Original Article

The Inter-relationship Between Nutrition and Infections in Older People: A Review

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Article History
Submitted: 10/11/2023; Accepted: 07/12/2023: Published: 22/12/2023

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ABSTRACT

Old age is variously described as referring to individuals older than 60 or 65 years of age. The proportion of elderly patients is steadily on the rise. These elderly individuals have an increased propensity for sickness and death due to progressive age-related effects in their physical constitution. Increased rates of youth migration and changes in traditional support for older people predisposes them to the effects of poverty and socio-economic inequality in our environment. This review sought to evaluate the interconnections between infection and nutrition amongst the elderly population. A literature search was done for publications referencing the elderly, infections, and nutrition. The review showed that elderly patients, are predisposed to infection and malnutrition because of specific changes in the various tissue and organ functions. While the nutritional requirements reduce in old age, the ability to take in nutrients decreases to a larger degree, leading to a negative balance in nutrition. Age-related changes in innate and adaptive immunity also predispose elderly people to different forms of infection. Infection and malnutrition in elderly people create a vicious cycle feeding into each other to negatively impact on the health and quality of life of this group of people. As our elderly population increases, we recommend specific attention be paid to the twin problems of infection and malnutrition, in order to maintain the health status of the elderly.

Keywords: Elderly; Infection; Immunity; Malnutrition; Old age; Frailty.

INTRODUCTION

Aging is an inevitable process associated with anatomical structure and physical function changes that occur without disease[1]. By convention, the elderly or older people are those aged at least 65 years based on their chronological age or aged over 60 years according to the United Nations[4,2]. This time of life is when the rates for sickness and death begin to show a marked increase compared to the earlier years, hence the threshold for old age.[4] Older people can be divided into the "fit older people" and "frail older people".[5] The frail older people are at least 65 years old, cannot live independently, and may have a comorbid illness (clinically or by laboratory

Article Access

Website: www.wjmbs.org.ng
10.5281/zenodo.15336137

How to cite this article
Ibraheem GH, Ibraheem RM. The Inter-relationship Between Nutrition and Infections in Older People: A Review. West J Med & Biomed Sci. 2022;3(3-4):43-51. DOI:10.5281/zenodo.15336137.

examination).[5] Conversely, fit older people live independently and have no comorbid diseases[5]. Also, frailty in old age has been defined based on phenotype as an elderly person with at least three of the following: weight or muscle loss, muscular weakness, poor endurance, slow walking speed, or low activity[6]. Gerontologists divide old age into three categories, namely 'young' old age (defined as 65 to 74 years old), 'middle' old age (defined as 75 to 84 years old), and 'advanced' age (defined as over 85 years old)[7].

In Nigeria, Africa's most populous nation, the proportion of Nigerians over the age of 65 years has remained around 2.8% of the total population since at least 1980; however, the projection is a steady increase in the older population to 2.9% by 2030, 4.0% by 2050, and 10.1% by 2100.[8] Indeed, Nigeria already has the highest number of aged people in Africa[9]. The increasing poverty in the country, socio-economic inequality, poor health care services with out-of-pocket expenses for health, increased migration of the younger people and decline in the traditional care and support of older people are all contributory factors to an increase in the proportion of older people with malnutrition and infections[9].

It is thus important to evaluate and understand the interconnections between old age, nutrition, and infection with a view to reducing the result antmorbidity and mortality in this group of people.

MATERIALS AND METHODS

We conducted a comprehensive literature search using PubMed, EMBASE, and Google Scholar to identify relevant articles on the interconnection of nutrition and infections in older people. The search terms were “aging”, “ageing”, “older people”, “elderly”, “infection”, community-acquired infections”, healthcare-associated infections”, immunosenescence, “malnutrition”, and “nutrition.” We confined our search to articles published in English between 1980 and December 2022, and we identified relevant articles through a systematic process that included screening of article titles, abstracts, and full texts. Manual searches of reference lists of relevant articles provided additional articles. Inclusion criteria for the review were articles that discussed elderly people, ageing and infections, ageing and nutrition, immunity, immunosenescence, nutrition and infections in older people. Two reviewers independently performed the data extraction and synthesis, with the resolution of any discrepancies through discussion and consensus.

