



## **The Role of Chronic Inflammation in Stunting: A Systematic Literature Review**

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### **A B S T R A C T**

Chronic inflammation can overactivate the body's immune system, causing excessive release of cytokines and inflammatory substances. This can affect the balance between the inflammatory response and the immune response, so that the immune system may be more focused on fighting inflammation rather than protecting the body from infection. Chronic inflammation can disrupt the body's growth pathways. Some molecules involved in the growth process, such as growth hormone, can be disrupted by inflammation. Additionally, inflammation can affect the development of the body's organs, tissues, and cells in ways that inhibit linear growth. This study aims to explore the role of chronic inflammation in the incidence of stunting. The literature search process was carried out on various databases (PubMed, Web of Sciences, EMBASE, Cochrane Libraries, and Google Scholar) regarding the role of chronic inflammation in the incidence of stunting. This study follows the preferred reporting items for systematic reviews and meta-analysis (PRISMA) recommendations. Chronic inflammation plays an important role in the occurrence of stunting in children. Chronic inflammation can influence various aspects that contribute to the growth and development of children's bodies, including nutrient absorption, growth hormone regulation, nutrient metabolism, and immune system function. This can result in stunted child growth, malnutrition, weight loss, and negative impacts on child well-being.

### **1. Introduction**

Stunting, or stunted growth, is a global health problem that has a significant impact on the well-being of children around the world. This refers to a condition where children have a shorter height than should be appropriate for their age. Stunting is not just a physical problem, it also has a serious impact on an individual's cognitive development, long-term health and productivity as they mature. In recent decades, medical research has revealed that chronic inflammation, namely a sustained and excessive inflammatory response in the body, can play an important role in the development of stunting. Chronic inflammation refers to inflammation that lasts for a long period of time and tends to occur continuously.

Factors that trigger chronic inflammation, such as repeated infections, exposure to toxic substances, or lack of nutrition, can have a negative impact on children's growth and development.<sup>1,2</sup>

Chronic inflammation can interfere with nutrient absorption in the intestine. An ongoing inflammatory process can damage the intestinal wall, reduce the surface area for nutrient absorption, and disrupt nutrient transport to body cells. This results in children having difficulty getting the nutrition needed for optimal growth. Chronic inflammation can overactivate the body's immune system, causing excessive release of cytokines and inflammatory substances. This can affect the balance between the inflammatory response and the immune response so

that the immune system may be more focused on fighting inflammation rather than protecting the body from infection. Chronic inflammation can disrupt the body's growth pathways. Some molecules involved in the growth process, such as growth hormone, can be disrupted by inflammation. Additionally, inflammation can affect the development of the body's organs, tissues, and cells in ways that inhibit linear growth.<sup>3-6</sup> This study aims to explore the role of chronic inflammation in the incidence of stunting.

**2. Methods**

The literature search process was carried out on various databases (PubMed, Web of Sciences, EMBASE, Cochrane Libraries, and Google Scholar) regarding the role of chronic inflammation on the incidence of stunting. The search was performed using

the terms: (1) "infection" OR "inflammatory" OR "Inflammation" OR "stunting" AND (2) "stunting" OR "inflammatory." The literature is limited to clinical studies and published in English. The literature selection criteria are articles published in the form of original articles about the role of chronic inflammation on the incidence of stunting. Studies were conducted in a timeframe from 2013-2023, and the main outcome was the role of chronic inflammation on the incidence of stunting. Meanwhile, the exclusion criteria were studies that were not related to the role of chronic inflammation on the incidence of stunting, the absence of a control group, and duplication of publications. This study follows the preferred reporting items for systematic reviews and meta-analysis (PRISMA) recommendations.

