



# A Literature Review: Understanding TNF and IL-1 of the Main Cause of Thrombo-occlusive in Lucio's Phenomenon

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## ABSTRACT

Last year, it was 0.5 out of every 10,000 people, but now it has increased. Lucio's Leprosy, also known as Leprosy Bonita, is a very uncommon type of serious leprosy. The Lucio phenomenon is a severe reaction that can occur in individuals with Lucio's leprosy. It causes a skin condition called "necrotizing erythema". This study used reliable and important scientific databases like PubMed, ScienceDirect, Google Scholar, as well as official databases from health organizations. These reactions occur in the cells of body's immune system, specifically the T helper 1 cells, in response to antigens from mycobacteria. Research has shown that certain substances produced by Th1 cells, such as IL-1 $\beta$ , TNF- $\alpha$ , IL-2, and IFN- $\gamma$ , are very important. High amounts of TNF- $\alpha$ , soluble IL-2 receptors, and adhesion molecules show how serious the local inflammation is. Patients with a mild form of leprosy who are experiencing a specific type of immune response have higher levels of a molecule called TNF- $\alpha$  in their nerves and skin. Type 1 reactions are caused by certain types of immune cells called Th1 lymphocytes. The WHO said it's important to make sure patients and communities know about leprosy so they can get help on their own. They think this is a very important part of their plan to fight leprosy worldwide.

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## 1. INTRODUCTION

According to the Ministry of Health (Kemenkes), there is 0.55 leprosy cases for every 10,000 people in Indonesia in 2022. This is more common now than last year. Last year, it was 0.5 out of every 10,000 people, but now it has increased. Lucio's Leprosy, also known as Leprosy Bonita, is a very uncommon type of serious leprosy. The Lucio phenomenon is a severe reaction that can occur in individuals with Lucio's leprosy. It causes a skin condition called "necrotizing erythema" (1,2).

In Indonesia, the number of new leprosy cases identified in 2021 reached 10976 cases, as stated by the World Health Organization (WHO). Compared to the 75,394 cases in India and 18,318 cases in Brazil, this discovery demonstrates a notably lesser number of cases.

The available information about Lucio's leprosy and its association with the Lucio phenomenon is limited and not well-documented. The precise number of deaths or illnesses resulting from this disease remains unknown as a consequence. This report mainly comes from Mexico and Costa Rica. There have been a few cases reported in Brazil, Argentina, India, and Singapore. The first reported case of the Lucio phenomenon in Malaysia happened in 2009. Out of three patients, one died from the disease (3).

Leprosy with diffuse lepromatous type was found in Brazil in 1844 by Ladislao de la Pascua. This type of leprosy has sores on the skin of both legs that are spread out and not clearly defined. The sores also cause damage to the skin tissue because of multiple necrotic cells. Lucio and Alvredo also discussed about a similar situation in the year 1852. This text discusses a form of leprosy known as diffuse lepromatous leprosy or Lucio's leprosy. A few doctor found a connection between this illness and a newly found type of organism called M. Lepromatosis is a medical condition. Historically, the Lucio phenomenon resulted in numerous fatalities in numerous instances. To fully comprehend the lucio phenomenon, it is crucial to have a comprehensive understanding of the workings of TNF and IL-1. In this literature review, the author will explore the effects of TNF and IL-1 on the Lucio phenomenon (3,4).

## 2. METHODOLOGY

This research collected and analyzed information from different sources of literature about understanding TNF and IL-1 of the main cause of thrombo-occlusive in Lucio's Phenomenon used a method called literature review to do this. The method was chosen because it allows us to find, put together, and analyze different research findings in order to give a comprehensive and detailed overview of the research topic. This study used reliable and important scientific databases like PubMed, ScienceDirect, Google Scholar, as well as official databases from health organizations. We choose this database to make sure that the information we used for our research was valid and correct.

We set up certain detailed rules to decide which studies are relevant for this research topic. The inclusion criteria for this study were focused on understanding TNF and IL-1 of the main cause of thrombo-occlusive in Lucio's Phenomenon. The study only included research articles written in either Indonesian or English. Meanwhile, the exclusion criteria were studies that were not related to the research topic, did not have enough data, or focused on different types of risk factors. Information by searching for certain words like "TNF and IL-1 in Lucio's Phenomenon", "thrombo-occlusive in Lucio's Phenomenon", "TNF and IL-1 of the main cause of thrombo-occlusive" and so on. We searched for literature in a careful and thorough way to find all the necessary studies.

