length of stay of the patients was around twelve days and ranges from five to thirty days.

Additionally, of these ten patients, five underwent leg ultrasound, and more or less the conclusion was similar "diffuse subcutaneous and soft tissue edema, non-specific myofascitis with no sonographic evidence of deep vein thrombosis". PICT was performed and all patients were non-reactive.

Among these ten patients, one died, and the remaining nine were discharged from our hospital with significant improvement after five to thirty days of inpatient management.

#### Case I

A 25-year-old male patient presented with a complaint of left leg swelling of twenty days duration with associated pain and dark color change. Vital signs at the emergency triage were:- blood pressure = 79/36mmHg; pulse rate = 112; respiratory rate = 22 Saturation; oxygen – 97% on atmospheric air and he had a pale conjunctiva; left leg pitting edema with shiny appearance as shown in Figure 1; tender to palpation; restriction of extension of the knee joint; shortness of breath; and dry cough of one-week duration. In the ED with initial diagnosis of Left leg cellulitis, hypovolemic shock, and severe anemia secondary to? Initial resuscitation was performed, and vital signs were corrected, and the patient was started on an antibiotic (ceftriaxone 1g IV BID) and put on maintenance fluid.

CBC showed a white blood cell count of  $5.16 \times 10^3$  /mL (Neutrophil% –47.57%, Lymphocyte% –50.5%), hemoglobin of 6.3 g/dL (Reference range, 12.5–16.3 g/dL), with normal RBC indices and platelet count and renal function test, serum electrolytes as well as liver function tests were within the normal range. Peripheral morphology showed normocytic, normochromic anemia, leg ultrasound revealed left leg subcutaneous tissue and calf muscle edema with a differential diagnosis of cellulitis with myositis, and there was no sonographic evidence of deep vein thrombosis. Chest radiography findings were unremarkable.

Subsequently, the patient was given cefepime, vancomycin, and metronidazole and stayed in the hospital for one month, required multiple transfusions of packed RBC, and later developed leukopenia and thrombocytopenia. Ascorbic acid therapy was considered while he was in the ED, but was not available due to the absence of the assigned attendants and also due to financial problems. Later, he was started on ascorbic acid 500mg + zinc 15mg chewable tablet, took for three days but succumbed to death due to ? Uncontrolled sepsis.



Figure I Left leg pitting edema, with hyperpigmented skin and flexion-contraction of the knee.

The second case came on May 27th of 2023 to our hospital ED, a 29-year-old male, with a compliant of right leg swelling of one-month duration. He came with a right leg swelling of one-month duration with associated pain, easy fatiguability, dry intermittent cough and history of gum bleeding. Vital signs at the ED triage were blood pressure, -98/64 mmHg; pulse rate, - 110; respiratory rate, - 24; body temperature  $- 37^{\circ}$ C and saturation of oxygen on atmospheric air, 95% and he also had pale conjunctiva; Hypertrophied gum (see Figure 2, right); right leg edema with shiny skin (see Figure 3, left); and tenderness to palpation with a leg-leg discrepancy of 2 cm. With an initial diagnosis of right leg cellulitis, severe anemia secondary to? And he was started on ceftriaxone 1 g IV BID and 325 mg of iron sulphate (65 mg elemental iron) orally daily.

Up on investigations on CBC, the WBC was  $5.17 \times 10^3$  /mL (Neutrophil -70.9%, Lymphocyte-22.7%) and hemoglobin of 4.3 g/dL (Reference range, 12.5–16.3 g/dL), with normal range of RBC indices and platelet count. Serum electrolytes level and liver and renal function test result were within the normal ranges. Right knee joint radiograph visible opacity at the suprapatellar bursae and recommended joint ultrasound.

After six days as an inpatient, it was decided to administer ascorbic acid 500 mg+ zinc 15 mg PO BID and zinc, and the patient was discharged after three days with improvement.



Figure 2 Showing gum hypertrophy.



