How to Cite:
Paul, P. Y., Satya, L. K., Satyanath, D., & Muralidharan, S. (2022). Role of vitamins and minerals in immunity: A scoping review. *International Journal of Health Sciences*, *6*(S1), 9686–9698. https://doi.org/10.53730/ijhs.v6nS1.7267

Role of vitamins and minerals in immunity: A scoping review

Dr. P Yuvaraj Paul
National Institute of Naturopathy, Ministry of AYUSH, Government of India, Pune-411001, India

Dr. Satya Lakshmi K
National Institute of Naturopathy, Ministry of AYUSH, Government of India, Pune-411001, India

Dr. Satyanath D
National Institute of Naturopathy, Ministry of AYUSH, Government of India, Pune-411001, India

Dr. Shrikanth Muralidharan*
National Institute of Naturopathy, Ministry of AYUSH, Government of India, Pune-411001, India
*Corresponding Author

***Abstract*---**Immune system is defined as the variety of cells and molecules that have involved in protecting humans/animals from the invasion of pathogenic microorganisms/antigens. The immune system structures; thymus spleen, lymph nodes and specific immunity cells which plays a major role in the immune mechanism. This review paper describes the various effects of micro and macro nutrients on the immune system of the human body.

***Keywords*---**Nutrition, Immunity, Vitamins, Minerals.

Introduction

Immune system is defined as the variety of cells and molecules that is involved in protecting humans/animals from the invasion of pathogenic microorganisms/antigens. The immune system structures; thymus spleen, lymph nodes and specific immunity cells which plays an essential part of the immune mechanism.

Effects of nutrition on immune system

The dietary factors that harm the immune system functions are majorly either due to lack of intake of macro-nutrients or deficiency in some specific micronutrients. Intake of nutrition that is balanced with regards to vitamin, mineral and proteins enhance the ability to resist communicable infections and also supplements the system to carry out its essential functions.[1]

Carbohydrates (CHO):

Carbohydrates are the important nutrient and are found in diet rich with carbon, hydrogen and molecules of oxygen.[2, 3] They are simple sugars or complex starch. Carbohydrates are an essential fuel element for immune system. Glycogen is mostly present in liver and in other organs and muscles. Glycogen in the form of blood glucose, is essential for providing constant energy to the cells and the tissues.[3-5] Lack of carbohydrates in diet may lead to abnormal performance of immune system.

Fats

Fats are one of the most significant nutrition sources and are needed for proper mechanism of the immune system. Fats are involved in various functions like absorption of vitamins (A, D, E, K), it acts as a source for omega 3 and omega 6 oil acid, essential for neural functions, provision of permeability and stability for cell membranes. [6] One gram of fat provides double the energy than protein and also essential for mechanism. [4] Diets, containing high amount of fats can reduce inflammatory action at the cellular levels. [7]

Proteins

Proteins are mainly needed for the immune mechanism. Intake of protein rich foods enhances the immunity. It is rich in cereals, nuts, sprouts and others. They the framework of body defense systems, enzymes that control body functions, and some hormones.[5] Lack of proteins suppresses the immune system. Too much consumption of certain amino acids can cause defects in the functioning of the immune system.[7]

Enhancement of immune system
Milk as unique source of immunomodulatory ingredients

Milk contains casein and whey protein along with milk fat.[8] Lactoferrin (LF) as well as caseinoglycopeptides (CGP) enhance the functions of the lymphocytes.[9] Blood cells have shown to possess enhanced phagocytic functions post milk consumption.[10] Conjugated linoleic acid (CLA), helps to improve the lymphocyte response and function.[11] Whey proteins on the other hand help to gain weight in immune compromised cases [12] and it raises the tissue concentrations of glutathione; that is actively involved with cellular immunity.[13] It also inhibits biding of the virus to the receptors on the surface of the T cells in HIV patients.[14] Bovine milk which has a higher concentration of immunoglobulins also enhances the immune response.[15]

