Review Article

The Relationship between Nutrition and Infectious Diseases: A Review

Sedigheh Farhadi[1], Roman S. Ovchinnikov[2]

[1]Department of English, Marvdasht Branch, Islamic Azad University, Marvdasht, Iran, [2]Department of Bioactive Nanostructures, Microbiology Group, Federal Research Centre for Microbiology and Epidemiology, N.A. N.F. Gamaleya, Moscow, Russia

Abstract

Nutrition and infectious diseases are related to each other in some aspects. First, nutrition affects the development of human body immune system. Moreover, nutrition can influence emerge of infectious diseases (e.g., gastrointestinal infections), food poisoning, intestinal diseases, and systemic infectious diseases. In this review, the mentioned aspects of the relationship between nutrition and infections are discussed. Furthermore, the relationship between malnutrition and infectious diseases, nutrition in patients with severe combined immunodeficiency and relationship between overeating and infection are reviewed. Overall, some factors can weaken the body's ability to fight infection and cause malnutrition. The factors include anorexia, traditional behaviors, reduction of intestinal absorption, metabolic damage, disorder metabolism of lipids and carbohydrates, reduction of vitamins, iron, zinc, and copper. In the case of the relationship between malnutrition and infection, a large number of studies have illustrated a bidirectional interaction of malnutrition and infection. In this aspect, to treat serious acute malnutrition and limit the rate of death, some preventive studies applied antibiotics, probiotic bacteria, and prebiotic foods. In the future, studies may be conducted on intestinal or systematic immunomodulation.

Keywords: Human body immunity, infection, malnutrition, nutrition

Introduction

The relationship between nutrition and infectious diseases can be divided into five groups as follows[1]: (1) the effect of nutrition on the development of human immune system; (2) the effect of nutrition on emerge of infectious diseases (e.g., gastrointestinal infections), food poisoning (e.g., botulism), intestinal diseases (e.g., microbial diarrhea), and systemic infectious diseases (e.g., brucellosis and typhoid); (3) relationship between malnutrition and infectious diseases; (4) nutrition in patients with severe combined immunodeficiency; and (5) relationship between overeating and infection [Figure 1]. These five groups of balance between nutrition and infection are discussed below.

The effect of nutrition on the development of human body immune system

The effect of diet on the development of human immune system begins from the embryonic stage. If during pregnancy, especially in the first trimester of pregnancy, the mother receives enough protein, vitamins, and minerals, the embryonic tissues will develop very well. If a fetus develops sufficiently, it will have normal weight and size. The normal weight of the fetus is an important criterion for his/her health.[2] Fetal malnutrition has unfavorable effects on the development of immune system. If the immune system does not efficiently develop in this period, it cannot defense against pathogens in the future.

After birth, breast milk provides sufficient vitamins and minerals to a baby that can guarantee the baby's growth and health.[2] Breastfeeding is the second-most important step to develop a vigorous immune system.[2] A malnourished baby who does not receive enough protein and vitamins is prone to infectious diseases and does not respond well to vaccines.[3] Therefore, nutrition is critical to provide high immunity in humans against environmental pathogens.

Access this article online

Quick Response Code:

Website: www.bmbtrj.org

DOI: 10.4103/bbrj.bbrj_69_18

Address for correspondence: Dr. Roman S. Ovchinnikov, Federal Research Center for Microbiology and Epidemiology, N.a. N.F. Gamaleya, 123098, Gamaleya St., 18, Moscow, Russia.
E-mail: rsovchinnikov@mail.ru

How to cite this article: Farhadi S, Ovchinnikov RS. The relationship between nutrition and infectious diseases: A review. Biomed Biotechnol Res J 2018;2:168-72.

