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# Protein Energy Malnutrition and Susceptibility to Viral Infections as Zika and Influenza Viruses

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## Abstract

Infection and malnutrition have constantly been intricately related. Malnutrition is the primary motive of immunodeficiency worldwide, and we're getting to know more and more about the pathogenesis of this interaction. Malnutrition is the main cause of immunodeficiency international, with infants, children, youth, and the aged most affected. There is a strong courting between malnutrition, contamination and mortality, due to the fact bad nutrients leading to kids underweight, weakened, and susceptible to infections, mainly considering that of epithelial integrity and irritation. The most consistent changes in immune competence in protein energy malnutrition are in cell-mediated immunity, the bactericidal function of neutrophils, the complement system, the secretory immunoglobins A, and antibody response. This direct relationship between malnutrition and immunodeficiency reflected on susceptibility to infection by influenza and Zika viruses.

**Keywords:** Malnutrition; Infection; Immunity; Zika virus; Influenza virus

## Introduction

Most attention during the period of immuno-nutritional reemergence focused on effects of protein energy malnutrition on the immune system and other host defensive mechanism. The myriad observations, some quite old and some quite new clearly show that the immune system cannot function optimally if malnutrition is present. Malnutrition also produces adverse effects on antigenically nonspecific mechanism of host defense. Careful observation showed a correlation between nutritional status and morbidity and mortality largely due to infections [1].

Zika virus is a global spread sickness, also it is called Zika fever, is an arthropod - borne viral (arboviral) sickness. Discovered in Uganda in the late 1940s, the virus remained restrained to a slender area of equatorial Africa and Asia previous to 2007 [2]. These countries suffered from malnutrition can be a consequence of energy deficit (protein-energy malnutrition - PEM) or a micronutrient deficiency. In any case, it is still a major burden in developing countries and is considered the most relevant risk factor for illness and death, affecting particularly hundreds of millions of pregnant women and young children [3]. This direct relationship between malnutrition and immunodeficiency reflected on susceptibility to infection by influenza and Zika viruses. It is estimated that 852 million peoples have been undernourished between 2000 and 2002, with most (815 million) residing in establishing nations, particularly in southern Asia and sub-Saharan Africa [3,4].

The virus has unfolded to different regions of Africa and Southeast Asia, in addition to diverse Pacific Islands, South the United States and the Caribbean. Zika virus transmitted to people through the bite of infected mosquitoes belonging to the Aedes species (frequently, *Aedes aegypti*) [2,5].

In 2007, the first documented outbreak of Zika virus disease was reported in Yap State, Federated States of Micronesia; 73% of the population aged ≥3 years is estimated to have been infected [2]. Subsequent outbreaks occurred in Southeast Asia and the Western Pacific [6]. In May 2015, the World Health Organization reported the first local transmission of Zika virus in the Region of the Americas (Americas), with autochthonous cases identified in Brazil [7]. In December, the Ministry of Health estimated that 440,000–1,300,000 suspected cases of Zika virus disease had occurred in Brazil in 2015 [8]. By January 20, 2016, locally-transmitted cases had been reported to the Pan American Health Organization from Puerto Rico and 19 other countries or territories in the Americas [9]. Further spread to other countries in the region is being monitored closely (Figure 1).

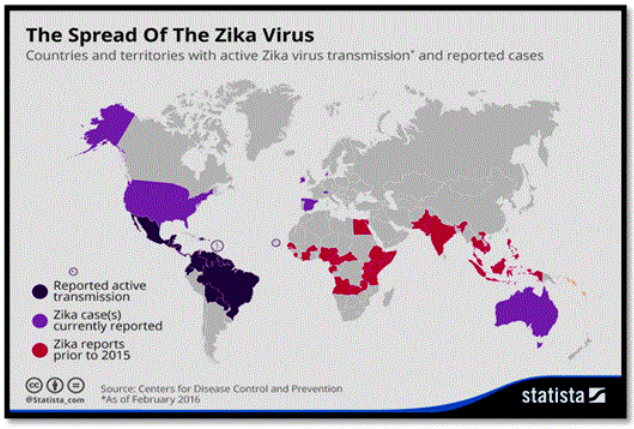


**Figure 1:** Spread of Zika virus.

Zika virus is a single stranded RNA *Flavivirus* belonging to the *Flaviviridae* own family [1,5]. Till lately, the virus turned into judged to