Colostrum and strengthening the immunity of infants

- Colostrum is the breast secretion that follows the release of mature milk, which is different in form and nutritional properties, it is yellow liquid water, but it forms a high degree of immunity to infants. The colostrum is exposed from 5-10 days after birth, remains its nature until it reach at the tenth day after that its properties has been turned to mature milk.[16,17]
- It is responsible for the anti-infection and stable in the acidic environment of the stomach and resistant to digestive enzymes.[18]
- Lysozymes, which has a concentration of 300 times when compare to cow's milk, which attacks and destroys the cell membranes of bacteria after inhibition of pathogens. Peroxides found in breast milk, infant saliva and vitamin C found in colostrum.[19]
- Lacto peroxidase in breast milk kills *Streptococcus* bacteria.[20]
- Lactoferrin in milk, protein containing iron that has immunological properties.[21,22]
- *Lactobacillus bifidus* creates an environment in the digestive tract activates the growth of *Lactobacillus bifidus* bacteria, produce acetic acid or lactic acid from lactose, which inhibits the growth of pathogenic microbes, reduces the infant's susceptibility to infectious diseases and inhibits the growth of *E. coli.*[23,24]
- In addition, a group of proteins (Immunoglobulins) in breast milk play an important role in protecting the body against infectious diseases. Immunoglobulin such as IgA, which are present at high concentrations in the early days of the infant's life, because they contain many antibodies that act as anti-viral, antibacterial against pathogens, effective against the diseases such as viral diseases, *Streptococcus* infection, and pneumonia, as well as its resistance to enzyme activity, and it is stable in the high acidic medium of stomach.[25,26]

The role of dairy products

Dairy products such as fermented milk and skimmed yogurt made from unpasteurized milk, yogurt, and turkey cheese are rich in natural yeast. They play a vital role in fermenting undigested plant fibers and converting them into products and strengthen the immunity system.[27] it lowers cholesterol, which decreases the risk rates of associated with cardiac diseases, and increase the useful microorganisms that reduce the allergist, malignant tumors, intestinal ulcers, and diarrhea and reduce high blood pressure. It is necessary to increase the intake of skimmed yogurt because it increases the growth of useful bacteria, especially in cases of illness or weakness or in cases of convalescence after surgery, so it is necessary to take one or two cups per meal.[28,29]

Fruits, vegetables and juices

Fruits such as apples, pomegranate, grapefruit, orange, strawberry, avocado, bananas, grapes, green apples, pears, melons, berries, cherries, kiwi, pineapples, apricots, lemons, peaches and dates.[30-32] Cabbage, broccoli, broccoli, cauliflower, beetroot, carrots, pepper, radish, watercress, parsley, celery, red onion, garlic, pumpkin, eggplant, tomatoes, green beans, potatoes, spinach, artichoke,

turnip.[33-35] Intake of fresh fruits, vegetables and salads increase the efficiency of the immune system.[36]

Juices of beet root, celery, fresh cabbage, asparagus, black grape, carrot, fresh apple, fresh lemon, orange, pineapple, pomegranate, cranberry, raspberry, apricot, peach, pear juice, strawberry, cucumber with lemon and grape fruit with lemon.[35,37] It supplies essential nutrients and enhance the function of immune system.

The role of drinking water

Drinking two to three cups on the stomach early morning as well as drink extra amounts of water throughout the day is essential. Consumption of a glass of water half an hour before meals helps digestion and similarly a glass of water before the bath helps to reduce the blood pressure. One glass of water prior going to sleep reduces the risks of heart attack. It works on the sedimentation of mucous membranes lining the respiratory tract, which helps the production of antibodies and white blood cells, thereby strengthening the immune system's performance.[38, 39]

Role of green foods

Juices extracted from the organic wheat plant and small organic barley leaf extract, organic oats grasses extract, spirulina, chlorella, organic green dandelion, green broccoli, organic spinach, organic kale, organic parsley, organic cauliflower, sea kelp, sea dulse, marine green algae and marine vegetables.[40,41] Supplementation of balanced diet containing organic sprouts, super seeds, medicinal crops and probiotics in the diet. These natural resources have demonstrated enormous health benefits and also boost up the immunity.[42]

Functional foods

Fiber rich foods, fish, fish oils, mushroom, tempeh (fermented soybean product), turmeric, black tea, green tea, oligosaccharides, fermented dairy products, wheat germ, wheat germ oil, flaxseed oil, olive oil, corn oil, ginger, garlic, berries, lignin, lycopene, sea food rich in omega-3.[41,43] It supplies essential nutrients and increases the production of white blood cells. Vitamins such as E, D, C, A, and B, which plays a role in improving the immune system.[44]

Minerals

Metal elements such as iron, zinc, selenium, and copper also help to strengthen the immune system.[45, 46]