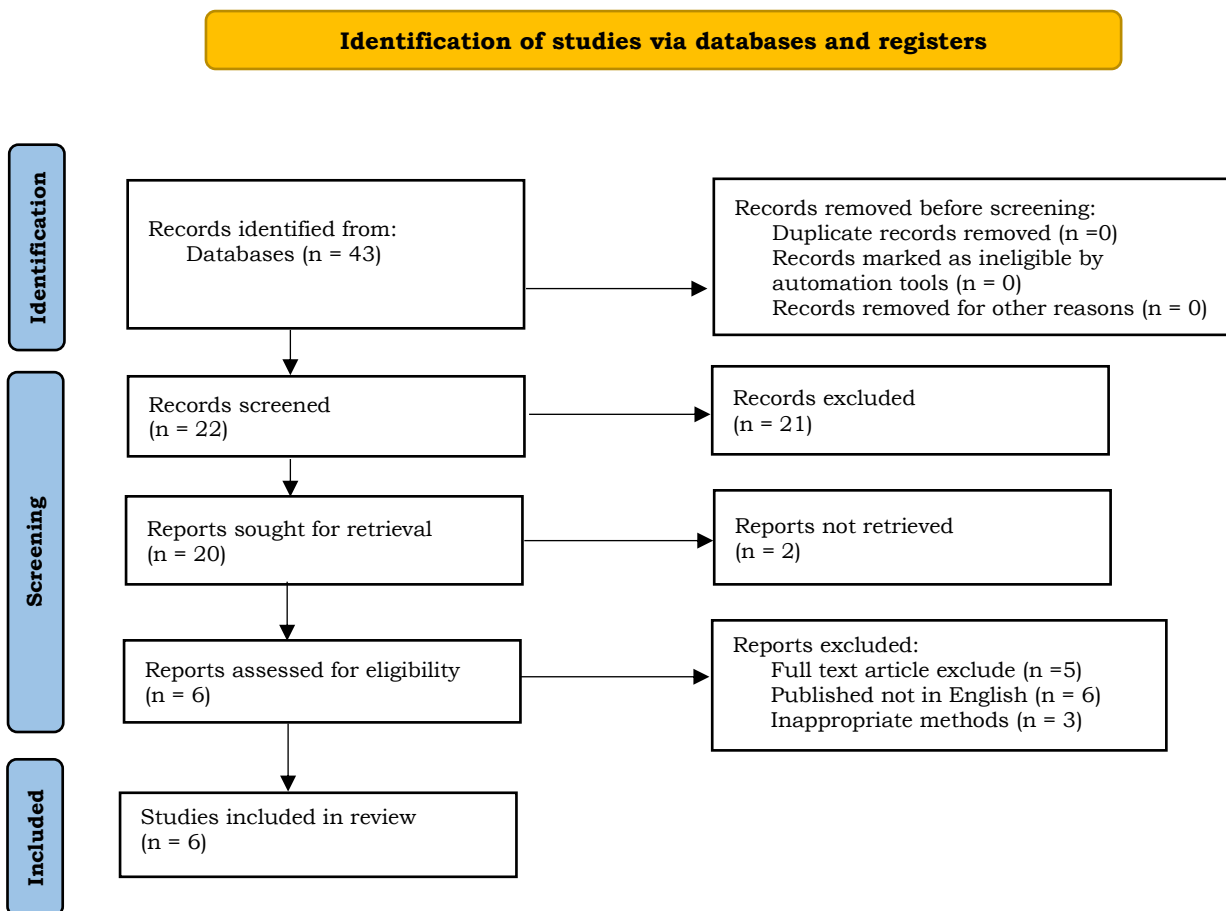


Figure 1. PRISMA flowchart.

### 3. Results and Discussion

#### Disorders of nutrient absorption

Chronic inflammation can result in pathological changes in the intestinal wall, involving damage to the microvilli, which are small structures on the surface of the intestine that play an important role in nutrient absorption. Chronic inflammation can damage and disrupt the microvilli, and this has several consequences that impact the gut's ability to absorb nutrients efficiently. Chronic inflammation can cause physical damage to the microvilli located on the surface of intestinal cells. Microvilli are responsible for increasing the intestinal absorptive surface area so that they can absorb nutrients from the food consumed. Damage to microvilli can reduce this surface area, which in turn limits the ability of the intestines to absorb nutrients. By reducing the intestinal absorption surface area due to damage to the microvilli, the intestine will be able to absorb nutrients in more limited quantities. Nutrients that are not absorbed efficiently will pass through the digestive system and then be excreted from the body through feces. Conditions, where the intestines have damaged or disturbed microvilli, will make it difficult for children to get the nutrients needed for their optimal growth and development. Important nutrients such as protein, vitamins, minerals, and carbohydrates may not be absorbed properly. Therefore, microvilli damage is one mechanism that explains why chronic inflammation can lead to nutritional deficiencies in children, which in turn can contribute to stunting.<sup>7-10</sup>