INFECTIONS IN THE ELDERLY

Infections cause morbidity and mortality worldwide, especially in older persons[10, 11]. It accounts for a third of deaths in the frail elderly[10, 11]. Their predisposition to infections may be associated with age-related immunosenescence and changes in organs, malnutrition, and underlying pathological changes from comorbid illness[10, 11]. Unlikefit older people, frail older people with comorbid diseases are more susceptible to common infections and exhibit weaker vaccine responses[10, 11]. Table 1 highlights other risk factors for infection in older persons. Respiratory, urinary, and gastrointestinal infections are the most common infections in the elderly[10,12].

Table 1: Causes of increased susceptibility to infections in the elderly[10]

- Reduced functional reserves
- Altered pathogen spectrum
- Reduced defence mechanisms
- Repeated/multiple hospital stay
- Delayed diagnosis and initiation of care
- Delayed response to antibiotics
- Increased occurrence of adverse drug reactions

CHANGES IN THE IMMUNE SYSTEM OF THE ELDERLY

Immunoscenesence, the gradual deterioration of the immune system due to ageing, increases the susceptibility of older people to infections[13]. The host-defence mechanism against infections includes physical barriers and innate and adaptive immune responses. In older people, the following changes occur:

Physical barriers

The diminished mucociliary clearance and cough reflex reduces the ability to clear organisms that enter the lungs, predisposing them to respiratory infections[13]. The elasticity of the bladder decreases with age. Consequent impairment in bladder capacity and emptying of the bladder predisposes to urinary tract infections (UTI)[14]. The combination of diminished gastric acid secretion, increased pH and reduced intestinal motility predisposes to bacterial

overgrowth and altered gut flora. Thus, the susceptibility to enteric infection increases[10] Furthermore, the reduction in the integrity of the epithelial barriers of the skin, lungs, and gastrointestinal tract (GIT) enables the invasion of the mucosal tissues by pathogens[15].

Innate immune response

Components of the innate system are complements, polymorphonuclear cells, macrophages, monocytes, dendritic cells, natural killer cells (NK-cells), and cytokines[16]. The innate system is the first defence against infection. Its role is to phagocytose the pathogen, initiate an inflammatory response, recruit NK cells, and facilitate the maturation of dendritic cells[16]. Table 2 shows the effect of ageing on the various cells of the innate system.

Table 2: Effects of ageing on the cellular components of the innate immunity in the frail elderly[17]

	Neutrophil	Macrophage	Dendritic cell	NK cell
Preserved	• Number • Phagocytosis • TLR2 and TLR4 expression • CM-CSFR expression	• Number		CD16-mediated cytotoxicity
Reduced	• Superoxide production • Chemotaxis • Apoptosis • Signal transduction • Molecular recruitment into lipid rafts	• Phagocytosis • Superoxide production • Chemotaxis • Signal transduction • Cytokine production • MHC class II expression	• Antigen presentation • Number of Langerhans cells • Langerhans cell migration	• Overall cytotoxicity • Pre cell cytotoxicity • Signal transduction • Response to cytokines • Cytokine production • Number of CD16+
Increased		• PGE2 production		

Abbreviations: TLR=Toll like receptor; GM_CSFR=granulocyte monocyte colony stimulating factor receptor; MHC= major histocompatibility complex; PG=prostaglandin; CD=cluster of differentiation

The quantity and phagocytic function of neutrophils are generally preserved in older persons, whereas other functions like superoxide production, chemotaxis, and apoptosis decline[17]. For monocytes and macrophages, the quantities are maintained,[15] but there is impaired phagocytic function[17]

The phagocytic function decreases in tandem with the amount of macrophage-derived cytokines[15,18.] Conversely, Prostaglandin E(2) production increases, contributing to dysfunctional immune responses in older people by suppression of interleukin (IL)-2 and IL-12 secretion and hence decrease T-cell function[18]. The reduced superoxide production of neutrophils and macrophages predisposes them to infections by catalase-positive organisms like *Staphylococcus aureus, Mycobacterium tuberculosis,* Enteric Gram-negative organisms, *Aspergillus*spp,and *Candida*spp.

Dendritic cells present antigens to T-cells in secondary lymphoid organs to initiate an immune response[16]. The number and function of both the plasmacytoid dendritic cells (pDC) and myeloid dendritic cells (mDC) are decreased in frail older people, while only the pDC is affected in healthy elderly[13]. Also, frail older people have reduced NK-cell activity compared to healthy older persons[19, 20] Furthermore, NK-cells' response to stimulation by IL-2 decreases[19]. Indeed, the NK-cells in older people tend to shift from a T helper (Th)-1 towards a Th-2 cytokine profile[13]. Consequently, there's an increase in the susceptibility of frail older people to viral infections[17,19].