The role of nutrition to provide vigorous immunity against infectious diseases has been vastly investigated. For example, it has been shown that if a group of children receives enough food and another group of children receives tuberculosis vaccine, those who have a good diet are less affected with tuberculosis than those who vaccinate. The risk of developing tuberculosis is significantly reduced in people who have healthy nutrition and are vaccinated.[4-6]

Nutrition effects on emergence of infections

If food, as a source of energy for human body, has microbial contamination, it can cause various diseases including digestive diseases and food poisoning. People are exposed to various food poisonings in different seasons. In hot weather, intestinal diseases are highly observed, which the most dangerous one is cholera.[7] Food poisoning is also caused by the consumption of contaminated foods. In many cases, eating the spoiled canned foods can be very dangerous. Typhoid fever, caused by *Salmonella* species, is also one of the most dangerous diseases transmitted through contaminated water and food.[8] It causes many problems for patients since the pathogen is antibiotic resistance.[8]

Besides, microbial contaminations transmitted through water and food can cause severe diarrhea and infectious diseases in children.[9] Brucellosis is an infectious disease caused by the ingestion of contaminated food and water. Brucellosis is a common disease between humans and animals. Bacterium *Brucella* can cause illness in sheep, goats, cows, pigs, and dogs. Humans become infected with *Brucella* by consuming unpasteurized milk or undercooked meat from infected animals.[10] Close contact with secretions of infected animals can also transmit the infection to human.[10] Amoebiasis is a major disease caused by consumption of contaminated water and food. Likewise, toxoplasmosis is caused through ingestion of raw or undercooked meat. As the parasitic cyst enters the human stomach, it is released by the action of gastric acid and absorbs into the liver through the intestinal mucosa and then enters the lymph nodes.[11] Pinworm infection is another parasitic disease transmitted through food. The infection is prevalent in all countries with more prevalence in children compared to adults. Parasitic worm infections such as teniasis and hookworm infection are also caused by inappropriate nutrition.[12]

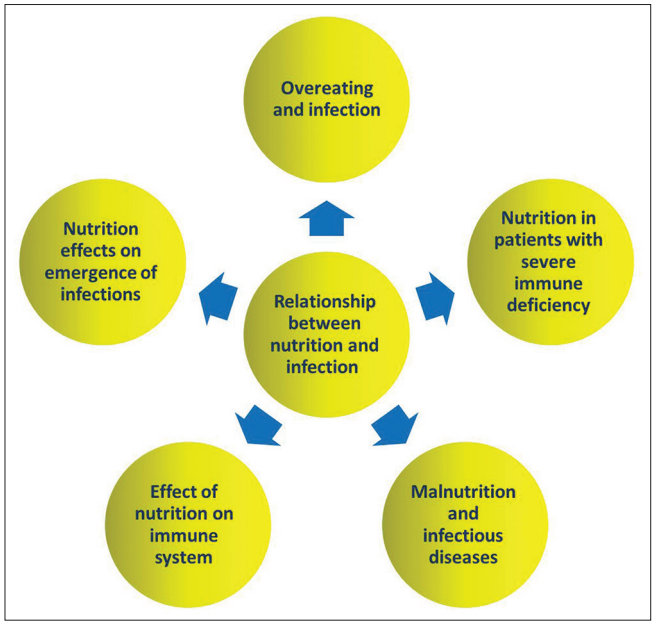

Figure 1: The relationship between nutrition and infectious diseases

Malnutrition and infectious diseases

Effects of malnutrition on emergence the infectious diseases

The effect of protein-energy malnutrition on the increase of infectious diseases has been studied extensively. In regions that there is malnutrition of proteins, microbial contamination is a health problem and affects the entire community of children. In such poor societies, the Vitamin A deficiency, which is one of the important immune system boosters, should be added to diet. The lack of the mentioned nutrients, protein, and Vitamin A has caused prevalent infections in the world's poorest areas.[13]

Effects of infections on malnutrition

In 1968, the World Health Organization reported that the infection could worsen malnutrition in humans.[14] This kind of enhancement relationship is called synergy. It is believed that the infection can negatively influence the subjects' nutritional status that results in reduction the body's ability to fight infection. Consequently, infection can cause malnutrition and malnutrition may increase the infection.[14]

Some factors can weaken the body's ability to fight infection and cause malnutrition [Figure 2]. First, anorexia can cause malnutrition and weaken the body's immune system against infection.[15] The traditional behaviors can also exacerbate malnutrition and infection. For example, in some societies, people who have fever or diarrhea are banned from eating.[15] Reduced intestinal absorption due to intestinal infections

