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# The Vicious Cycle of Malnutrition and Childhood Infections – What are the policy implications?

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**Abstract**

*Malnutrition refers to a deficiency or imbalance in the intake of energy and nutrients and is an underpinning factor for child mortality in developing countries. Undernutrition predisposes children to repeated infections, increases the severity and delays recovery from illness. In addition, repeated infections deplete patients of valuable micronutrients required for functioning of acquired and innate immunity. The integrity of natural protective mechanisms such as naso-oesophageal linings, gastrointestinal and genito-urinary tracts may also be affected. These children frequently have bacterial overgrowth in their small bowel as well as insidious infections. Undernutrition therefore creates a potentially lethal cycle of prolonged illness and deteriorating nutritional status which predisposes to further infection. The policy implication of this negative synergism is that suspected infections in malnourished children should be promptly and effectively treated with antibiotics. This strategy will disrupt the vicious cycle and contribute towards reduction of mortality in children.*

**Keywords:** *Malnutrition, infections, children*

## Introduction

Malnutrition is the failure of the body to get appropriate amounts of nutrients to maintain healthy tissues and organ function [1]. Whether acute or chronic, malnutrition conventionally indicates a state of deficiency of energy, protein and other nutrients or an excess of these nutrients in other cases. Severe acute malnutrition (SAM) is a medical emergency because it accounts for a higher burden of mortality in young children especially those less than 5 years. It is classified as "complicated" if there are clinical features of infection, metabolic disturbance, severe oedema or poor appetite, and "uncomplicated" if the patient is clinically well, alert with appetite retained [2]. Although malnutrition refers to both states of under and over-nutrition, this review will focus on states of undernutrition and use the term interchangeably with malnutrition.

Worldwide, malnutrition affects about 852 million people with 815 million living in developing countries [3]. Nearly half of deaths in children under 5 years are attributable to malnutrition which translates to preventable loss of about 3 million young lives a year. Undernutrition not only puts children at risk of dying from common infections, but also increases the frequency and severity of such infections thereby contributing to delayed recovery. In addition, the interaction between undernutrition and infection can create a potentially lethal cycle of worsening illness, deteriorating nutritional status and repeated infections.

Since infections are ubiquitous in developing countries, the convergence of malnutrition and infectious diseases results in high morbidity and mortality in children[4].

The goal of this article is to explore the plausible link between infection and malnutrition and the effect of the synergism of these factors in child health.

## Impact of Malnutrition on the Pathogenesis of Infections

Host defence mechanisms depend upon the activities of white blood cells to function. In severely malnourished children host defence mechanisms, both acquired (lymphocyte functions) and innate (macrophages and granulocytes) are affected. Diminished immune functions render malnourished children more susceptible to infections, notably by opportunistic pathogens commonly prevalent in patients with HIV/AIDS and in other immunocompromised states [5]. Multiple immune system abnormalities including lymphoid organ and thymic atrophy, preformed T-cell deficiency, altered ratio of T-cell subsets, decreased natural killer (NK) cell activity and cytokine production are noted in malnourished children. In addition, there is decreased T-cell function and the ability of lymphocytes to respond appropriately to cytokines. In essence, both acquired immunity and innate host defences are compromised by malnutrition [6].

Innate immunity comes first in the defence against pathogens but if the infection is not cleared, the adaptive immune responses are activated. Innate immune defences allude to macrophages, monocytes and neutrophils that function without requiring exposure to a specific antigen. Whereas, the acquired immune system develops in response to specific antigens and pathogens; exhibit memory qualities and rapidly responds if the same antigen is encountered in the host's lifetime [6]. The combination of these two different but complementary systems defends the host against infections.

For the body to effectively fight infections, protective mechanisms such as intact skin surface and naso-oesopharyngeal linings, gastrointestinal and genito-urinary tracts are necessary to provide a barrier to invasion. In addition, the epithelial lining should have capability to produce mucous secretions. In order for the body to mount an adequate protective response against infection, a range of nutrients are needed [7]. These include antioxidant enzymes with iron, zinc, copper, manganese, and selenium and antioxidant vitamins such as vitamin E and vitamin C. In malnutrition, especially SAM, varying degrees of mucous membrane disruptions, abnormalities in protective secretions and nutrient deficiencies are observed, thus making the malnourished child prone to infections which could be very severe and life threatening. Furthermore, SAM predisposes to gastrointestinal and respiratory infections. The first line of defence against these types of infections is the innate immune response, particularly epithelial barriers and the mucosal immune response. Defects in mucous membrane barriers are critical in the pathogenesis of respiratory and gastrointestinal tract infection; SAM severely compromises mucosal epithelial barriers in the gastrointestinal, respiratory and urogenital tracts [6,8]. A plausible explanation for this is the loss of protective intestinal barrier which increases susceptibility to infection by pathogens that normally would be trapped and cleared away by the mucus produced by the epithelial lining.