Figure 3 Shiny, edematous and hyperpigmented right leg.

The third case presented on June 20<sup>th</sup> 2023, a 25-year-old male, with complaints of left leg pain of one-month duration with associated swelling and limitation to movement. The pain and swelling had progressively worsened. He also had a dry cough, low-grade fever, and fatigue.

He had been diagnosed with epilepsy, using Phenobarbital for the past 10 years. In the ED, the vital signs were stable and he had a pale conjunctiva as well as palmar pallor and left leg and thigh has pitting edema, tender to palpation and there is joint stiffness at the knee joint which restricts full extension of the knee joint (as shown in Figure 4) and hypertrophied lower gingiva (see Figure 5). CBC showed a hemoglobin of 5.6 g/dL (Reference range, 12.5–16.3 g/dL), and the other parameters were within the normal range. Leg ultrasonography revealed diffuse subcutaneous and soft tissue swelling in the left thigh and proximal calf regions secondary to cellulitis, with no evidence of abscess formation. Left leg radiography and chest radiography findings were unremarkable. After three days of inpatient management, the patient was started on ascorbic acid 500 mg PO BID and was discharged with improvement after one week of inpatient management.

# Case 4

The 4th patient was a 17-year-old male, visited the ED on June 23rd, 2023, presented with right leg swelling and pain for a one-month duration. Vital signs at the ED triage were stable, and his right leg and thigh were edematous, shiny, hot, and tender on palpation. Circumferential leg-leg discrepancy of 10 cm on the calf and 4 cm in the thigh area (see Figure 6). Up on investigation the hemoglobin level was 2.9 g/dL (Reference range, 12.5–16.3 g/dL), and the other CBC parameters were within the normal range. Ascorbic acid powder 1000 mg mixed with 300 mL of water and 150 mL of this mixture was given on BID base and had two units of whole-blood transfusion. He was discharged after six days of inpatient management, with significant improvement.

## Case 5

A 28-year-old male presented to the ED on July 10<sup>th</sup>, 2023, with progressively worsening fatigue and shortness of breath of one-month duration. In addition, he had light headedness, vertigo and tinnitus, loss of appetite, unquantified weight



Figure 4 Diffuse left leg and thigh swelling with semi flexed position.



Figure 5 Gum hypertrophy and mucosal hyperpigmentation.



Figure 6 Right leg shiny diffuse swelling with a right leg flexion at knee joint and visible leg-leg discrepancy.

loss, and gum bleeding. Significant fatigue limited his activity, and he noticed reddish discoloration of the urine in the past three weeks. He had cough for two weeks and had swollen gums, which limited his chewing resulting in fluid diet. He also had difficulty of walking.

The vital signs at the ED were stable, and he had pale conjunctiva. Both the upper and lower gingiva were severely hypertrophied, with ecchymosis and ulceration over the left upper inner part of the gum (as shown in Figure 7A) and a pale tongue with erythematous patch and perioral hyperpigmentation (as shown in Figure 7B). The right leg was tender on palpation, but no leg-leg discrepancy and he had a trace pedal edema (as seen in Figure 8). He also had palmar pallor, perifollicular hyperpigmentation and macule to patchy hyperpigmentation over the dorsum of the hand (as seen in Figure 9). There was also restriction of movement of the left knee to extend it fully either actively or passively.

CBC showed a hemoglobin level of 3.2 g/dL (Reference range, 12.5–16.3 g/dL), and MCV of 62.2 fL (Reference range, 78.3–96.2 fL) and RDW of 17.9% (Reference range, 12.1–14.2%) and the other parameters as well as organ function tests were within the normal range. Ascorbic acid 1000mg in 300mL of water and iron sulfate 325mg PO daily were started after one day of stay in the ED. Subsequently, he was transferred to the medical ward and stayed for sixteen days as in patient, and on the eleventh day of admission the gum hypertrophy decreased significantly (see Figure 10A) and the patchy hyperpigmentation over



Figure 7 (A) Severe gum hypertrophy with erythema and ulceration. (B) Pale tongue with overlying erythematous patch and perioral hyperpigmentation in a young male patient prisoned for 15 months.