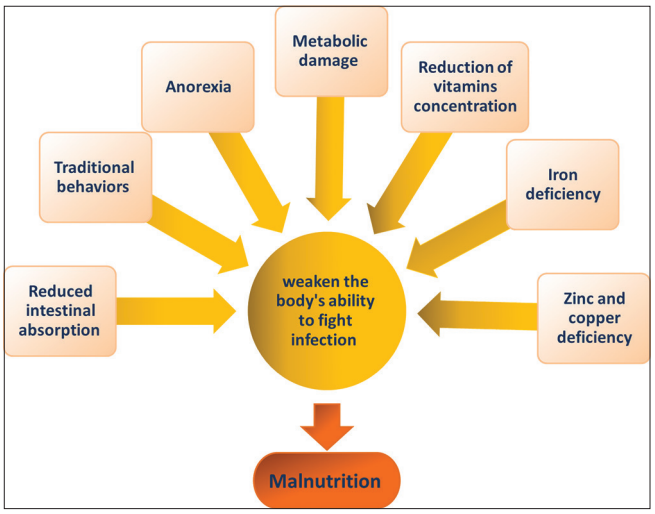

Figure 2: The factors that weaken the body's ability to fight infection and cause malnutrition

can reduce protein, carbohydrate, and fat absorption by 43%, 42%, and 72%, respectively. Of course, these values depend on the type of infection.[16] Metabolic damage such as losing proteins during the infection can increase the need for dietary protein.[17] Disorder metabolism of lipids and carbohydrates (e.g., disorder in fatty acid self-assembled structure, ketone bodies, and triglycerides) may be observed in various infections. In addition, the infection can transmit amino acids to carbohydrates via gluconeogenesis pathway that makes new glucose from noncarbohydrate precursors.[14] The concentration of Vitamin A may be reduced in blood during respiratory infections. Diseases such as hepatitis, acute tonsillitis, and rheumatoid arthritis can also reduce serum Vitamin A concentration.[13] The concentration of Vitamin C is reduced in patients' blood with infections. As a result, the concentration of Vitamin C increases in the urine. This situation is even seen in people who have received measles and smallpox vaccine. Obviously, people who have received the vaccine have an imitation infection.[18] Amount of Vitamin B2 (riboflavin) in the body decreases following infection. Reduction of Vitamin B2 due to infection is statistically significant.[2] Iron is another nutrient that is reduced in the body due to infection. Iron efficiency can help to reduce the activity of pathogens and aid to treat infections.[2] Zinc and copper are other elements whose concentration decreases when infections occur. Studies have shown that the balance of copper and zinc in infections is negative. In the blood, the concentration of copper increases, however, levels of copper may significantly decrease in the infected body.[19]

In order to treat malnutrition caused by infection, it is necessary to compensate for energy and weight loss. Overall, nutrition is critical in the treatment of malnutrition caused by infection.[13]

Nutrition in patients with severe immune deficiency

In severe immune deficiency, the susceptibility to infection can occur. A healthy person may eat some poisoned canned food and do not get infection. However, patients with severe immune deficiency may develop disease if they eat the same. Physicians emphasize that patients with severe immune deficiency, especially those with white blood cells below 1000 or less, should not use raw foods and fruits. Such foods may transmit pathogens. It is also recommended that the patients avoid eating dried fruit when the white blood cells are under 1000.[20]

Overeating and infection

The relationship between overeating and infection is not vastly investigated. However, in some studies, it is shown that overweight persons are at more risk for respiratory tract infections.[21] In addition, obese people have potential for get diabetes and all diabetic people are sensitive to infections.[21]

Relationship between Malnutrition and Infection Globally; Some Examples

In this section, some recent studies that focused on relationship between malnutrition and infection are discussed. A large number of studies have illustrated a bidirectional interaction of malnutrition and infection [Figure 3].[16] The figure is adapted from Brown.