## Impact of Infectious States on Malnutrition

While malnutrition can predispose to infection or increase its severity, infectious states could also contribute to malnutrition through several mechanisms. For example, a gastrointestinal infection can cause prolonged diarrhoea leading to loss of nutrients and consequently malnutrition. HIV/AIDS, tuberculosis and other chronic infections can cause cachexia and anaemia potentiating undernutrition while intestinal parasites cause anemia and nutrient deprivation [5]. Immune response stimulation by infection increases the metabolic demands for energy and associated substrates, leading over time to adverse nutritional status and increased susceptibility to further infection [5].

Infections can also alter the nutritional status, mediated by changes in dietary intake, absorption, nutrient requirements and loss of endogenous nutrients. A metabolic consequence of infection is a decrease in serum iron, zinc and vitamin A [7]. Gastrointestinal and respiratory tract infections have also been shown to cause malnutrition by causing a deficit in crucial body supplies of protein, energy, minerals and vitamins [8].

The first line of defence against gastrointestinal and respiratory infections is the innate immune response, particularly epithelial barriers and the immune response [8]. These infections might cause anorexia, malabsorption, intestinal damage, diarrhoea, excess protein catabolism, increased metabolic rate, redistribution of nutrients and activation of inflammatory and/or immune responses. The consequences are reduced nutrient intake, reduced nutrient absorption, nutrient losses, and increased nutrient requirement [7,9].

Micronutrient deficiencies are therefore major complications of SAM, which in a cyclical manner, promotes infections and diseases. Additionally, if micronutrients are deficient in infectious states, oxidative stress is worsened. Micronutrients such as vitamin A, β carotene, folic acid, vitamin B12, vitamin C, riboflavin, iron, zinc and selenium have immuno-modulating functions and influence both the susceptibility of the host to infections as well as the clinical course and outcome of disease [10].

## The Vicious Cycle – A Negative Synergism

Given the interaction between infection and malnutrition, all possible measures should be undertaken to break the negative synergism and the vicious cycle of infections leading to loss of nutrients and malnutrition which further predisposes to infections (see figure 1).

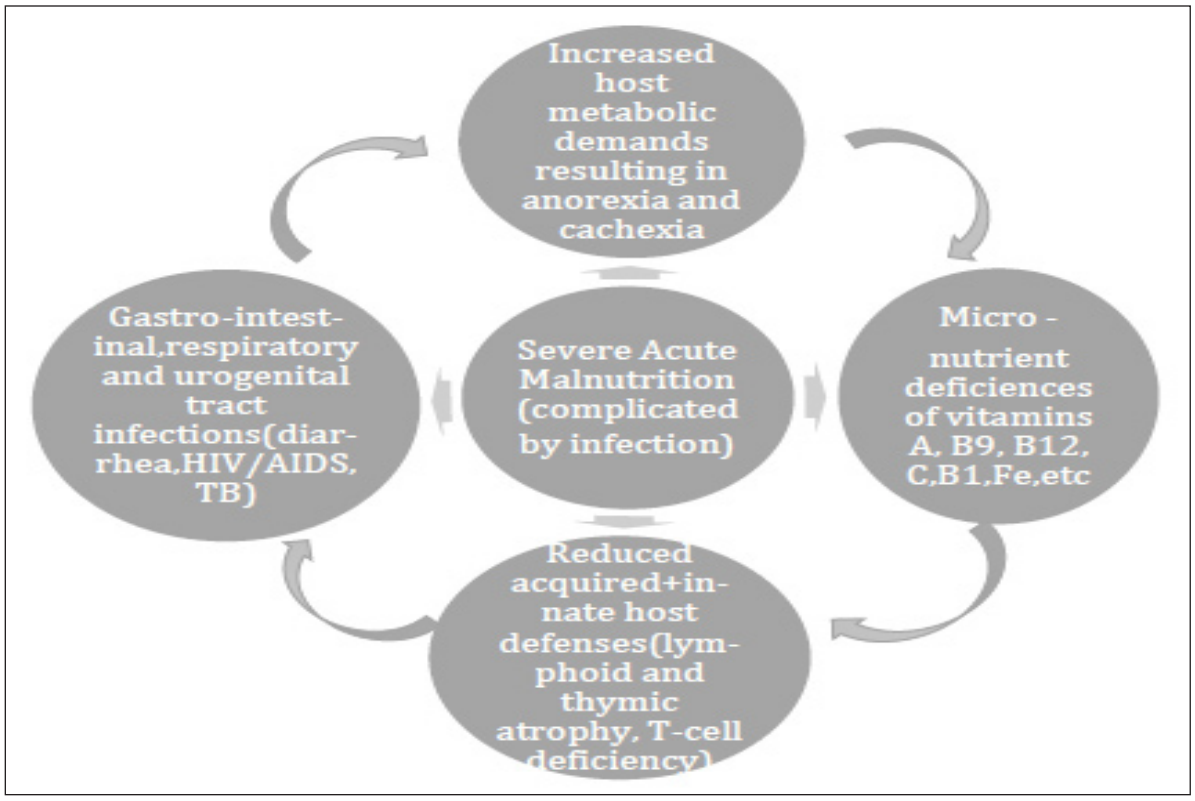


**Figure 1.** *Conceptual framework for the cycle of malnutrition and infection*

Where it is considered necessary, suspected infections in malnourished children should be treated with broad spectrum antibiotics. The rationale for this treatment are that: malnourished children frequently have bacterial infections [2, 11, 12]. Diagnosing infections in malnourished children based on signs or symptoms is often difficult because clinical manifestations of infection may not be apparent and malnourished children have insidious bacterial overgrowth in their small bowel [2].