Figure 8 Hyperpigmented, trace pedal edema of both right and left leg.



Figure 9 Hyperpigmented (macule-patchy) skin lesion over the dorsum of the left hand.

the dorsum of the hand **is gone** (see Figure 10B). Without any blood transfusion, the hemoglobin level increased to 5.4g/dL with MCV of 73.3 fL and RDW of 33.2%, and there was significant improvement in the functional status of the patient.

## Case 6

A 30-year-old male was presented with swelling and pain in the right leg for one month with associated pain. The limp started at the onset of leg swelling. Vital signs were stable in the medical OPD and he had pink conjunctiva, minimal gum hypertrophy and right leg is having a pitting edema with a shiny appearance (as shown in Figure 11) and tenderness on palpation. A complete blood count showed a hemoglobin of 7.9 g/dL (Reference range, 12.5–16.3 g/dL), and the other parameters were in the range and right leg x-ray showed right leg soft tissue swelling, and visible bones were unremarkable. Ascorbic acid 1000 mg powder mixed with 300 mL of water was initiated and six days after admission the patient was discharged with improvement.



Figure 10 (A) The same patient on Figure 7A, 11 days after ascorbic acid initiation the severe gum hypertrophy regressed significantly. (B) The same patient on Figure 9, 11 days after ascorbic acid initiation, the hyperpigmentation over the dorsum of the hand is fully subsided.



Figure 11 Right leg swelling with shiny appearance, darkening and flexion contracture at the knee joint.

A 35-year-old male came with complaint of left leg pain of three weeks duration with associated swelling and limitation of movement. The pain and swelling had progressively worsened. Vital signs were stable in the medical OPD, with poor dentition, perioral darkening, grossly edematous; shiny left leg and palmar pallor. CBC showed a hemoglobin level of 6.6 g/ dL (Reference range, 12.5–16.3 g/dL), and the other parameters were within the normal range. Bilateral leg radiography was unremarkable, and bilateral Leg Doppler ultrasound showed normal findings. Ascorbic acid 1000 mg with 300 mL of water was administered for two days after admission, and the patient was discharged after five days of stay as inpatient.

## Case 8

A 28-year-old male who presented with difficulty of extension of the left leg of two months duration. Swelling of the left leg and easy fatigability of one-month duration. In addition, he had an unquantified yet significant weight loss and dry cough of one-month duration. The vital signs in the ED were as follows:

Blood Pressure =92/63 mmHg	Pulse rate- 120	Respiratory rate - 22	Body temperature =37.2
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He had pale conjunctiva and, non-icteric sclera, and there were small ecchymotic lesions (as shown in Figure 12) over the upper and lower gingiva, but no gum hypertrophy. Furthermore, the patient had a Grade II bilateral pitting edema (as seen in Figure 13B) and hyperpigmented dorsal surface of the ankle of both extremities with contracted and a semi flexed left knee (as seen in Figure 13A) and also the left knee could not be extended fully, either actively or passively (as seen in Figure 14). Up on investigation, CBC showed a white blood cell count of  $1.83 \times 10^3$  /mL (Neutrophil -47.57%, Lymphocyte-50.5%), hemoglobin level of 2.8 g/dL (Reference range, 12.5-16.3 g/dL), with MCV of 110.1fL (Reference range, 78.3–96.2fL) and RDW of 30.7%, (Reference range, 12.1-14.2%) and a platelet count of  $10 \times 10^3$ / mL and peripheral morphology showed dimorphic (mixed nutritional deficiency) anemia + thrombocytopenia + leukopenia. Serum electrolyte levels and renal and liver function test results were within the normal ranges. Urinalysis results were positive for urobilinogen, and the ESR was 100. Bilateral duplex study of the lower limb – normal bilateral lower limb veins duplex study, inflammation of the subcutaneous tissue, fascia, and muscles non-specific myofascitis. The left knee and leg X-rays were unremarkable, although the chest X-ray showed right mid and lower zone opacity secondary to pneumonia. Abdominal ultrasound: ascites with serosal thickening, intra-abdominal necrotic lymphadenopathy, and mild splenomegaly (13.8 cm) likely disseminated tuberculosis to (lymph node, peritoneum, and spleen).