The role of volatile oils and aromas

Volatile oils and aromas such as chamomile and lavender oils, coconut oil are used as an ointment to increase the immunity of the skin since they consider as protective substances that protect the body from infection.[46]

Micronutrients and immunity
Vitamins and immunity

Vitamins in many ways affect the immune response of our body.[47] Antioxidants decrease cancer risks and also protect against minor infections.[48] the micronutrients such as vitamins A, C and E have shown significant effect on various aspects of the immune system.[49]

Vitamin A

According to World Health Organization, deficiency of vitamin A is a serious public health menace which affects 127 million children in the preschool age group. It has also around 20 million deaths in the low income nations that is estimated to be 2.4% of the total deaths globally. Among children, lack of vitamin A causes mortality and morbidity due to resulting measles, infections leading to diarrheal, and night blindness apart from severe anemia. Among women hypovitaminosis of A is correlated to pregnancy related mortality rates. Its daily consumption needs to be raised based for better and healthy life.

β- Carotene derived from provitamin A prevents the phagocytic cells from undergoing auto oxidative damage. It also enhances the proliferative responses of T and B lymphocyte, stimulates functions of T cell, promotes cytokines production and increases the tumoricidal capacity of macrophage, cytotoxic T cell and natural killer cell.[50] Vitamin A acts by the following functions:

1. Modification of integrity and functions of the epithelium.
2. Lymphoid mass
3. Host immunity (specific/ nonspecific)

Is deficiency may increase the risk of congenital HIV.[51] Vitamin A supplementation has proven to significantly reduce all mortality when administered between 6-59 months.[52] Dietary sources of Vitamin A include- sweet potatoes, pistachio nuts, broccoli, spinach, egg, carrots, peppers, cheese, apricots and green vegetables.

Vitamin D

Vitamin D receptors are expressed on the cells and hence it helps to alter the innate as well as adaptive immunity.[53] It improves pulmonary Also, vitamin D plays an important role in pulmonary resistance and its deficiency has been linked to various respiratory infections. It affects both cytokine and immunoglobulin production. Besides it has a beneficial effect in autoimmune thyroiditis, multiple sclerosis and rheumatoid arthritis. It upregulates the lipopolysaccharide receptor on the surface of T lymphocyte and suppresses the vitamin A induced immunoglobulin E expression.[54, 55] Vitamin D3 protects against the adipose tissue inflammation by causing disruption to the cycle of recruitment of macrophages.[56] Sources of Vitamin D are all dairy products like milk and cheese apart from liver oil and tuna. Exposure to sunlight also helps to activate the vitamin D metabolism.

Vitamin E

It is an anti-oxidant which enhances the immune system.[57,58] Large doses of vitamin E stimulates the humoral and cell mediated immunity.[59] Vitamin E decreases the production of prostaglandin E2 (PGE2) and hydrogen peroxide along with other immunosuppressive agents.[60,61] Sources of Vitamin E are peanuts, sunflower, tomato, wheat germ, broccoli and spinach.

Vitamin B

B complex includes thiamine (B_1), riboflavin (B_2), niacin (B_3), pantothenic acid (B_5), pyridoxine (B_6), biotin (B_7), folic acid (B_9) and cobalamins (B_{12}). Vitamin B_6 deficiency impairs lymphocyte maturation, growth and proliferation, and antibody production. It suppresses the production of Th1 cytokines and helps to promote Th2 action.[62] Among healthy adults as a supplement, Vitamin B_6 increases mitogen assisted proliferation of lymphocyte and helper T cells.[63] Its deficiency can lead to defective IL-2 production and delayed or no response to T and B cell mitogens.[64] Another study reported of decreased immune competency among cases undergoing dialysis due to Vitamin B_6 deficiency.[65]

Vitamin B_{12} enhances T cell response to concanavalin A (Con A) and also to the B cells synthesis by pokeweed mitogen (PWM). [66] It is reported that its deficiency can cause suppression of immunity to viral/bacterial infections in animal models.[67] Among children its deficiency can cause white blood cell related abnormalities.[68] Reduced folate levels can result in abnormality with the neutrophil functioning.[69] Sources of Vitamin B_6 include tuna, salmon, beef chick peas, liver, cereals, rice onions. Sources of Vitamin B_9 include spinach, avocado, lettuce, salmon, egg, kidney beans, shellfish, peanuts and rice. Sources of Vitamin B_{12} are all dairy products and green leafy vegetables along with cereals.