ADAPTIVE IMMUNE RESPONSE

Humoral response

There is a decline with age in the clonal proliferation and differentiation of pro-B lymphocytes into pre-B lymphocytes in the bone marrow[13]. However, the peripheral B-lymphocytes remain normal[13]. Also, the B-cell receptor repertoire of B-cells is altered with a decrease in affinity and diversity of antibody response. Plasma immunoglobulin (Ig) levels, especially IgA and IgG, increase with age[21]. However, the antibodies have reduced avidity because of impaired somatic hypermutation[13,15]. The T-cell-dependent antibody response is specifically affected.Subsequently, there is a decrease in their ability to respond effectively against some viruses and bacteria[15]. Influenza and respiratory syncytial virus are some viruses that commonly affect elderly patients as a result of impaired humoral function.

Cell-mediated response

An ageing-related decrease in the thymus size and function occurs with a resultant decline in T-cell output to the peripheral blood[13, 15]. Also, a restricted T-cell repertoire occurs, which increases susceptibility to infections in older people[13,21]. There are fewer mature T-cells compared to naïve T-cells[21] The decreased CD4+ T-cell function impairs the T-cell-dependent antibody response. Furthermore, aged naïve CD4+ T-cells cannot produce IL-2 when stimulated by T-cell receptors. Consequently, there

is the generation of poorly polarised Th-1 and Th-2 subsets and a propensity to generate functional Th-17 subsets[13]. Indeed there is an imbalance in Th-17/Treg ratios (high Th-17 and low Tregs). These contribute to an imbalance in the pro-inflammatory and anti-inflammatory responses predisposing to inflammatory diseases in older people[15]. The decrease in CD8+ T-cell repertoire diversity impairs cytotoxicity and,thus, the ability to respond to intracellular infections such as viral infections[13]. Indeed, the age-related decline in delayed-type skin hypersensitivity (DTH) reflects the reduced ability of the older person to mount a substantial T-cell response[21].

The nutritional requirements and nutritional status of the frail elderly

Generally, a change in body composition with increasing age results in decrements in lean body mass[22]. This decline is rapid after 60 years. Consequently, the energy requirements decrease by about 100kcal/day/decade[23]. Yet, frail older peopleoften cannot meet the daily nutrient requirements (micronutrient and macronutrient) for this low caloric intake[23]. The energy intake and physical activity levels in frail elderly are reduced compared to healthy elderly[24].

Anthropometry is one of the assessment methods utilised in the frail elderly[23,25,26.] Other methods are the biochemical assessment (for micronutrients), clinical assessment, and dietary questionnaires[25,26]. The Mini-Nutritional Assessment (MNA) tool combines these methods for frail older people[23]. A weight loss of 5% or more in a month is a predictor of mortality, and should warrant an immediate evaluation by the physician[23].

Undernutrition is a problem in frail older people[27]. Low dietary intakes of protein, fibre, carbohydrates, and micronutrients are associated with frailty[28,29]. The prevalence of undernutrition was 3-10% in healthy elderly compared to 30–60% in institutionalised patients and 15–65% of hospitalised patients[27]. A recent systematic review on undernutrition in community-dwelling elderly in Africa reported an overall prevalence of 20.9%; for Nigeria, the range was 7.3-25.1%.[30] For those seen within the hospital in Nigeria, the prevalence of undernutrition from previous Nigerian studiesranges between 7.8%-25.3%.[31-33]. In frail older people, there are insufficient macronutrients and micronutrients to meet optimal physiological requirements, causing consequences of undernutrition and micronutrient deficiencies[27]. The predisposition to nutritional deficiencies arises from various factors, as shown in Table 3.

