# Porotic Hyperostosis and Cribra Orbitalia as Indicators of Nutritional Problems in Ancient Population

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## Abstract

**Background** One of the most studied pathological conditions in human bone remains is porotic hyperostosis and cribra orbitalia, where the condition of porosity or bone tissue is porous and looks like a coral, sieve or sponge-like formation, and is often associated with a history of anemia. nutritional deficiencies, certain diseases and so on. This is often seen in the skull because the bone tries to increase the marrow space available for increased red blood cell formation. Porotic hyperostosis and cribra orbitalia (some paleopathologists put into the same category as porotic hyperostosis) occur due to conditions caused by the body's attempts to produce more red blood cells in the marrow to compensate for iron deficiency. The longer this iron deficiency continues, the more clearly these lesions will form. **Objective** This study was conducted to see the picture of the lesion porotic hyperostosis and criba orbitalia associated with anemia and nutritional deficiencies. **Methods** This study is a case study by observing an intact skull without a mandible, by inspecting the regions of the skull and the roof of the orbit. **Results** Found coral, sieve or spongy formations on the roof of the skull and the roof of the orbit. The presence of a skull lesion can be an indicator of the fragility of an individual's bones. **Conclusion** Anemia and deficiency conditions can result in the formation of lesions in the skull.

***Keywords****: porotic hyperostosis, cribra orbitalia, iron deficiency anemia*

## Background

The study of human physiology that comparing of human health status in the past, aims to understand the pattern of human life so that can be evaluated in the present. A health condition of an individual or population can become a reference in physical anthropology as a new way to interpret human behavior and biocultural adaptations in the past and the present. One of the markers of human health status can appear in individual organs due to stress over a long period of time and a poor health status can affect the human condition, such as skeletal parts. So by analyzing the condition of human skeleton from the remains can be used to observe, predict, and explain the interactions between the human condition and the environment in the past.[1]

Paleopathology is a study to understand the causes, frequency, characteristics, signs, and degrees of disease severity that existed in past populations in the prehistoric era. The study of paleopathology is often used as a measure of the health quality of a population in prehistoric era. Paleopathology can directly study a disease that has emerged and experienced by populations in the past through the discovery of prehistoric human skeletal remains, artifacts, and surviving medical records. Pathological findings of human skeletal remains are usually found in skull bones and teeth. Pathological conditions found in the skull include porotic hyperostosis and cribra orbitalia, while pathological conditions commonly found in dental findings include caries, tooth attrition, periodontitis, antemorthem toothloss, and

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enamel hypoplasia.[2]

Stress and health status that considered in human interaction with the environment can be a guide for interpreting the situation in the past, can be an anticipation for human health and condition for the present and future. The remains of human skeletons can provide very important and in-depth information about activity patterns, diet, demographics, stress and diseases that have been suffered. The human skeletons can provide information about the health status and lifestyle of humans in the past. Health status is most commonly understood as something that can be affected by the history of disease, infection, nutritional status, and psychological factors. Other factors that may affect include an individual or group's access to good sanitation, proper nutrition, malnutrition, and resistance and resistance to stress and disease both genomically and epigenically.[1]

Some studies explained that the etiology of porotic hyperostosis and cribra orbitalia are the presence of pathogenic microorganisms that depend on the source of supply and the content of host's iron. This can be exacerbated by the presence of iron deficiency conditions which are a physiological response that evolves to an increased pathogen load. Therefore iron deficiency is one of the clinical symptoms of anemia caused by nutritional deficiencies.[3]

The the cribra orbitalia has a similar clinical characteristics of porotic hyperostosis, but the difference is that the orbital cribra is present only in the orbital roof. Many researchers treat cribra orbitalia as a symptom resulting from the same etiological and pathological processes as porotic hyperostosis. Iron deficiency anemia does not always result from malnutrition, but can also be caused by conditions of large amounts of blood loss in a short time, pregnancy, growth, menstrual conditions, chronic systemic diseases, poor personal hygiene, vitamin C deficiency, gastrointestinal ulcers, and parasites infection.[4] This study aims to support previous theories about dietary patterns and poor environmental conditions in ancient populations that could lead to anemia and nutritional deficiencies, and to support evidence that severe anemia can result of lesions in the cranium, namely porotic hyperostosis and criba orbitalia.