Vitamin C

Vitamin C deficiency results in decreased bactericidal activity and reduced movements of neutrophils and macrophages. It also reduces the resistance to microbial infection. Several mechanisms have been put forward were Vitamin C plays an essential role, [70, 71] such as:

- modulation of levels of intracellular cyclic nucleotide,
- synthesis of prostaglandins
- protection of 5'- lipoxygenase,
- production of cytokines,
- antagonism of leukocytes and histamine,
- neutralization of oxidants

Intake of vitamin C shows significant increase with serum IgG and IgM levels especially in older women.[72] Sources of Vitamin C include all citrus fruits apart from tomato, red and green pepper along with green peas.

Minerals and immunity
Selenium (Se)

Selenium is mostly found in aquatic products, kidney, heart and liver and also in whole wheat [73,74] .Selenium (Se) via its incorporation into cytosolic glutathione peroxidase (GSHPx) and bio membranes has been associated with the expression of specific, non specific and cell mediated immune response.[75,76] Se deficient mice were more susceptible to infections by coxsackie virus as well as influenza virus. [77] Moreover, Se decreases the possibilities of AIDS virus infection. [78]

Zinc

The best zinc sources are giblets like liver, meat aquatic products, eggs, cheese, walnut, hazelnut, whole wheat and whole wheat bread.[79-80] It acts as a catalytic, structural and regulatory role for enzymes, proteins and transcription factors and plays a key role in immune responses. Dietary zinc supplementation has been shown to enhance immune response in elderly.[81-83] Zinc has been reported for its detrimental effects of toxic dietary metals, such as nickel, on the immune response.[84] Copper/zinc superoxide dismutase (SOD) is directly involved in immunity and antioxidant defenses. In addition, thymulin a key thymic factor is zinc dependent.

Iron supplementation

Iron salts add to immunity.[83] Metalloenzymes and proteins rich in iron are essential for roles such as catalase, lactoferrin formation.[85] It acts via innate immunity. The iron deficiency reduces morbidity due to infection or diarrheas. Iron deficiency anemia has been shown to decrease the morbidity from infections and diarrheal diseases.[84]

Copper

Copper regulates the action of superoxide dismutase. Mice that received excess of copper for 8 weeks showed suppressed lymphoproliferative response.[85] T along with B lymphocytes responses to stimulation of mitogen were found to be decreased in subjects who had copper deficiency.[86] It is also shown to increase antitumor activity in drug resistant types of tumours.[87] A research reported that deficiency of copper deficiency caused significant reduction in the process of phagocytosis.[88]

Trivalent chromium

It is a trance element which stimulates the cellular activity associated with macrophages as well as phagocytosis function.[89,90] It raises the total serum immunoglobulin level (IgM) and reduces the levels of serum cortisol.

Magnesium
Magnesium affects both innate and acquired immunity. But its actions as a standalone element needs to be explored more.

Conflict of Interest: The authors declare no conflict of interest
Funding- Nil.