As one example, a study was conducted to show relationship between infections and malnutrition in children. Results showed that malnourished children often suffered from diarrhea.[22] In these children, the rate and severity of diarrhea was high.[22] The results indicate a direct relationship between malnutrition degree and risk of diarrhea. In another study, the influence of diarrhea was evaluated in infants from birth until 24 months of age. Results showed that impaired growth was increased (about 16%) for every 5% increase in diarrhea incidence.[23] It has been also found that frequency of diarrhea has a variable relationship with linear growth.[24] In a study conducted in Western Kenya (2005–2007), 1146 children hospitalized with moderate-to-severe diarrhea were examined. It was found that children with severe malnutrition died from diarrhea four times more than healthy children.[25]

The global enteric multicenter study conducted a study in seven countries in Africa and Asia. In the study, 9439 children with moderate-to-severe diarrhea and control children without diarrhea were enrolled.[26] Results showed that there was a direct relationship among diarrhea, impaired growth and rate of postdiarrhea death during 90 days.[26]

A direct association has been found among malnutrition, increase risk of pneumonia episodes and fatality. For example, results of a study on 16,475 Malawian children demonstrated that severe malnutrition has a predictive value for hypoxemia and coma in children with pneumonia.[27] In Kenya, 25% of 4187 hospitalized children with severe pneumonia were reported to be severely malnourished. Thirty-seven percent of children were died after discharge from hospital. Effective factors on postdischarge mortality included malnutrition, HIV status, young age, and prolonged length of stay. Malnourishment was found as a strong risk factor for inpatients mortality and severity signs of the disease.[28]

There is variable relationship between malnutrition and bacteremia risk and malnourished children are more likely to

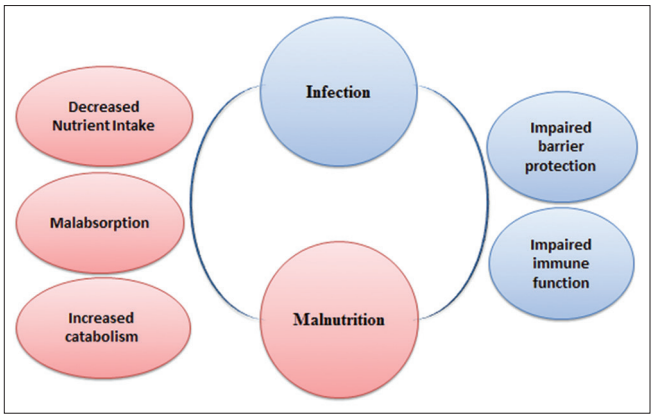

Figure 3: Interaction of nutrition and infection. Adapted from Brown 2003[16]

have Gram-negative bacteremia.[1] However, in underdeveloped countries, there is a similarity in the range of bacterial species in blood of both malnourished and nonmalnourished children. A blood culture study was conducted in Tanzania and the results showed that *Pseudomonas* spp., *Enterobacter* spp., and *Staphylococcus aureus* are of high prevalence with low sensitivity to ampicillin and gentamicin as the first-line therapies.[29] In Kenya, no association was found between coagulase-negative staphylococci identified in blood culture and death rate or length of stay in hospital.[29,30]

A study was conducted on 335 children in Colombia. The statistical population was children <6 years of age who were hospitalized due to severe or moderate acute malnutrition related to their primary disease. Diarrhea was the most frequent complication at the admission time, and sepsis was the most frequent complication during hospitalization. The death rate and complication were similar between moderate and severe acute malnourished children.[16]

In 2006, Mondal *et al*. examined the relationship between diarrhea caused by gastrointestinal infections and nutritional quality in children.[31] Considering to their results, there was a strong relationship between amebiasis caused by parasite *Entamoeba histolytica,* and increased rate and severity of diarrhea in malnourished children.[31] Amebiasis can be transmitted through fecal-contaminated water and food. It has been observed that *E. histolytica* infection can cause the incidence of diarrhea 2%–10% in children living in the developing countries. The annual global rate of mortality and infection caused by amoebiasis is estimated to be about 100,000 and 50 million, respectively.[32] Secretory antibodies (immunoglobulin A) promote immune protection against *E. histolytica* diarrhea.[33] Hence, decrease in a number of IgA-secreting cells in malnourished children can increase the incidence of infection caused by *E. histolytica*.[34]