Continuous inflammation can cause villus atrophy, which is a decrease in the length and area of the microvilli on the intestinal wall. Villus atrophy is one of the pathological changes that occur in the intestine in response to chronic inflammation. Villus atrophy can have several important consequences that affect nutrient absorption in the intestine. Microvilli function to expand the absorption surface area of the intestinal wall. When microvilli atrophy, this surface area becomes smaller, meaning the area available for nutrient absorption becomes limited. This reduces the ability of the intestines to absorb nutrients from the food consumed. Because villus atrophy reduces the

intestine's ability to absorb nutrients efficiently, nutrients present in food may not be absorbed properly. This results in reduced nutritional intake necessary for children's growth and development. When nutrient absorption is impaired due to villus atrophy, children become more susceptible to malnutrition. This can cause various nutritional deficiencies, which can worsen stunting.<sup>11,12</sup>

Chronic inflammation can also affect nutrient transport in the body, which can negatively impact nutrient absorption. Continuous inflammation can disrupt the transportation process of nutrition from the digestive tract into the blood circulation, and this prevents nutrients from reaching the body's cells efficiently. Inflammation can disrupt the activity of nutrient transporters in intestinal cells. These transporters are responsible for transporting nutrients across intestinal cell membranes and moving them into the blood circulation. Inflammation can disrupt the function of these transporters so that nutrients cannot be absorbed efficiently. Inflammation can cause damage to the blood vessels that supply the intestines. This can inhibit blood flow to the intestines, which in turn can reduce the supply of nutrients and oxygen to intestinal cells. As a result, the intestines may not be able to absorb nutrients properly. Inflammation can disrupt nutrient metabolism in the body. This can change how the body processes and uses nutrients. For example, inflammation can increase the use of nutrients to combat inflammation, meaning those nutrients are no longer available for the body's growth and development. As a result, inflammation influences Nutrient transport can contribute to nutritional deficiencies and stunting. Children who experience chronic inflammation may have difficulty getting the nutrition needed for optimal body growth.<sup>13,14</sup>

Chronic inflammation can influence the composition of the gut microbiota, namely the community of microorganisms that live in the digestive tract. Changes in the composition of the gut microbiota can have significant consequences on health and nutrient absorption. Chronic inflammation can trigger changes in the type and abundance of

microorganisms that inhabit the intestine. This can disrupt the normal balance between the various species of microorganisms in the gut. Several microorganisms in the intestine have an important role in producing substances that help in the absorption of nutrients, such as short-chain fatty acids. Inflammation can reduce the number of these microorganisms, which in turn can interfere with the body's ability to get the nutrients it needs. A disturbed balance in the composition of the intestinal microbiota can cause changes in the fermentation processes that occur in the intestine. This can alter nutrient metabolism, reducing the production of compounds that support nutrient absorption. Chronic inflammation can disrupt the function of the normal intestinal barrier, which separates microorganisms in the intestine from body tissues. This may allow bacteria or products of microorganisms to pass through this barrier and trigger a further inflammatory response. As a result, changes in the composition of the gut microbiota caused by chronic inflammation can be seen to influence the body's ability to obtain nutrients from food efficiently. This can contribute to malnutrition and stunting in children.<sup>15</sup>

### **Disorders of immune system function**

Cytokines are molecules that function as messages between immune cells and play a role in coordinating the body's response to infection, inflammation, and other factors that affect the balance of the immune system. In chronic inflammatory conditions, the immune system can produce and release excessive amounts of cytokines, which can trigger inflammation that lasts for a long time and has the potential to be detrimental to health. Excessive release of cytokines can result in persistent inflammation and can cause tissue damage and an imbalance in the body's immune response. Understanding the role of cytokines in chronic inflammatory processes is important in treating and controlling this condition, especially in the context of stunting problems in children. In an effort to prevent and overcome stunting caused by chronic inflammation, controlling cytokines and

inflammation are aspects that must be considered and intervened.<sup>16</sup>

A healthy immune system works in fine balance, allowing for a timely and efficient immune response to infections, while protecting the body from damage caused by excessive inflammation. When the immune system is more focused on fighting inflammation, the body becomes more susceptible to infection. The immune response to pathogens and infections may become weakened, which can lead to recurrent or more frequent infections. In the case of chronic inflammation, the body may not be able to control or stop the inflammation efficiently. This results in continued and ongoing inflammation, which can damage body tissue and disrupt the normal function of organs and systems. In the context of stunting in children, an imbalance in the immune response can lead to nutritional deficiencies and stunted growth. Over time, this condition can have serious impacts on a child's health and development. Efforts to prevent and treat chronic inflammation must consider the appropriate balance of immune response and inflammation. This involves controlling chronic inflammation, restoring normal function of the immune system, and paying special attention to infection prevention.<sup>17</sup>