References

1. Chandra RK. Nutrition and the immune system: an introduction. The American Journal of Clinical Nutrition. 1997; 66: 460S-463S
2. Basoglu S, Turnagol H. Egzersiz ve immün sistem: Karbonhidratlar ETKisi. Hacettepe. Journal of Sport Sciences. 2004; 15: 100-123.
3. Sayan A. Beslenme Aliskanliklari ve Temel Besin Gereksinimleri. Atatürk. Üniversitesi Hemsirelik Yüksekokulu Dergisi. 1999:2: 2.
4. Baysal A, Beslenme G, Yayinevi H, Coskun T. Fonksiyonel Besinlerin Sagligimiz Üzerine Etkileri. Çocuk Sagligi ve Hastaliklari Dergisi. 2005; 48: 69-84.
5. Sahingöz SA. Omega-3 Yag Asitlerinin Insan Sagligina Etkileri Gazi Üniversitesi Endüstriyel Sanatlar Egitim Fakültesi Dergisi. 2007;15: 1.
6. Hüner GF. Çocuklarda Beslenme ve Infeksiyon Iliskisi. Ankem Dergisi. 2004;18: 26-31.
7. Li M, Monaco MH, Wang M, Comstock SS, Kuhlenschmidt TB, Fahey GC, et al. Human milk ligosaccharides shorten rotavirus-induced diarrhea and modulate piglet mucosal immunity and colonic microbiota. International Society for Microbial Ecology Journal. 2014; 8(8): 1609-1620.
8. Sfeir RM, Dubarry M, Boyaka PN, Rautureau M, Tomé D. The mode of oral bovine lactoferrin administration influences mucosal and systemic immune responses in mice. Journal of Nutrition. 2004; 134(2): 403-409.
9. Brosche T, Platt D. Nutritional factors and age-associated changes in cellular immunity and phagocytosis: A mini review. Aging Immunology and Infectious Disease. 1995; 6: 31-42.
10. Chew BP, Wong TS, Shultz TD, Magnuson NS. Effects of conjugated dienoic derivatives of linoleic acid and B-carotene in modulating lymphocyte and macrophage function. Anticancer Research. 1997; 17: 1099-1106.
11. Bounous G, Létourneau L, Longshan PA. Influence of dietary protein type on the immune system of mice. Journal of Nutrition. 1983; 113(7): 1415-1421.
12. Bounous G, Gold P. The biological activity of indentured dietary whey proteins: role of glutathione. Clinical and Investigative Medicine. 1991; 14(4): 296-309.
13. Neurath AR, Li YY, Strick N, Jiang S. A herpesvirus inhibitor from bovine whey. Lancet. 1996; 347: 1703-1704.
14. Goddeeris RML, Morrison WI. Cell mediated immunity In: Immunity in Ruminauts, CRe Press, London. 1994.
15. Gephart S M, Weller M, Gephart S. Colostrum as oral immune therapy to promote neonatal health. Advances in Neonatal Care. 2014; 14(1): 44-51.
16. Cacho NT, Lawrence RM. Innate immunity and breast milk. Frontiers in immunology. 2017; 8; 584.
17. Ballard O, Morrow AL. Human milk composition: nutrients and bioactive factors. Pediatric Clinics. 2013; 60(1):49-74. Food Science and Quality Management
www.iiste.org.
18. Fichter M, Klotz M, Hirschberg DL, Waldura B, Schofer O, Ehnert S, et al. Breast milk contains relevant neurotrophic factors and cytokines for

enteric nervous system development. Molecular Nutrition and Food Research. 2011; 55(10): 1592-1596.
19. Magacz M, Kędziora K, Sapa J, Krzyściak W. The Significance of Lactoperoxidase System in Oral Health: Application and Efficacy in Oral Hygiene Products. International Journal of Molecular Sciences. 2019; 20(6): 1443.
20. Campos LF, Repka JCD, Falcão MC. Effects of human milk fortifier with iron on the bacteriostatic properties of breast milk. Journal de Pediatria (Versão em Português), 2013; 89(4): 394-399.
21. Siqueiros-Cendón T, Arévalo-Gallegos S, Iglesias-Figueroa BF, García-Montoya IA, Salazar-Martínez J, Rascón-Cruz Q. Immunomodulatory effects of lactoferrin. Acta Pharmacologica Sinica. 2014; 35(5): 557.
22. Schepers AW, Thibault J, Lacroix C. Lactobacillus helveticus growth and lactic acid production during pH-controlled batch cultures in whey permeate/yeast extract medium. Part I. Multiple factor kinetic analysis. Enzyme and Microbial Technology. 2002; 30(2):176-186.
23. Reddy G, Altaf MD, Naveena BJ, Venkateshwar M, Kumar E V. Amylolytic bacterial lactic acid fermentation- A review. Biotechnology Advances. 2008; 26(1): 22-34.
24. Hurley W L, Theil PK. Perspectives on immunoglobulins in colostrum and milk. Nutrients. 2011; 3(4): 442-474.
25. Kaetzel CS. Cooperativity among secretory Ig A, the polymeric immunoglobulin receptor, and the gut microbiota promotes host–microbial mutualism", Immunology Letters. 2014; 162(2): 10-21.
26. Conlon M, Bird A. The impact of diet and lifestyle on gut microbiota and human health. Nutrients. 2015; 7(1): 17-44.
27. Balch PA. Prescription for nutritional healing. Penguin. 2006.
28. Hunter BT. Probiotic foods for good health: Yogurt, sauerkraut, and other beneficial fermented foods. Basic Health Publications, Inc. 2008.
29. Sinha N, Sidhu J, Barta J, Wu J, Cano MP. Handbook of fruits and fruit processing. John Wiley & Sons. 2012.
30. Kushi LH, Doyle C, McCullough M, Rock CL, Demark-Wahnefried W, Bandera EV. American Cancer Society Nutrition and Physical Activity Guidelines Advisory Committee. American Cancer Society Guidelines on nutrition and physical activity for cancer prevention: reducing the risk of cancer with healthy food choices and physical activity. CA: A Cancer Journal for Clinicians. 2010; 62(1): 30-67.
31. Calder PC. Feeding the immune system. Proceedings of the Nutrition Society. 2013; 72(3): 299-309.
32. Balch PA. Prescription for dietary wellness. Penguin.2003.
33. Donsbach KW. Donsbach's Guide to Good Health- Long. Shadow Books. 1985.
34. Steinmetz KA, Potter J D. Vegetables, fruit, and cancer prevention- A review. Journal of the American Dietetic Association. 1996; 96(10): 1027-1039
35. Dhandevi PEM, Jeewon R. Fruit and vegetable intake: benefits and progress of nutrition education interventions-narrative. Review article. Iranian Journal of Public Health. 2015; 44(10): 1309.
36. Jacobson MF, Lefferts LY, Garland AW. Safe food: Eating wisely in a risky. World. Living Planet Press. 1991.