In Kenya and Bangladesh, some interventions such as water treatment, improved sanitation, hygiene, and nutrition interventions had been done to reduce the rate of diarrhea. However, these interventions had low effect on diarrhea or children growth.[29] In a multicenter research trial in Kenya, it was shown that daily co-trimoxazole prophylaxis did not significantly reduce the severe infections after leaving the hospital and did not increase growth among critically malnourished children in a long time.[35] In some studies, other antibiotics were tested against intestinal bacteria to treat serious acute malnutrition and limit the rate of death after leaving the hospital.[36] As intestinal microbial flora was better recognized, some preventive studies applying suitable probiotic bacteria and prebiotic foods have been carried out *in vivo*.[37] In the future, studies may be conducted on intestinal or systematic immunomodulation.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Cervantes-Ríos E, Ortiz-Muñiz R, Martínez-Hernández AL, Cabrera-Rojo L, Graniel-Guerrero J, Rodríguez-Cruz L, *et al.* Malnutrition and infection influence the peripheral blood reticulocyte micronuclei frequency in children. Mutat Res 2012;731:68-74.
2. Kim DE, Jang MJ, Kim YR, Lee JY, Cho EB, Kim E, *et al.* Prediction of drug-induced immune-mediated hepatotoxicity using hepatocyte-like cells derived from human embryonic stem cells. Toxicology 2017;387:1-9.
3. Ezenwa BN, Ezeaka VC. Is canscore a good indicator of fetal malnutrition in preterm newborn. Alexandria J Med 2017;54:57-61.
4. Gupta KB, Gupta R, Atreja A, Verma M, Vishvkarma S. Tuberculosis and nutrition. Lung India 2009;26:9-16.
5. Jena L, Harinath BC. Anti-tuberculosis therapy: Urgency for new drugs and integrative approach. Biomed Biotechnol Res J 2018;2:16-9.
6. Aghajani J, Farnia P, Velayati AA. Impact of geographical information system on public health sciences. Biomed Biotechnol Res J 2017;1:94-100.
7. Davies HG, Bowman C, Luby SP. Cholera-management and prevention. J Infect 2017;74:66-73.
8. Farhadi T, Hashemian SM. Constructing novel chimeric DNA vaccine against *Salmonella enterica* based on SopB and GroEL proteins: An *in silico* approach. J Pharm Investig 2017. [In press]. [doi: 10.1007/s40005-017-0360-6].
9. Chatterjee A, Abraham J. Microbial contamination, prevention, and early detection in food industry. Microb Contam Food Degrad 2017;10:21.
10. Singh BB, Khatkar MS, Aulakh RS, Gill JPS, Dhand NK. Estimation of the health and economic burden of human brucellosis in India. Prev Vet Med 2018;154:148-55.
11. Protozoa GD. Malaria; toxoplasmosis; cryptosporidiosis; amoebiasis; trypanosomiasis; leishmaniasis; giardiasis; trichomoniasis. In Medical Microbiology (Eighteenth Edition) 2012. p. 642-54.
12. Molyneux DH. Control of human parasitic diseases: Context and overview. Advances in Parasitology 2006;61:1-45.
13. Sanson G, Bertocchi L, Dal Bo E, Di Pasquale CL, Zanetti M. Identifying reliable predictors of protein-energy malnutrition in hospitalized frail older adults: A prospective longitudinal study. Int J Nurs Stud 2018;82:40-8.
14. Krawinkel MB. Interaction of nutrition and infections globally: An overview. Ann Nutr Metab 2012;61 Suppl 1:39-45.
15. Solomons NW. Malnutrition, immunity and infection. In Diet, Immunity and Inflammation 2013. p. 686-717.
16. Brown KH. Diarrhea and malnutrition. J Nutr 2003;133:328S-32S.
17. Dos Anjos Garnes S, Bottoni A, Lasakosvitsch F, Bottoni A. Nutrition therapy: A new criterion for treatment of patients in diverse clinical and metabolic situations. Nutrition 2018;51-52:13-9.
18. Hunter JV, Goerner L. Infections. Handb Clin Neurol 2016;136:1173-98.
19. De Riccardis L, Buccolieri A, Muci M, Pitotti E, De Robertis F, Trianni G, *et al.* Copper and ceruloplasmin dyshomeostasis in serum and cerebrospinal fluid of multiple sclerosis subjects. Biochim Biophys Acta 2018;1864:1828-38.
20. Pai UA, Chandrasekhar P, Carvalho RS, Kumar S. The role of nutrition in immunity in infants and toddlers: An expert panel opinion. Clin Epidemiol Global Health. 2017. [doi: 10.1016/j.cegh.2017.11.004].
21. Hegde V, Dhurandhar NV. Microbes and obesity—interrelationship between infection, adipose tissue and the immune system. Clinical Microbiology and Infection 2013;19:314-20.
22. Guerrant RL, Schorling JB, McAuliffe JF, de Souza MA. Diarrhea as a cause and an effect of malnutrition: Diarrhea prevents catch-up growth and malnutrition increases diarrhea frequency and duration. Am J Trop Med Hyg 1992;47:28-35.
23. Checkley W, Buckley G, Gilman RH, Assis AM, Guerrant RL, Morris SS, *et al.* Multi-country analysis of the effects of diarrhoea on childhood stunting. Int J Epidemiol 2008;37:816-30.
24. Pickering AJ, Djebbari H, Lopez C, Coulibaly M, Alzua ML. Effect of a community-led sanitation intervention on child diarrhoea and child growth in rural Mali: A cluster-randomised controlled trial. Lancet Glob Health 2015;3:e701-11.
25. O'Reilly CE, Jaron P, Ochieng B, Nyaguara A, Tate JE, Parsons MB,