## Literature Review

Sieve-like porous lesions, identified as porotic hyperostosis in the skull dome and cribra orbitalia on the orbital roof, are generally known having the same haematological process. The process indicates an abnormal demand for a hematopoietic marrow increases, that cause marrow hyperplasia or hypertrophy and the production of red blood cells increases. This overproduction results in an increase in the physical size of the red blood cell production centers. As the marrow space develops, the outer layer of bone becomes very thin, often exposing diploe trabecular bone. Expansion in the trabecular bone (the marrow containing space) exerts pressure on the outer table and eventually expands through it. The resulting exposure of trabecular bone on the outer surface gives a characteristic porous appearance known as porotic hyperostosis and cribra orbitalia lesions.[5]

Porotic hyperostosis and cribra orbitalia are among the pathological lesions most frequently found in ancient human skeletal collections. Since the 1950's, chronic iron deficiency anemia has been widely accepted as a possible cause of both conditions. Based on this proposed etiology, bioarchaeologists use the prevalence of this condition to infer the condition of individuals during their lifetime with iron deficiency, iron malabsorption, and iron loss resulting from diarrheal disease and intestinal parasitic infections in previous human populations. Some evidence suggests that the loss of acceleration and red cell overcompensation seen in hemolytic anemia and megaloblastic anemia are the most likely causes of the discovery of porotic hyperostosis.[3]

Porotic hyperostosis lesions appear as macroscopic porosity on flat bones, especially in the frontal, parietal and occipital bones, where they produce a "coral-like" or "filter-like" shape in the solid bone of cranium.[6] The appearance of the orbital cribra lesion is similar to that of

porotic hyperostosis, but only found on the orbital roof. Many researchers find that cribra orbitalia as a symptom resulting from the aetiology and pathological processes are the same as hyperostosis. Some etiology for both conditions are iron deficiency anemia disease, pathogen resistance, hemolytic anemia, megaloblastic anemia, or other infections.

Anemia is a pathological symptom, not a specific disease, that has literal meaning of "bloodless". Anemia is defined as a pathological deficiency in either the red blood cells or the hemoglobin content. In a healthy homeostatic state, there is a balance between production and lysis of red blood cells in the spinal cord. There are three main causes of anemia, including masive blood loss, erythropoiesis disorders, and increased hemolysis. From an etiological perspective, anemia is divided into genetic and acquired (caused by infectious conditions, malignancy, or deficiency). The prevalence of anemia that is genetically acquired (eg, thalassemia and sicklemia) is less common than the prevalence of acquired anemia caused by excessive blood loss and nutritional deficiencies. The nutrients needed to maintain red blood cell homeostasis include essential amino acids, iron, and vitamins such as A, B12, B6, and folic acid. Iron is a key constituent of hemoglobin and thus iron deficiency is the most common cause of anemia. Although iron deficiency is frequently caused by blood loss, it can be caused by diet with iron deficiency, gastrointestinal iron malabsorption, or any combination of these factors. When the intake or absorption of iron or other essential nutrients is insufficient, red blood cell production is inhibited and can lead to anemia. The body increases its hierarchical response to anemia, shifting to cranial spinal cord expansion and remodeling only after easier measures fail to maintain homeostasis. Red blood cells usually mature over a seven day period and have a life span of about 120 days. The emergence of anemic conditions can cause hemoglobin levels to decrease and the body becomes deprived of oxygen. This hypoxic state triggers the release of erythropoietin, a hormone produced by the kidneys that accelerates the production and maturation of red blood cells.[7]

In chronic anemia, the cytokine response to the underlying condition (eg infection, inflammation or malignancy) occurs, via the anti-erythroprotein effect of tissue necrosis factor α (TFN-α), in suppressed mitotic activity in marrow erythroblasts. The supply of iron to the marrow for hemoglobin synthesis become impaired, resulting in the production of red blood cells with a reduced hemoglobin content (hypochromia). This is not due to iron deficiency stores, but indeed iron stores usually increase in these conditions. Thus, when iron deposits are reduced, iron supply is limited and hypochromic red blood cells are also produced. This is iron deficiency and a result of blood loss and / or a low iron diet. The functional difference between chronic anemia and iron deficiency anemia is that the erythropoietic activity is previously suppressed, whereas in iron deficiency anemia it is increased. However, since the rate of iron supply to stimulated red marrow is limited to iron deficiency, there are too many erythroblasts chasing too little iron. The result of this is that an increasing proportion will fail to make sufficient hemoglobin counts in the time available to become ready-to-function red blood cells; this is crushed in the marrow. In iron deficiency anemia there is a massive increase in intra-medullary ineffective erythropoiesis.[8]