His management course was as follows: he was started on ascorbic acid 1000 mg with 300 mL of water on the day of the admission at the ED with Iron sulphate 325 mg (65 mg elemental iron), folic acid 5 mg to be taken once daily, Cyanocobalamin 1mg IM daily and after five days of his admission to the medical ward and after collecting the investigations he was started on Anti-TB RHZE 03 tabs to be taken daily with 50 mg of pyridoxine daily and on the fourteenth day of stay as inpatient management he can extend his left knee completely without any restriction (see Figure 15) and the bilateral pitting edema has subsided (see Figure 16). During his sixteen days of stay as inpatient he was transfused with 02 units of whole blood and 01 unit of packed RBC, and up on discharge his CBC profile was; white blood cell count of  $5.7 \times 10^3$ / mL with neutrophil % of 48.2 and lymphocyte% of 35.5%, hemoglobin level of 7.3 mg/dL with MCV of 98.5 fL and RDW of 28.4%, and platelet count of  $138 \times 10^3$ /mL. Clinically, the patient's condition improved significantly.



Figure 12 Ecchymotic gingiva.



Figure 13 (A) Hyperpigmented dorsal surface of the ankle of both extremities with contracted and a semi flexed left knee at admission. (B) Bilateral pitting edema at admission.



Figure 14 Left knee during active extension, that failed to extend fully and stayed in a semi extended position at admission.



Figure 15 The same patient on Figure 14, fully extended left knee on active extension after 14 days of in-patient management with ascorbic acid.

An 18-year-old male presented with shortness of breath of five months, that had worsened over the past one month. The patient also complained easy fatigability, vertigo, light headedness, and tinnitus of the same duration. In addition, he reported that he noticed a dark skin color change over his legs on both side for one-month duration. Vital signs were stable in the medical OPD and then linked to the ED for blood transfusion, with a paperwhite conjunctiva, non-icteric sclera, and scaly hyperpigmented skin lesion over the bilateral dorsal surface of the foot on the flexural aspect of the ankle. Hyperpigmented patchy discoloration of both legs (as shown in Figure 17). Hyperpigmented perifollicular hemorrhagic lesion over the forehead (as shown in Figure 18) and left part of the face (as shown in Figure 19), and



Figure 16 The same patient on Figure 13B, the previous pitting edema has subsided after 14 days in patient management with ascorbic acid.



Figure 17 (A) Hyperpigmented patchy discoloration of the left leg and hyperpigmented skin lesion over the dorsal surface of the foot more on the flexural aspect of the ankle. (B) Hyperpigmented patchy discoloration of the right leg and hyperpigmented skin lesion over the dorsal surface of the foot more on the flexural aspect of the ankle.



Figure 18 Hyperpigmented perifollicular hemorrhages over the forehead.



Figure 19 Hyperpigmented perifollicular hemorrhagic lesion over the left part of the face.

there was no peripheral edema, although tenderness on both lateral malleoli on palpation and palmar pallor involving the creases was observed. CBC showed that hemoglobin level of 3.1 g/dL (Reference range, 12.5–16.3 g/dL), MCV of 57.2fL (Reference range, 78.3–96.2fL) and RDW of 21.7% (Reference range, 12.1–14.2%) with normal range of other parameters, stool exam showed ova of hook worm, abdominopelvic ultrasound – unremarkable abdominopelvic scan. Leg ultrasound – subcutaneous edema bilaterally and on the next day of admission he was dewormed with Albendazole 400 mg PO stat, transfused with 04 units of crossmatched whole blood and ascorbic acid 500 mg PO twice daily and iron sulphate 200 mg (elemental iron 65 mg) PO daily was initiated and he was discharged after five days of inpatient management and up on discharge his CBC showed a hemoglobin level of 7.9 g/dL, MCV of 72.8fL and RDW of 28.4%, with normal range of other parameters.