Excessive activation of the immune system in the context of chronic inflammation can negatively impact the body's ability to fight infection. This can occur because ongoing inflammation can disrupt several key aspects of the body's immune response, including the production of antibodies and important immune cells. Chronic inflammation can inhibit the production of antibodies by B cells in the immune system. Antibodies are important in fighting infection, and the body's inability to produce enough antibodies can increase susceptibility to infection. Chronic inflammation can also disrupt the function of immune cells, such as T cells and phagocytic cells. This can reduce the body's ability to detect, fight, and clear pathogens that enter the body. Ongoing inflammation can stress the immune system and disrupt the balance of the immune response. This can result in compromised and detrimental immune responses. As a result, although the body may experience excessive

activation of the immune system in response to chronic inflammation, the body's ability to fight infection and maintain immune health may be compromised. Therefore, it is important to understand the complexity of the relationship between chronic inflammation, immune response, and infection in the context of stunting, and to take appropriate steps to control inflammation, restore balance to the immune response, and support children's growth and health.<sup>18</sup>

Chronic inflammation can alter aspects of the body's metabolism, including nutrient use. In the context of chronic inflammation, there is an imbalance in the use of nutrients by the immune system and the body itself. This can have a significant impact on children's growth and well-being. In chronic inflammatory situations, the immune system often uses nutrients, especially protein and energy, to support a sustained immune response. This can cause a reduction in the availability of nutrients that should be used for body growth and development. Chronic inflammation can disrupt energy metabolism in the body, which can result in increased energy use for inflammation and disrupt the balance between energy intake and use. This can cause weight loss and lack of energy. Chronic inflammatory conditions can cause an imbalance in the nutritional intake needed for children's growth and health. Certain nutrients, such as vitamins and minerals, may be used by the immune system in greater amounts than intended. Some nutrients, such as antioxidants, can be used to help fight inflammation in the body. If the body experiences chronic inflammation, this can result in reduced nutrients available to support growth and development.<sup>16-18</sup>

### **Disorders of the body's growth process**

Chronic inflammation can interfere with the regulation of growth hormone, which is one of the key hormones in regulating body growth. Growth hormone, which is produced by the pituitary gland in the brain, plays an important role in regulating the growth, development, and regeneration of body tissue. Chronic inflammation can affect growth hormone production or inhibit the body's tissue response to this hormone in several ways. Chronic inflammation can

affect the pituitary gland in the brain, where growth hormone is produced. This can reduce the production of growth hormone, which in turn can stunt the child's growth. Inflammation can interfere with the body's tissue's ability to respond to existing growth hormones. This can reduce the effectiveness of existing growth hormones in triggering the growth and development of body tissue. In chronic inflammatory situations, the body may produce inflammatory hormones such as interleukin-6 (IL-6) which can inhibit the growth hormone response and suppress growth. All of this contributes to stunting, which is a condition where children's growth is stunted. In the case of stunting caused by chronic inflammation, controlling inflammation and restoring growth hormone regulation becomes very important in efforts to promote optimal child growth.<sup>17-19</sup>

Chronic inflammation can trigger catabolic processes in the body, which is basically the process of breaking down body tissue, especially protein, to meet the increased energy needs during inflammation. In chronic inflammatory situations, the body often requires more energy to support the inflammatory response and additional work of the immune system. Catabolic processes can result in the breakdown of muscle proteins, which reduces muscle mass. This can hinder the growth and physical development of children. Catabolic processes can also lead to weight loss and loss of body mass, which can negatively impact a child's health and development. Catabolic processes may lead to an imbalance in nutrient utilization, with nutrients used to meet additional energy requirements rather than for growth and development. Apart from muscle, catabolism can also influence other tissues in the body, including organ tissue. This can hinder the development of organs and body systems. To overcome the impact of catabolism caused by chronic inflammation on children's growth, it is important to control the inflammation itself and ensure an adequate supply of nutrients. Appropriate nutrition is key to supporting children with chronic inflammation so that they can achieve optimal growth and physical development.<sup>18-20</sup>

#### 4. Conclusion

Chronic inflammation plays an important role in the occurrence of stunting in children. Chronic inflammation can influence various aspects that contribute to the growth and development of children's bodies, including nutrient absorption, growth hormone regulation, nutrient metabolism, and immune system function. This can result in stunted child growth, malnutrition, weight loss, and negative impacts on child well-being.

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