The association between the incidence of porotic hyperostosis and cribra orbitalia with the incidence of iron deficiency is assumed to be the presence of known markers of skeletal conditions with clinically identified cases of hemolytic anemia, particularly sickle cell anemia and thalassemia. The premature destruction of defective red blood cells produced by this genetic condition is a contributing factor to marrow hyperplasia.[5] Anemic conditions can cause disruption of hematopoiesis (production of blood cells) in the trabecular bone marrow of the skull. Porotic hyperostosis was caused by the expansion of the diploë, cranial spongy bone, either due to bone marrow hypertrophy (increased cell size) or hyperplasia (increased cell count). This process is also followed by the formation of an irregular outer cranial table, which is reabsorbed over time, making it thinner and with a visible porous lesion. In the most

severe case ever found, diploë spongy bones can also be seen.[9] Within the cranial dome, diploe expansion occurs by gradually absorbing the outer dome of the skull. This resorption creates a porous formation which gives the hyperostotic porotid lesion that is characteristic of the "sponge" image. In extreme cases of anemia, as seen in the case of thalassemia major, diploe hypertrophy is found to be well beyond the srcinal ectocranial surface to create a palpable upper and distinct "hair-on-end" effect easily observable on radiographs. [6]

Another explanation of iron loss that related to the body's defense process against invading pathogens in the form of cutting iron. When faced with chronic infection and inflammatory conditions, the body's natural response is to place iron-binding proteins at the site of entry of pathogens, reduce the absorption of iron from the gut from food, prevent the release of iron into the blood from storage sites, and bind that which is available. All of these mechanisms serve to inhibit the growth and reproduction of microorganisms, which do not store their own iron stores, and therefore require and obtain it from their hosts. This pathogen has several methods of obtaining iron from the host. They usually produce siderophores, which are iron-binding proteins that extract iron from transferrin in the blood supply, or bind directly with transferrin and other iron-carrying molecules. Some pathogens also break down red blood cells directly. In addition to inflammatory porous skeletal lesions, the porosity observed in the skeletal tissue is due to the formation of new blood vessels to remove blood accumulated along the bone surface. Because these blood vessels penetrate the surface of the cortex of the bone, they can easily be confused with the porotic lesions that are usually associated with anemia.[5]

The general diagnosis of porotic hyperostosis is usually applied to cases of enlarged bone tissue that are porous, which can be caused by several types of systemic disease or lesions. Some diseases modify the cranial periosteum but do not affect the underlying tissue. A common type of pathology of the porotic state in the cranial, is the occurrence of hematopoietic marrow enlargement as a result of anemia, resulting in a visually porous-looking bone condition. This type of porotic hyperostosis usually results from a condition of thinning of the bone in the external lamina and exposure of the diploe, followed by hypertrophic radial growth of the trabeculae. Enlargement of the cancellous bone can eventually create bone thickening in the form of atrophy of the hair-at-ends or comb-like structures.[10]

In addition, pathological conditions caused by inflammatory conditions, such as periostitis, osteitis, and osteomyelitis, exhibit a different microscopic porosity structure than that observed in the appearance of hyperostotic porotic lesions. Because the disease-induced inflammatory response usually results in a combination of bone damage and reactive bone formation in areas of necrotic tissue. The resulting bone pathological condition appears as a rough surface with pitting space and new bone plaque. This is in contrast to porotic hyperostosis, where the remodeling of new bone only occurs with healed pathologies. In this early phase, porotic hyperostosis is triggered by anemia, thus showing a decrease in the structure of the bone marrow module, with the trabeculae occurring tangentially to the outside. After the outer table portion has been eroded, a thin flat squamous plate (osteophyte), in the form of an atrophic trabeculae, can be observed in its initial horizontal alignment. Since this is an early diagnosis of porotic hyperostosis (occurring before extreme hypertrophy) when the new cancellous bone appears as a radially patterned trabeculae - it cannot be mistaken for a pathological state caused by an inflammatory condition. The condition of the trabecular bone in the early stages of this pathological change has not yet formed hypertrophic bone beyond the area previously covered by the outer table, but at a more advanced stage the trabecula experiences a hypertrophic state that is expressed as generalized swelling of the cancellous bone. In addition, the marrow module exhibits a characteristic state, associated with anemia causing porotic hyperostosis, but not usually with pathologies caused by diseases related to the inflammatory response.[10]