## Case 10

The last case that came to the ED on July 18th 2023, and his presentation was a complaint of diarrhea for eight days, which was voluminous and 2–3 episodes per day as well as bilateral leg pain and swelling for three weeks and vital signs in the ED were:

Blood pressure -99/	Pulse rate	Respiratory	Body temperature -	Saturation of oxygen was 97% on
60 mmHg	-130	rate of 24	37.2°C	atmospheric air,

He had pale conjunctiva and tender, grade II bilateral pitting edema, with a shiny surface (as seen in Figure 20) and woody consistency of the lower extremity bilaterally. CBC showed a hemoglobin level of 2.9 g/dL (Reference range, 12.5–16.3 g/dL), MCV-78.5 fL (Reference range, 78.3–96.2fL) and RDW of 16.8% (Reference range, 12.1–14.2%) with other parameters fall in the normal range. Stool tests showed no ova parasites, although many pus cells were present. He was started on ciprofloxacin 500 mg po BID and ascorbic acid 1000 mg was dissolved in 300 mL of water daily, and he had a significant improvement and discharged after ten days of inpatient management.

#### Descriptive Epidemiology of the On-Site Observational Study

On July  $15^{\text{th}}$  of 2023, among a total of 3300 prisoners in the prison 67 cases were identified based on unilateral or bilateral leg swelling and/or pain initially by the prison paramedics later by physicians from HUCSH and onsite history, physical examination was done with four physicians from Hawassa University Comprehensive specialized hospital. The mean age was  $23.57\pm6.4$  years, ranges between 15 up to 42 years (as shown in Figure 21).

All clinically confirmed cases were male, with a mean age of  $23.5\pm6.4$  years and none of the female prisoners had symptoms of scurvy that is probably due to; the female prisoners cook their own food in the prison and their diet consists of green vegetables and potatoes.

On onsite clinical evaluation, all of the clinically confirmed cases had either a unilateral or bilateral leg pitting edema and hyperpigmented skin (Table 1).

Among the 67 cases two were completely unable to move, nineteen of them used a stick to walk, and twenty-one of them were limping.

#### Environmental Investigation

At the time of the investigation, 3300 prisoners were in the prison and held in 26 rooms. With a direct interview with the prison head and nursing staff, the diet prior to the occurrence of the scurvy outbreak used to consist of vegetables such as cabbage, and the prisoner families could provide any type of meal to the prisoners, five months prior to the first case that came to our hospital, there was an outbreak of cholera in the prison; due to fear of this, the prison changed its regular diet plan and it was devoid of any vegetable and fruits, and it also closed its gate to the foods that were being delivered by the families.



Figure 20 Bilateral tender Grade II pitting edema with a shiny skin appearance on a male prisoner who was behind the bars for 7 months.



Figure 21 Age in years of the patients from the on-site prison investigation.

## Treatment and Public Health Actions

Onsite direct observed therapy of ascorbic acid 500 mg PO daily was initiated, active surveillance was performed two weeks later, and only two new cases were identified, four weeks after the initiation of ascorbic acid, no new additional scurvy case was identified in the prison or visited our hospital medical outpatient department or the emergency department. All patients showed significant improvement in leg swelling and pain, and those who were unable to extend their limbs were able to walk (as seen in Figures 22 and 23). Unless there was a prompt treatment, this scurvy outbreak could be the largest and with a highest case fatality in prison history.