37. Popkin BM, D'Anci KE, Rosenberg IH. Water, hydration, and health. Nutrition Reviews, 2010; 68(8): 439-458.
38. Petraccia L, Liberati G, Masciullo SG, Grassi M, Fraioli A. Water, mineral waters and health. Clinical Nutrition. 2006; 25(3), 377-385.
39. Wardlaw GM, Kessel MW. Perspectives in Nutrition. 5th Edition McGraw-Hill Education, New York, 2002.
40. David A, Gail D, Adrianne B. Diet and human immune function. New Jersey: Humane Press. Inc. 2004.
41. Lokhande P, Kharche A, Wagh SG, Manithe D, Harke S. Immune boosting super food supplement from natural resources. Journal of Pharmacognosy and Phytochemistry. 2019; 8(5):2108-13.
42. Munkyong P, Simin M. Dayong Wu. The Role of Nutrition in Enhancing Immunity in Aging. Aging and Disease. 2012; 3 (1): 91-129.
43. Ronald W. Hand Book of Nutrition in the Aged, 4th Edition. Taylor and Francis Group - New York. 2009.
44. Hodkinson CF, Kelly M, Alexander HD, Bradbury I, Robson PJ, Bonham MP, et al. Effect of zinc supplementation on the immune status of healthy older individuals aged 55–70 years: the ZENITH Study. The Journals of Gerontology Series A: Biological Sciences and Medical Sciences, 2007; 62(6): 598-608.
45. Food Labeling: Health Claims; Calcium and Osteoporosis, and Calcium, Vitamin D, and Osteoporosis". U.S. Food and Drug Administration. 29 September 2008.
46. Mora JR, Iwata M, von Andrian UH.Vitamin effects on the immune system: vitamins A and D take centre stage. Nature Reviews Immunology. 2008; 8(9): 685-698.
47. Hughes DA. Effects of dietary antioxidants on the immune function of middle-aged adults. Proceedings of the Nutrition Society. 1999; 58: 79-84.
48. Erickson KL, Medina EA, Hubbard NE. Micronutrients and innate immunity. The journal of Infectious Diseases 2000;182: S5-S10.
49. Bendich A. Carotenoids and immunity. Clinical Applied Nutrition. 1991; 1:45-51.
50. Cunningham-Rundles S, Ahrn S, Abuav-Nussbaum R, Dnistrian A. Development of immunocompetence: Role of micronutrients and Microorganisms. Nutrition Reviews. 2002; 60(S5): S68-72.
51. WHO. Guideline: Vitamin A supplementation in infants and children 6–59 months of age. Geneva: World Health Organization. 2011.
52. Aranow C. Vitamin D and the immune system. Journal of Investigative Medicine. 2011;59(6): 881-886.
53. De Tena JG, Debekc AE, Gutiérreza CH, Alonso JLI. The Role of Vitamin D in Chronic Obstructive Pulmonary Disease, Asthma and Other Respiratory Diseases. Archivos Bronconeumologia. 2014; 50: 179-84.
54. Zhang Y, Leung DY, Richers BN, Remigio LK, Riches DW, Goleva. E. Vitamin D inhibits monocyte/macrophage proinflammatory cytokine production by targeting MAPK phosphatase-1. The Journal of Immunology. 2012; 188 (5): 2127-2135.
55. Gao D, Trayhurn P, Bing C. 1, 25-Dihydroxyvitamin D3 inhibits the cytokineinduced secretion of MCP-1 and reduces monocyte recruitment by human preadipocytes. International Journal of Obesity 2013;37(3): 357-365.