Inherited hemoglobinopathy conditions, such as sickle cell anemia and thalassemia, are associated with

the wide range of skeletal anatomical changes found in children. One of the changes observed, which is relevant here, is the expansion of the diploic bone and the thinning of the outer table in the frontal and parietal parts in particular; the occipital are generally spared because of their relatively lower bone marrow content. Such skeletal anatomical changes have also been observed in the previous literature with respect to the condition of iron deficiency anemia and at face value appear to support an association between iron deficiency anemia and subadult bone to skull changes. However, more research needs to be done to refute or support this theory of apparent relationships. In adult humans, at least, there is almost always room for the erythropoietic marrow to accommodate increased erythropoietic activity without disturbing the surrounding bone. Indeed, there is some evidence showing in adults that increased erythropoiesis can be accommodated without the need for physical expansion or changes in the ratio of fat cells. The wider distribution of erythropoietic marrow in children would be more likely to be, as mentioned, less accommodating, although again, more research is needed with respect to deficiency diseases in childhood (eg iron and B12 deficiency) and associated bone changes.[8]

These age-related changes in bone marrow production are supported by the hypothesized association between severe anemia and increased child mortality consistent with bioarcheological studies that show porotic hyperostosis is much more common in pediatric skeletons than in adult skeletons. Although iron deficiency from anemia can also be ruled out on the basis of hematology, the extensive work by researchers seeking to establish a causal link between iron deficiency anemia and porotic hyperostosis clearly has implications for nutritional deficiency of diet and unhealthy living conditions in its etiology. The effects of an inadequate diet, poor sanitation, infectious disease, and related cultural practices during pregnancy and child feeding, provide a plausible explanation for the high prevalence of the prevalent porotic hyperostotic lesion. However, this reason can be debunked by the fact that porotic hyperostosis often occurs in cranial bones that do not have orbital crib lesions. Another possibility that can be presumed is that these two types of lesions reflect changes associated with the locus of the body's hemopoietic response to anemia. Finally, it is possible that the higher off-table remodeling rate of the cranial sac relative to the orbital roof reduces the ability of paleopathologists to identify lesions that are porotic hyperostotic in older individuals.[3]

The apocryphal diagnosis that results from postmortem lesions, hypervascularization and osteitis is also influenced by other factors. Likewise, etiologies other than anemia, scurvy, rickets, hemangiomas and traumatic lesions can produce subperiosteal inflammation or hematoma. During the healing process, these blood clots turn into new, highly vascular, superiosteal bone plaques that on rough examination can appear identical to those of an orbital cribra lesion. Many factors aggravate chronic iron deficiency anemia and megaloblastic anemia, such as prolonged breastfeeding, weaning periods with low-iron cereals, and diarrheal diseases that have a different effect on childhood. [3]

## Methods

This research is a qualitative study with a case study approach, by observing the presence of porotic hyperostosis and cribal orbital in an intact cranium without mandible of an adult human as the study sample (Figure 1). This research was conducted in April 2019 and was carried out at the Ethnography and Anthropology Museum, Master Program of Forensic Sciensic, Faculty of Social and Political Sciences, Universitas Airlangga, Surabaya, Indonesia.

## Results

In the observed cranium, there were found lessions that look alike porosity, sponge, coral-like or filter-like formation in the region of the cranial dome (Figure 2) and in the orbital roof (Figure 3).

**Figure 1. an intact cranium without mandible**

**Figure 2. Porotic hyperostosis in the form of porosity on the cranial dome**

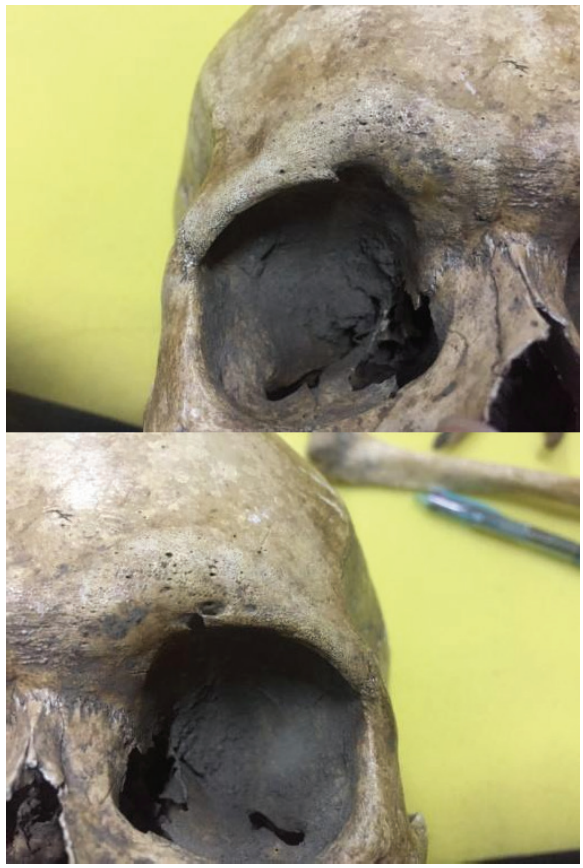

**Figure 3. Cribra orbital in the form of porosity on the roof of the right (top figure) and left (bottom figure )of orbital**