## Discussion

At the end of May 2023, we started to see patients who were prisoners of Hawassa central prison. The diagnosis of scurvy was based on the clinical manifestations, dietary history, and response after initiation of ascorbic acid, and the

Patient Characteristics	Value			
Male Sex %	100			
Musculoskeletal Findings %				
Unilateral leg edema	46.2			
Bilateral leg edema	47.7			
Tenderness up on palpation	89.1			
Affected range of motion of knee joint (on Extension)	23.1			
Limping   Inability to walk without assistance	30.8			
Dermatologic Findings %				
Hyperpigmentation	100			
Hyperkeratotic, papules	50.8			
Clinical Signs of Anemia* %	56.9			
Gum involvement (Hypertrophy or Bleeding)	44.6			

Table IPercentage of Clinical Symptoms of Scurvy, Hawassa City,Sidama Regional State, Ethiopia, July 2023

Note: \*Clinical signs refer to either pale conjunctiva or palmar pallor.



Figure 22 A prisoner with right contracted knee and heel is off -ground in standing position and stick use as a walking-aid also other prisoners are seen having stick on their hands.

main aim of our study was to describe the clusters of cases that came to Hawassa University Comprehensive Specialized Hospital with either a unilateral or bilateral leg swelling starting from May 25th up to July 18th, 2023.

In our study, all patients who presented with this compliant were male, which is similar to that of previously published articles, with a mean age of  $25.6\pm5.33$  years, ranging between 15 and 42 years, and the mean age for a study conducted in 2010 in one of the South Ethiopian prison was  $25.36 \pm 8.53$  years.

The actual date when the scurvy outbreak started in prison is unknown, yet the need for seeking better health care emerged after two prisoners died in prison in April. As previously reported in the literature, scurvy is not a new entity in prison settings, especially in a third world setup.

Scurvy models accurately predicted the time taken for clinical symptoms to appear. Forty-one days after beginning a diet low in vitamin C, serum ascorbic acid levels were no longer detectable. Cell depletion occurred after 121 days, and the first skin lesions appeared after 132 days. Dental anomalies began to appear after six months. After one to three months of consuming no vitamin C, a constellation of clinical symptoms appeared. When the total body pool of vitamin C fell below 300 mg, and the serum ascorbic acid level drops below 2.5 mg/l.<sup>17,18</sup>

These descriptions of the onset of scurvy goes in line with the outbreak of the scurvy in the prison, as described earlier there was a cholera outbreak in the prison five months before the first case to our hospital where the diet was changed to be devoid of any Vitamin C source.

Lower extremity pain was also the major reason of difficulty walking by 3 children.<sup>19</sup> The clinical findings of longstanding vitamin C deficiency in 7 patients the outstanding features are a curious "woody" oedema of the legs associated with pain and discoloration.<sup>20</sup> These manifestations of scurvy are very similar to our study in which all of the cases had either unilateral or bilateral leg swelling and hyperpigmented skin with a "woody" consistency.

The anemia profile of our cases varies greatly there is a patient with MCV of 57.2fL in case-9 and on the other side with MCV 110.1fL in case-8 and the other patients MCV being in between these two measurements and this wide range



Figure 23 The same prisoner on Figure 22, after onsite evaluation and initiation of therapeutic doses of ascorbic acid 500mg PO daily on direct observational therapy. Note: Fourteen days later, the right heel touching the ground in standing position and no use of stick to walk.

of MCV can be supported by that Scurvy can cause microcytic, normocytic and macrocytic anemia.<sup>21</sup> The Scurvy in Adult Africans: A Clinical, Hematological, and Pathological Study reported that the anemia was normochromic and normocytic in every instance.<sup>22</sup> Our case series also had a similar anemia profile in six patients out of the ten admitted, in which they had a normocytic and normochromic anemia and the remaining three had a microcytic anemia and one had di-morphic anemia (both microcytic and macrocytic). But Serum iron studies as well as thiamine, folate and Vitamin B12 levels should have been determined to diagnose an additional cause of anemia in these patients, though we relied on the CBC parameters and peripheral morphology reports solely due to unavailability and cost issues of these investigation modalities in our setup and a component of concomitant micro-nutrients deficiency cannot be ruled out.