56. Meydani SN, Leka LS, Fine BC, Dallal GE, Keusch GT, Singh MF, Hamer DH. Vitamin E and respiratory tract infections in elderly nursing home residents. The Journal of the American Medical Association. 2004; 292(7): 828-836.
57. Maslova E, Hansen S, Strøm M, Halldorsson TI, Olsen SF. Maternal intake of vitamins A, E and K in pregnancy and child allergic disease: a longitudinal study from the Danish National Birth Cohort. British Journal of Nutrition. 2014; 111(6): 1096- 1108.
58. Bauersachs S, Kircbgessener M. Paulicks BR. Effect of different levels of dietary selenium and vitamin E on the humoral immunity of rats. Journal of Trace Elements and Electrolytes in Health and Disease. 1993; 7: 145-152.
59. Pallast EG, Schouten EG, de Waart FG, Fonk HC, Doekes G, Blomberg BM, Kok FJ. Effect of 50- and 100-mg vitamin E supplements on cellular immune function in noninstitutionalized elderly persons. The American Journal of Clinical Nutrition. 1999; 69: 1273-1281.
60. Pae M, Meydani SN, Wu D. The role of nutrition in enhancing immunity in aging. Aging and Diseases. 2012;3(1): 91-129.
61. Maggini S, Wintergerst ES, Beveridge S, Hornig DH. Selected vitamins and trace elements support immune function by strengthening epithelial barriers and cellular and humoral immune responses. The British Journal of Nutrition. 2007; 98: S29-S35.
62. Talbott MC, Miller LT, Kerkvliet NI. Pyridoxine supplementation: Effect on lymphocyte response in elderly persons. American Journal of Clinical Nutrition. 198; 746: 659-664.
63. Meydani SN, Endres S, Woods MM, Goldin BR, Soo C, Morrill-Labrode A, et al. Oral (n-3) fatty acid supplementation suppresses cytokine production and lymphocyte proliferation: comparison between young and older women. The Journal of Nutrition. 1991; 121(4): 547-555
64. Casciato DA, McAdam LP, Kopple JD, Bluestone R, Goldberg LS, Clements PJ, et al. Immunologic Abnormalities in Hemodialysis Patients:Improvement after Pyridoxine Therapy. Nephron. 1984; 38: 9-16.
65. Sakane T, Takeda S, Kotani H, Tsunematsu T. Effects of methyl-B12 on the in vitro immune functions of human T lymphocytes. Journal of Clinical Immunolology. 1982; 2(2): 101-109.
66. Vellema P, Rutten VP, Hoek A, Moll L, Wentink GH. The effect of cobalt supplementation on the immune response in vitamin B12 deficient Texel lambs. Veterinary Immunology and Immunopathology. 1996; 55(1-3): 151-161.
67. Crist WM, Parmley RT, Holbrook CT, Castleberry RP, Denys FR, Malluh A. Dysgranulopoietic neutropenia and abnormal monocytes in childhood vitamin B12 deficiency. American Journal of Hematology 9(1):89-107. Cross, M.L. and Gill, H.S. 2000. Immunomodulatory properties of Milk. British Journal of Nutrition. 1980; 84 Suppl 1: S81-89.
68. Youinou PY, Garre MA, Menez JF, Boles JM, Morin JF, Pennec Y, et al. Folic acid deficiency and neutrophil dysfunction. The American Journal of Medicine. 1982; 73(5): 652-657
69. Anderson R, Smit MJ, Joone GK. Vitamin C and cellular immune functions. Protection against hypochlorous acid-mediated inactivation of glyceraldehyde-3-phosphate dehydrogenase and ATP generation in human leukocytes as a possible mechanism of ascorbate-mediated