## Discussion

Porotic Hyperostosis and Cribra Orbitalia are the pathological conditions that most frequently found and reported in archaeological collections. This finding is important to assess the general condition or disease of human population in the past.[11] The lesions are the result of pathological conditions, such as anemia, chronic metabolic disease, malignancy, chronic scalp infections, other chronic diseases, infection, or malnutrition.[7] However, the only condition that is found or not present should not be considered as an indication of the health and / or nutritional status of the individual at the age of their death, because healed lesions can occur due to the condition or situation of the individual years before, and the individual. can be in good shape for a long time before dying. As suggested by the paradox theory of osteology, Wood in 1992[12], investigators should be careful when interpreting the indicators of the physiological stress framework, as some may actually indicate a disease,

which has been resolved due to the overall good health status of the individual, and thus shows no weakness.

Hemolytic anemia conditions such as thalassemia or sickle cell anemia (which occurs when red blood cells lysis prematurely) or megaloblastic anemia (resulting from dietary deficiency and malabsorption of folic acid and vitamin B12) are etiologies of porotic hyperostosis which refers to the presence of hemolytic anemia. Chronic hypoferremic (or iron deficiency) is a physiological response to an increased pathogen load, coupled with symptoms of iron deficiency anemia caused by nutritional deficiencies. Several studies have noted that the cases observed by archaeologists of porotic hyperostosis are of increasing frequency, especially in equatorial populations, which may reflect microorganisms that thrive in hot and humid climates. When the body becomes hypoxic, it releases the hormone erythropoietin, which stimulates the acceleration and maturation of red blood cell production. Only if this initial hormonal response fails will the bone marrow go into action to produce more red blood cells. Because the erythropoiesis process is responsible for bone marrow hypertrophy which then manifests as porotic hyperostosis, and because erythropoiesis requires an adequate supply of iron, iron deficiency anemia is effectively associated with reducing the production of mature red blood cells, thereby expanding the hemopoietic marrow that paleopathologists recognize as porotic hyperostosis. and cribra orbitalia. Similar features found in the postmortem skeleton, hypervascularization and osteitis are also influenced by other factors. Likewise, etiologies apart from anemia, other factors such as scurvy, rickets, hemangiomas and traumatic lesions can also cause subperiosteal inflammation or hematoma. Study by Walker *et al* in 2009 [3] reported that during the healing process, this blood clot transformed into a new, highly vascular, superiosteal bone plaque which on rough examination may appear identical to the orbital cribra. Many factors aggravate chronic iron deficiency anemia and megaloblastic anemia, such as long breastfeeding periods, weaning periods on cereals with low iron content, and diarrheal diseases that will have different effects on childhood health, especially those related to the condition.

Porotic hyperostosis in adults is most likely a lesion that heals from marrow hyperplasia that previously occurred during childhood, this is because children have bone plasticity and iron requirements are greater than adults. However, apart from that, anemia persisted in some adults, because the lesions in this case remained active and occurred until the death of the individual.[13]

## Conclusion

Porotic hyperostosis and cribra orbitalia are the common lesions that are identified on human bones and a are result from thickening of the skull diplo in response to spinal hypertrophy, resulting in thinning and porosity of the outer part of the bone. These lesions were commonly used as indicators of the health, nutritional status, and anemia evidence of the ancient human population. Knowing the condition of an individual or a group through findings on the remains of a human skeleton can improve our understanding of the etiological, pathophysiological and physical manifestations of the skeleton with the living conditions of the past individual or group health. The result study can be a guide to overcoming the health problems for human life in the present and in the future.

**Ethical Clearance:** The academic institute declared there is no need an ethical clearance for studies that including media collections in laboratory and the action during research was a low risk/no cause a harm to the sample. The sample had been already got a prior approval by the academic institute.

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**Conflict of Interest:** There is no conflict interest in this study

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