What are the policy implications of this negative synergism? The recommendations of the World Health Organization (WHO) as detailed in figure 2 below, are that children with SAM and complications such as septic shock, hypothermia, skin infections, respiratory/urinary tract infections, should be given parenteral antibiotics (IM or IV) such as cephalosporins and gentamicin; while children admitted with SAM who have no apparent signs of infection and no complications should be given an oral antibiotic such as amoxicillin[11]. Children with uncomplicated SAM not requiring any admission and managed as outpatients should also receive a course of oral antibiotics. However, children who are malnourished, with no SAM should not receive antibiotics unless they show signs of clinical infection [2, 12].

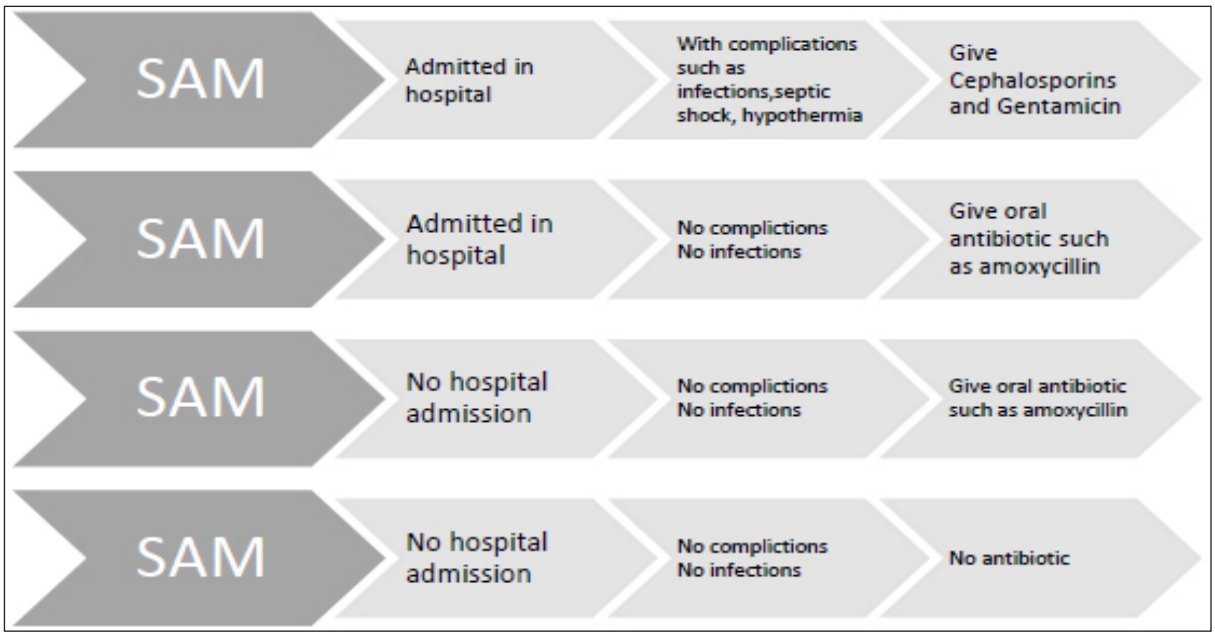


**Figure 2.** *Antibiotic treatment protocol for states of malnutrition as recommended by WHO [11]*

Metronidazole is also recommended for its anti-anaerobic and anti-protozoal activity. Moreover, metronidazole is active against giardia and small intestinal bacterial overgrowth [2, 11, 12].

On the other hand, some authors argue that metronidazole has potential side effects in children which may complicate its use in SAM. Such side effects include nausea, diarrhoea, thirst disturbance, anorexia, and potential metronidazole induced hepatotoxicity. Proponents of metronidazole use, recommend that doses be reduced to 10mg/Kg/day. Evidently tuberculosis, HIV infections, measles, and malaria should be adequately treated in SAM patients [2, 11, 12].

## Conclusion

Malnutrition and infection constitute a devastating vicious cycle which can be life threatening to patients, especially children under 5 years of age. On one hand, children are more vulnerable because of their relatively weak immune system and high incidence of gastrointestinal and respiratory infections which can result in malnutrition. On the other hand, those with severe acute malnutrition have increased susceptibility to infections which might be life-threatening because of their compromised immune status. Within this cycle, repeated and chronic infections tend to compromise the nutritional status of children or worsen the nutritional status of an already malnourished child. The existence of this vicious cycle provides justification for active treatment of childhood infections in order to increase survival rates and the possibility of meeting the sustainable development goals and targets relating to childhood mortality in many developing countries.

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