be of youth significance. Most individuals (80%) infected with Zika virus are asymptomatic, whereas the other patient suffered from moderate signs and symptoms, include of fever, vomiting, rash, joint pain, and purple eyes (conjunctivitis). In the majority of instances, the signs and symptoms last from a few days as much as per week, with full healing in a while [10].

Zika infection is equipped for transmitting the infection to her infant amid pregnancy. Alarmingly, alongside the late pandemic of Zika infection sickness, especially in Brazil, there has been an emotional increment in the vitality of infants which influenced by microcephaly [2,10].

## Pathophysiology of malnutrition in relation to immune response

Severe PEM is typically characterized via the occurrence of fats degeneration in diverse organs together with the liver and coronary heart. The loss of subcutaneous fat, which markedly reduces bodily ability to regulate temperature and additionally to keep water, can also arise, frightening dehydration, hypothermia and hypoglycemia [11,12]. Moreover, PEM is related to atrophy of the small gut that triggers the lack of each absorption and digestion potential [13].

From a critical point of view, it is impossible to separate innate and acquired immunity due to the fact they work in an intrinsically linked manner in the body. Nonetheless, for the sake of readability, we will be able to first refer to a couple mechanisms viewed innate, i.e., those used in opposition to any variety of pathogen. For instance, availability of complement components and phagocyte operate are compromised in the course of malnutrition, in order to directly influence pathogen elimination. This happens considering the fact that the complement itself can kill bacteria or viruses. Presence of complement receptors on the phagocytic cell surface enhances capture of pathogens. *There are three pathways of complement activation: the classical pathway, which is triggered by antibody or by direct binding of complement component C1q to the pathogen surface; the MB-lectin pathway, which is triggered by mannan-binding lectin, a normal serum constituent that binds some encapsulated bacteria; and the alternative pathway, which is triggered directly on pathogen surfaces. All of these pathways generate a crucial enzymatic activity that, in turn, generates the effectors molecules of complement. The three main consequences of complement activation are opsonization of pathogens, the recruitment of inflammatory cells, and direct killing of pathogens. Significantly decrease in the levels of complements; chiefly C3 that's the principal opsonic factor leading to decrease phagocytic ability to ingest and kill pathogens [14,15].

## Malnutrition raises chance of viral infection

Malnutrition, a major dangerous reason for a number of infectious illnesses as influenza virus, is widely generic in growing international locations [16]. Consequently, it is vital to recognize the effects of malnutrition on morbidity and mortality related to influenza infection. Several studies display the deleterious impact of PEM on influenza virus disease and subsequent immune responses and moreover display that supplementing protein can restore immune characteristic and improve the final results of influenza infections in the mouse model [17]. Comparable statement may be found in case of Zika virus infection is scarce however mosquito-borne *Flaviviruses* are thought to replicate initially dendritic cells close to site of inoculation then unfold to lymph nodes and the bloodstream [18]. Even though flaviviral replication is idea to arise in cell cytoplasm, Zika antigens can be located in infected cell nuclei [19].

PEM is a common motive of secondary immune deficiency and susceptibility to infection in human. This immunodeficiency represents a key thing in susceptibility to infections. PEM termed as nutritionally acquired immunodeficiency syndrome. In seriously malnourished patients, both received immunity - i.e., lymphocyte functions - as well as innate host defense mechanisms - i.e., macrophages and granulocytes - is influenced [20].