Many nutritional disorders do not present as the primary problem but are detected when patients present with an acute co-existing problem or problem that complicates the underlying deficiency. In the foregoing, there has been frequent reference to the close relationship between scurvy and the incidence of the infectious diseases to the fact that a scorbutic condition increases the susceptibility to infection.<sup>23</sup> Scurvy, generally is more severe and involves more systems than experimental scurvy. One might speculate that this results from multiple deficiencies or from associated infectious diseases. Nonetheless, the similarities between experimental and spontaneous scurvy are remarkably close.<sup>5</sup> These reports support the idea that our patients might have a concomitant micronutrient deficiency associated infectious diseases are seen in our patients like case-1 who had a full-blown sepsis, case-10 had acute gastroenteritis, case-8 was diagnosed with disseminated tuberculosis (Peritoneum, Spleen and lymph node).

## **Conclusion and Recommendations**

Scurvy, which is not being considered as a differential diagnosis in modern clinical practice, may be costing patients their lives – especially in the prison setting. We identified an outbreak of scurvy in a prison that included two deaths in the prison and one death in the HUCSH, resulting in a total of three deaths. Thus, health professionals working in prison clinics should have a high index of suspicion when prisoners present with unilateral or bilateral leg swelling or pain.

There is a need to train such professionals in the early identification and management of such populations when they present with signs and symptoms of scurvy. Furthermore, active surveillance systems and posters that can explain oral, musculoskeletal, and dermatologic findings should be posted in prison clinics, so that a patient will not be misdiagnosed by the front-line healthcare provider in prison clinics.

#### Limitations

The limitation of this report is that the vitamin C, thiamine, folate, Vitamin B12 level and Iron studies were not determined due to the unavailability or cost issues of the test in the country for the admitted patients in HUCSH, and for any of the patients seen in prison as part of the on-site study, CBC was not determined due to financial constraints.

## **Abbreviations**

BID, Twice daily; CBC, Complete blood count; cm, Centimeter; ED, Emergency department; fL, Femtoliter; g/gm, Gram; g/dL, Gram per deciliter; HUCSH, Hawassa University Comprehensive Specialized Hospital; IM, Intramuscular; IRB, Institution review board; IV, Intravenous; MCV, Mean corpuscular volume; mg, Milligram; mL, Milliliter; MRC, Medical Research Council; OPD, Outpatient department; PICT, Provider initiated counseling and testing; PO, per os; RBC, Red blood cell; RDA, recommended daily allowance; RDW, Red cell distribution width; RHZE, Rifampicin-Isoniazid-Pyrazinamide-Ethambutol; SPSS, Statistical Package for Social Sciences; TID, Three times a day; WBC, White blood cell; WHO, World Health Organization.

## **Ethical Issues**

Ethical clearance was obtained from the IRB of HUCSH before the study was conducted. For the cases series in our university hospital the entire patient's written consent which included their consent for the publication of their images was obtained and documented in their medical charts and the participation of the observational study in the prison study was discussed in detail with higher prison officers and head of the Central Hawassa Prison and after we get the green light for the study; the study was voluntary and a written consent which included their consent for the publication of their images was obtained from the prisoners prior to the administration of ascorbic acid and before the prison was screened by the screening tool for the scurvy and each of the patients in the study in the prison has signed on the first page of the screening tool. Ascorbic acid is a vitamin that can be safely administered to all patients. It is non-toxic as long as therapeutic doses of ascorbic acid (Vitamin C). All of the study participants in the case series as well as the prison observational study have given consent regarding publication of this study.

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