et al. Risk factors for death among children less than 5 years old hospitalized with diarrhea in rural Western Kenya, 2005-2007: A cohort study. PLoS Med 2012;9:e1001256.
26. Kotloff KL, Nataro JP, Blackwelder WC, Nasrin D, Farag TH, Panchalingam S, *et al.* Burden and aetiology of diarrhoeal disease in infants and young children in developing countries (the global enteric multicenter study, GEMS): A prospective, case-control study. Lancet 2013;382:209-22.
27. Hooli S, Colbourn T, Lufesi N, Costello A, Nambiar B, Thammasitboon S, *et al.* Predicting hospitalised paediatric pneumonia mortality risk: An external validation of RISC and mRISC, and local tool development (RISC-malawi) from malawi. PLoS One 2016;11:e0168126.
28. Ngari MM, Fegan G, Mwangome MK, Ngama MJ, Mturi N, Scott JA, *et al.* Mortality after inpatient treatment for severe pneumonia in children: A cohort study. Paediatr Perinat Epidemiol 2017;31:233-42.
29. Walson JL, Berkley JA. The impact of malnutrition on childhood infections. Curr Opin Infect Dis 2018;31:231-6.
30. Obiero CW, Seale AC, Jones K, Ngari M, Bendon CL, Morpeth S, *et al.* Should first-line empiric treatment strategies cover coagulase-negative staphylococcal infections in severely malnourished or HIV-infected children in Kenya? PLoS One 2017;12:e0182354.
31. Mondal D, Petri WA Jr., Sack RB, Kirkpatrick BD, Haque R. *Entamoeba histolytica*-associated diarrheal illness is negatively associated with the growth of preschool children: Evidence from a prospective study. Trans R Soc Trop Med Hyg 2006;100:1032-8.
32. Long SS, Pickering LK, Prober CG. Principles and practice of pediatric infectious disease. Elsevier Health Sciences; 2012.
33. Ragazzo LJ, Zohdy S, Velonabison M, Herrera J, Wright PC, Gillespie TR, *et al. Entamoeba histolytica* infection in wild lemurs associated with proximity to humans. Vet Parasitol 2018;249:98-101.
34. Isanaka S, Langendorf C, Berthé F, Gnegne S, Li N, Ousmane N, *et al.* Routine amoxicillin for uncomplicated severe acute malnutrition in children. N Engl J Med 2016;374:444-53.
35. Versloot CJ, Attia S, Bourdon C, Richardson SE, Potani I, Bandsma RH, *et al.* Intestinal pathogen clearance in children with severe acute malnutrition is unrelated to inpatient morbidity. Clin Nutr ESPEN 2018;24:109-13.
36. Pekmez CT, Dragsted LO, Brahe LK. Gut microbiota alterations and dietary modulation in childhood malnutrition – The role of short chain fatty acids. Clin Nutr 2018. pii: S0261-5614(18)30077-3.
37. Black RE, Morris SS, Bryce J. Where and why are 10 million children dying every year? Lancet 2003;361:2226-34.