After looking at the title and summary of the study, a selection process was done to make sure the study fit the requirements. The studies that fit the requirements will be found and reviewed further. To analyze the data, we collected information from important studies and showed it in tables or summaries of the exact words and ideas from those studies. Different information will be brought together and studied to provide clear and complete results about TNF and IL-1 of the main cause of thrombo-occlusive in Lucio's Phenomenon.

This study aims to use a method called literature review to provide accurate and clear results about the connection between understanding TNF and IL-1 of the main cause of thrombo-occlusive in Lucio's Phenomenon. This research wants to find out how TNF and IL-1 are related to the main cause of thrombo-occlusion in Lucio's Phenomenon. They are going to use a method called literature review to give accurate and clear results. Through this method, the fair examination of important research allows for a thorough comprehension of the primary cause of blood clotting in Lucio's Phenomenon, which is TNF and IL-1.

## 3. RESULTS AND DISCUSSION

Diffuse lepromatous leprosy was first identified in 1844 by Ladislao de la Pascua in Brazil. This type of leprosy causes sores on the legs that blend together and hurt the skin. Lucio and Alvredo found a similar case in 1852. This type of leprosy is also called Lucio's leprosy. This disease is thought to be caused by a recently identified species known as *M. lepromatosis*, according to certain scientists. Lepromatosis is a type of medical condition. This type of leprosy can make the skin on the face look smooth and shiny. There are no red spots or lumps, and no lines on the skin. In Spanish, it is called "Lepra Bonita" which means "beautiful leprosy". Apart from that, you may also experience classic signs of losing eyebrows and eyelashes. Peripheral neuropathy and destructive rhinitis frequently happen. The skin on the face and earlobes gets thicker, and the skin overall looks swollen and wet. However, patient might not see any skin bumps. During the operation, the surgeon will open the patient's stomach and extract the organ that is indicated. The incision will then be stitched up using sutures. The patient will be given anesthesia to ensure they do not feel any pain during the surgery. After the procedure, the patient will be monitored closely to ensure they are recovering well and to manage any potential complications. (3,4,5,6)

Because there are no superficial abnormalities on the skin, making a diagnosis of Lucio leprosy requires caution. Generally, patients seek treatment after skin abnormalities manifest as many necrotic sores on both legs. It is difficult to assess the presence of numb areas since they are hidden by wounds, especially if there is a secondary infection. Lucio's leprosy is characterised by an uncommon, violent, and occasionally fatal type 2 necrotization reaction (3,4,5).

However, the reaction is frequently classified as a type 3 leprosy reaction or a very severe leprosy reaction (7). The occurrence of this reaction is observed in leprosy cases that have not been cured previously. This is related to a large amount of cell death in small blood vessels caused by an invasion of *M. bacteria*. The bacteria called leprae, can be found in large amounts in the cells on the surface of blood vessels. This discovery might be the reason for the serious problems with blood vessels that happen during the reactive phase. The inflammation of blood vessels in the body and the formation of blood clots in both surface and deep vessels can lead to bleeding and the development of necrotic skin tissue (8).

The Lucio phenomenon is when people get painful sores on their legs that can recurrent and again for 2 months to 10 years. The clinical manifestation such as pink patches on the skin that are spread out and have an irregular shape. These patches can be painful. Injuries, especially in the arms or legs, then move to other parts of the body. Severe sores look reddish and have purple spots. They can also have blisters, and then turn into dead tissue and painful sores quickly. The healing process of the cut requires a significant duration and eventually results in the formation of a scar (3,4,5).

Vasculonecrotic erythema nodosum, systemic vasculitis, disseminated intravascular coagulation, TB cutis, deep mycoses, and tertiary syphilis are among the differential diagnosis (5).