immunostimulation. Annals of the New York Academy of Sciences. 1990; 587: 34-48.
70. Sorice A, Guerriero E, Capone F, Colonna G, Castell G, Costantini S. Ascorbic acid: Its role in immune system and chronic inflammation diseases. Mini Reviews in Medicinal Chemistry. 2014; 14(5): 444-452.
71. Ziemlanski S, Wartanoicz M, Klos A, Raczka A, Klos M, Ziemlanski S, et al. The effect of ascorbic acid and alphatocophrol supplementation on serum protein and immunoglobulin concentration in elderly. Nutrition International. 1986; 2: 1-5.
72. Muscaritoli M, Molfino A, Laviano A, Rasio D, Fanelli FR. Parenteral nutrition in advanced cancer patients. Crit Rev Oncol Hematol. 2012
73. Brozmanová J. Selenium and cancer: from prevention to treatment. Klin Onkol. 2011; 24: 171-179
74. Spallholz JE. Selenium and glutathione peroxidase: Essential nutrient and antioxidant component of the immune system. Advances in Experimental Medicine and Biology. 1990; 262: 145-158.
75. Teixeira AG, Lima FS, Bicalho ML, Kussler A, Lima SF, Felippe MJ, et al. Effect of an injectable trace mineral supplement containing selenium, copper, zinc, and manganese on immunity, health, and growth of dairy calves. Journal of Dairy Science. 2014; 97(7): 4216-4226
76. Beck MA. Antioxidants and viral infections: host immune response and viral pathogenicity. Journal of the American College of Nutrition. 2001; 20 (5): 3845-3885.
77. Zagrodzki P. Selenium and the immune system. Postepy Higieny Medycyny Doswiadczalnej. 2004; 58:140- 149.
78. Turan H, Kaya Y, Balik SG. Etinin Besin Degeri ve Insan. 2006.
79. Onder F, Yildiz S. Çinko ve Bakir Yetersizliginin Bagisiklik Sistemine Etkileri. Kafkas Univ Ver Fak. Derg. 2002; 8: 183-187.
80. Schiffer RB, Sunderman FW, Baggs RB, Moynihan JA. The effects of exposure to dietary nickel and zinc upon humoral and cellular immunity in mice. Journal of Neuroimmunology. 1991; 34(2-3): 229-239.
81. Goldberg I. Nutrient control of immune function. In: Functional foods. pp. 88-108. Blumberg, J. B. (Ed.) Chapman & Hall press. London. 1994.
82. Chandra RK. Impact of nutritional status and nutrient supplements on immune responses and incidence of infection in older individuals. Aging Research Reviews. 2004; 3(1): 91-104.
83. Scrimshaw NS, Taylor CE, Gordon JE. Interactions of nutrition and infection. Nutrition Reviews. 1990; 48: 402-405.
84. Pocino MJ, Malave I Baute L. Zinc administration restores the impaired immune response observed in mice receiving excess copper by oral route. Immunophamlacology and Immunotoxicology. 1990; 12: 697-713.
85. Kelley DS, Daudu PA, Taylor PC, Mackey BE, Turnlund JR. Effect of low copper diets on human immune response. American Journal of Clinical Nutrition. 1995; 62(2): 412-416.
86. Chakraborty P, Das S, Banerjee K, Sinha A, Roy S, Chatterjee M, et al. A copper chelate selectively triggers apoptosis in myeloidderived suppressor cells in a drug-resistant tumor model and enhances antitumor immune response. Immunopharmacology and Immunotoxicology. 2014; 36(2): 165-175

87. Niederman CN, Blodgett D, Eversole D, Schurig GG, Thatcher CD. Effect of copper and iron on neutrophil function and humoral immunity of gestating beef cattle. Journal of the American Veterinary Medical Association. 1994; 204(11): 1796-1800.
88. Yuan K, Vargas-Rodriguez CF, Mamedova LK, Muckey MB, Vaughn MA, Burnett DD, et al. Effects of supplemental chromium propionate and rumen-protected amino acids on nutrient metabolism, neutrophil activation, and adipocyte size in dairy cows during peak lactation. Journal of Dairy Science. 2014; 7(6): 3822-3831.
89. Lee DN, Yen HT, Shen TF, Chen BJ. Chromium induced glucose uptake, superoxide anion production and phagocytosis in cultured pulmonary alveolar macrophages of weanling pigs. Biological Trace Element Research. 2000; 77 (I): 53-64.
90. Tam M, Gómez S, González-Gross M, Marcos A. Possible roles of magnesium on the immune system. European Journal of Clinical Nutrition. 2003; 57(10): 1193-1197