Table 3: Factors that contribute to the development of nutritional deficiency in older people[27]

Determinanats of nutritional deficiency	Consequences
Physical and physiological changes	
❖ Changes in body composition	
➢ Reduced amount of lean body mass	✓ Reduced metabolic rate
➢ Increased amount and distribution of fat stores	✓ Reduced energy requirements
➢ Reduced cellular capacity to store water	✓ Decline in strength and balance
	✓ Increased truncal obesity
	✓ Dehydration
❖ Changes to the gastrointestinal tract	
➢ Oral health problems including improperly fitted dentures, gingivitis, missing teeth	✓ Poor appetite ✓ Reduced food intake
➢ Reduced gastrointestinal motility, atrophic gastritis, reduced volume of digestive juices (e.g. hypochlorhydria, saliva)	✓ Reduced absorption of folic acid, vitamin B12, calcium, iron and beta-carotene
❖ Changes in sensory function	
➢ Diminished sense of taste possibly related to zinc deficiency and/or reduction in the number of taste buds/papilla (on the tongue)	✓ Poor appetite ✓ Inappropriate food choices
➢ Diminished sense of smell	✓ Decreased energy
❖ Changes in fluid and electrolyte regulation	
➢ Reduced glomerular filtration rate, decreased renal plasma flow, reduced ability to regenerate nephrons	✓ Dehydration ✓ Delirium
➢ Altered thirst sensation	✓ Dementia
Chronic diseases	
➢ Stroke, cancer, dementia, diabetes, depression, visual impairments, arthritis and osteoporosis	✓ Increased morbidity ✓ Loss of dexterity, coordination and mobility ✓ Increased metabolic rate ✓ Poor appetite ✓ Nausea ✓ Difficulty with food preparation
Medication and hospitalization	✓ Chemosensory impairments ✓ Altered absorption, utilization or excretion of nutrients
Psychosocial	
❖ Social determinants	
➢ Financial restraints and poverty	✓ Poor appetite
➢ Social isolation, reduced mobility and lack of transport	✓ Reduced food security
➢ Decreasing independence	✓ Innapropriate food choices
➢ Widowhood and bereavement	✓ Decreased energy ✓ Inability to self-feed ✓ Food aversion

Age-related changes

GIT: Changes in taste and smell, poor dentition or poorly-fitted dentures, and diminished saliva contribute to reduced food intake in older people.[23,34.] Others are decreased oesophageal motility, early satiety, delayed gastric emptying after a meal, atrophic gastritis, and decreased intestinal motility[23].

Kidney: Renal function declines with age with decreased responsiveness to antidiuretic hormone. Consequently, this affects thirst need and predisposes older people to dehydration[23]. Also, Vitamin D metabolism in the kidneys declines, predisposing to low serum levels of Vitamin D.

Skin: Aging decreases the skin content of the precursor of Vitamin D (7-dehydroxycholesterol), from which most Vitamin D requirements are met.This inability to get enough from the skin predisposes to Vitamin D deficiency[29].

Body mass: The rapid decline in lean body mass in older people is associated with low performance, loss of strength, decreased protein reserves, increased disability, and increased risk for falls and injuries[28,29]. These predispose to functional disabilities (poor coordination) that will result in diminished food intake.

Medical Factors

Chronic diseases may cause anorexia due to the illness or medications. Memory loss and confusion (dementia) result in reduced food intake[19].

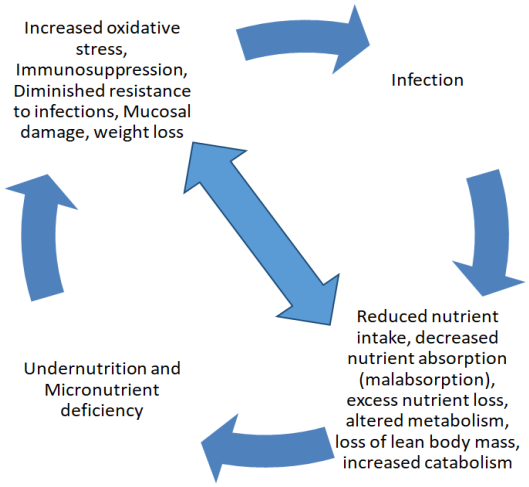
Social factors

Poverty, lack of regular caregivers, and a low zeal to cook a proper meal as it may be seen as a bother due to the time it takes, may predispose to undernutrition[34].

The relationship between infection and nutrition in the elderly

Infections in older people affect nutrition by causing low intake with resultant under nutrition. Also, malnutrition of frail older people negatively impacts their immune response, increasing their susceptibility to infections. These create a vicious cycle(Figure 1).

Figure 1: The vicious cycle of infection and malnjutrition[43]



Effects of infection on nutrition

Infections increase an individual's need for energy and protein, increasing their metabolic rate.[35] Furthermore, the rise in temperature associated with infections from pyrogens contributes to the increase in energy requirement[36]. Anorexia due to infections from the cytokines contributes to the poor appetite in frail older people. In addition, enteric infections compromise the intestinal mucosa and villi, resulting in the malabsorption of macronutrients and micronutrients[35,36]. Also, the cytokines released in response to an infection interfere with efficient fat utilisation. Indeed, there is a pro-inflammatory mediated redistribution of skeletal muscle and adipose tissue towards the host immune response[36].