These reactions occur in the cells of body's immune system, specifically the T helper 1 cells, in response to antigens from mycobacteria. Research has shown that certain substances produced by Th1 cells, such as IL-1 $\beta$ , TNF- $\alpha$ , IL-2, and IFN- $\gamma$ , are very important. High amounts of TNF- $\alpha$ , soluble IL-2 receptors, and adhesion molecules show how serious the local inflammation is. Patients with a mild form of leprosy who are experiencing a specific type of immune response have higher levels of a molecule called TNF- $\alpha$  in their nerves and skin. Type 1 reactions are caused by certain types of immune cells called Th1 lymphocytes. These cells release substances called proinflammatory cytokines, like IFN- $\gamma$  and IL-12, as well as harmful molecules called free oxygen radicals. Researchers have proven that inflammation can be initiated in nerves by macrophages, even without the presence of bacteria (18).

Fever, splenomegaly, swollen lymph nodes, kidney inflammation, small red blood cells, low albumin levels in the blood, abnormal immune response, and low calcium levels have been found to occur together in the Lucio phenomenon. The Lucio phenomenon is hard to tell apart from vasculonecrotic erythema nodosum leprosum (ENL). This looks like a painful sore with tissue necrotic, and it can cause overall symptoms, nerve inflammation, and sometimes affects internal organs. However, the specific signs and physical features can be used to tell the difference between the two. The ENL reaction is different from the Lucio phenomenon. In ENL, the necrotic area is only found where there are nodules. But in the Lucio phenomenon, necrotic lesions can show up anywhere, even without nodules. And these lesions do not get better with Thalidomide treatment (9).

Although the exact cause of the Lucio phenomenon remains unclear, thrombosis, the obstruction of blood vessels, is widely deemed as the main factor by most experts. The main idea is that certain parts of bacteria can make immune cells release specific substances. This product helps endothelial cells make prostaglandins, TNF, IL-6, and coagulation factor III. This makes blood clots form in blood vessels, which can lead to tissue death. This meant that something was blocking the blood flow, and the two big toes looked dead. The CT-Angiography test did not find any narrowing in the arteries of the legs. Nevertheless, it is crucial to acknowledge that this test exhibits greater efficacy in identifying issues within larger blood vessels (7).

The research findings on tissue samples indicate that Lucio's Leprosy arises from the intrusion of *Mycobacterium leprae* bacteria into the cells lining the blood vessels, leading to vascular complications. Bacteria that can get inside the endothelial cells can cause changes in the cells, like making them bigger, growing more, and causing swelling. This makes the walls of the blood vessels thicker. It also causes new blood vessels to form and makes the blood clot more easily, which can lead to blood clots. These changes are common in Lucio's Leprosy (10,11).

The term "Lucio phenomenon" should strictly be used when there is a correlation between clinical and anatomic findings and in accordance with strict clinical criteria. The predilection of the diffuse lesion in the Lucio phenomenon is mainly extremities, which may include nodules and heal with atrophic stellate scars (12).

The number of patients detected with leprosy before manifesting Lucio phenomenon symptoms was only four out of the total 30 individuals analyzed by Rea and Jerskey. This condition may not be easily noticed because it is rare in countries where it is not common, and it is similar to other symptoms of rheumatic disease and inflammation of blood vessels caused by other factors. A study in Malaysia found that between 2008 and 2013, 44% of patients in primary care were diagnosed incorrectly. This was despite the patient having common signs of madarosis (eyelash loss), thickened earlobes, and nails falling off. Being educated is very important for health professionals because the World Health Organization has identified leprosy as a neglected tropical disease (12,13,14,15).

Leprosy can cause people to lose their eyebrows and eyelashes, and rarely their body and scalp hair. Their facial skin and earlobes can become thickened, and their skin may have a waxy appearance. They may also experience peripheral neuropathy and nose problems. In countries where leprosy is not common, people usually have painless ulcers that get worse over time and may have other symptoms throughout their bodies. It has been reported that the Lucio phenomenon often occurs 1 to 3 years after the disease shows up.(11,12) Patients only realize they are sick when more obvious symptoms of the Lucio phenomenon appear. The WHO said it's important to make sure patients and communities know about leprosy so they can get help on their own. They think this is a very important part of their plan to fight leprosy worldwide (15).

#### 4. CONCLUSION

The available information about Lucio's leprosy and its association with the Lucio phenomenon is limited and not well-documented. The precise number of deaths or illnesses resulting from this disease remains unknown as a consequence. This news mainly comes from Mexico and Costa Rica. There have been a few cases reported in Brazil, Argentina, India, and Singapore.

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