Antigen-presenting cells (APC) assume a cardinal part of immune system which regulate and support of intrinsic and procured invulnerable reactions [20]. A progression of studies exhibited that the functional capacity of various cell sorts (B lymphocytes, macrophages and Kupffer cells) is obviously reduced at some stages in nutritional deficiencies [21-23].

## Effect of malnutrition on primary lymphoid organs

Malnourished patients considered as vulnerable to infections. Excessive protein malnutrition in newborns and babies is sincerely related to atrophy especially in the primary lymphoid organs, i.e., bone marrow and thymus. Effects are devastating due to those organs are generators of B and T cell repertoires. Furthermore, malnutrition truly influences hematopoiesis, determining anemia, leucopenia and extreme reduction in bone marrow. Manufacturing of IL-6 and TNF-α by bone marrow cells is also significantly decrease in malnourished animals [24].

The capability of malnourished hematopoietic stroma to aid the progress of hematopoietic stem cells (CD34+) *in vitro* can also be lowered. This can be a very important finding since CD34+ cells are able to generate more than one lympho-hematopoietic lineages as myeloid, erythroid and lymphoid (B and T) [25].

Extreme protein malnutrition, mainly in newborns and small youngsters, also provokes thymus atrophy and also critically influences the development of peripheral lymphoid organs [26]. The immediate consequence of this atrophy is leucopenia, reduced CD4/CD8 ratio and elevated number of immature T cells. Lower numbers of CD3+ lymphocytes had been present inside the spleen of critically malnourished rats. In addition they detected an extensive impairment of T cell activation characterized by decreased expression of CD25 and CD71 in these cells [25].

## Relation among malnutrition and immunosuppression

Malnutrition leads to immunosuppression via different mechanisms, inclusive of leptin and the hypothalamic-pituitary-adrenal axis. PEM reduces leptin concentrations and increases serum levels of stress hormones as glucocorticoids [26-28]. Thus, it is likely that the hypothalamic-pituitary-adrenal axis performs an important function in malnutrition related immune deficiency. In properly-nourished people, infection and inflammation increase leptin levels in an IL-1-dependent manner and increase glucocorticoid concentrations, which subsequently can control inflammation, which in the end can manage infection [27]. Under conditions of PEM, low leptin concentrations, glucocorticoids and impair of macrophage function [29].

Macrophages from mice with experimental PEM are less sensitive to activate with lipo-polysaccharides. Their capability to engulf pathogens

and to provide cytokines and reactive oxygen intermediate ROI are impaired. [30].

PEM, mainly in developing nations, represents one of the maximum commonplace sorts of adolescence malnutrition. PEM will increase susceptibility to a couple of infectious illnesses. In proceeding have a look at the outcomes of PEM on influenza a virulent disease infection in mice. They found that infection of mice manifesting symptoms of weight-reduction plan (VLP) - brought about PEM, with both a laboratory stress and a 2009 H1N1 pandemic virus, led to higher quotes of virus - brought on morbidity and mortality as compared with mice that obtained adequate nutrients. The VLP group of mice verified a sizeable lower in adaptive immune functions, inclusive of manufacturing of virus-unique antibodies, influenza (NP)-unique CD8+ T cells, and IFN-γ-producing T cells. Importantly, those outcomes will be reversed via supplementing additional protein inside the food regimen of the VLP institution of mice, which led to notably stepped forward immunity to influenza virus venture and improved host survival. Taken together, our results exhibit multiple immune deficits related to PEM and emphasize an immune stimulatory position for protein supplementation for the duration of influenza virus infection [30,31]. On other hand, Zika virus has been detected in human blood as early as the day of infection onset; viral nucleic acid has been detected as overdue as 11 days after onset. The virus was isolated from the serum of a monkey nine days after experimental inoculation [5].

## Conclusion

In these days, starvation and malnutrition are more effect on people distribution and politics than natural catastrophe. Infection is inevitably tied to diet in both developing and developed world. Malnutrition is the main cause of immunodeficiency and increase susceptibility to infection as influenza and Zika viruses.

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