Effects of nutrition on infection

Macronutrients- Frail older people with a reduced food intake cannot meet the elevated energy demand. Although the reduced physical activity level in frail older people reduces energy expenditure, the combined requirement due to the illness, the reduced intake, and losses from impaired kidney function outstrip it[20]. Hence, the carbohydrate body reserves are rapidly used in infections.

The body, therefore, breaks down the body tissues to generate the needed energy. The tissue breakdown causes weight loss[36]. During an infection, increases in protein and energy requirements occur from synthesising acute-phase proteins, complements, immunoglobulins, and proliferation of leucocyte needs for the immune response[36]. The protein synthesis also requires energy intake that the body cannot meet from the rapidly exhausting body reserves of carbohydrates alone. Indeed, in infections, the daily protein requirement for the immune response increases to 45 grams[37]. A frail elderly with low intake can't cope.

Fats can modify cytokine functions; hence, dietary fat influences the type of prostaglandins and leukotrienes produced by tissues targeted by cytokines[38]. The unsaturated fats can insert into the cell membrane and affect the phospholipid contents of the membrane[38]. The dietary consequence is an anti-inflammatory response by either*n-3* polyunsaturated fatty acids [PUFA] from seafood or monounsaturated fatty acids from butter and olive oil) for example. A pro-inflammatory response (*n-6*PUFA derived from corn or sunflower oil) is also likely[38, 39]. In frail older people, *n-3*PUFA could ameliorate inflammatory symptoms.

Micronutrients: Consists of vitamins, minerals, and trace elements essential for basic metabolic processes such as protein synthesis, cell proliferation, and cell differentiation[39]. They are germane for immune response to infection. For example-

- Vitamin E increases cytokine production, and its deficiency in older people affects the antioxidant function and impairs humoral and cell-mediated immune responses[35,40]. In frail older people, Vitamin E supplementation reduces the incidence of

upper respiratory tract infections[41].

- Vitamin A also increases cytokine production, maintains epithelium integrity, modulates lymphocyte activation and proliferation, and enhances NK-cell activity[32,40]. B-carotene has an antioxidant effect in frail older people[21]. Its' deficiency in older people may affect the epithelium of the respiratory tract and mucociliary function, with high susceptibility to respiratory infections. Vitamin A deficiency affects cell-mediated immunity and can cause an impaired response to delayed cutaneous hypersensitivity (DCH) tests.[40]
- Vitamin B6 is a cofactor for enzymes of amino acid metabolism, thereby affecting the immune system. It increases IL-2 production in older people. Vitamin B6 deficiency has been associated with a decrease in both humoral and cell-mediated immune responses.[39]
- Iron is essential for lymphocyte proliferation and acts as a metalloenzyme for myeloperoxidase.[39] Myeloperoxidase in phagocytes catalyses the oxidative burst-derived hydrogen peroxide to form reactive halide radicals.[42] Hence, iron deficiency decreases the bacterial killing capacity of the phagocytes. It also reduces cytokine production.[42] Excess iron causes an increase in cellular cytokine production, impairs immune function by reducing reactive oxygen intermediaries produced by neutrophils, and makes iron available to pathogens[42]. These all predispose to infections, e.g. *Yersinia* spp.
- Zinc acts as a metalloenzyme for gene expression in lymphocytes, regulates acute-phase protein production, and supports the differentiation of T-cells in the thymus[39]. Zinc deficiency reduces lymphocyte production, causes a low ratio of mature to immature T-cells, and impairs the host defence. These result in an impaired DCH response[39]. Hence, the increase in susceptibility of frail elders to infections.

CONCLUSION

Frail older people are vulnerable to infections and nutritional deficiencies due to age-related changes in organs and immune responses, chronic illnesses, and social factors. An interplay between infections and malnutrition creates a vicious cycle. Strategies to manage frail elderly patients need to balance the interplay between infections and malnutrition to improve the health and quality of life of this important segment of the society. It is important to pay specific attention to the nutritional status of the elderly to maintain their immunity and resistance to infections. Geriatric care should include specific macro and micro-nutrient supplementation in the same way we provide Vitamin A and D supplementation to growing children.

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