

# Dietary Patterns for Immunity Support and Systemic Inflammation against Infections: A Narrative Review

*Budhi Setiawan and Masfufatun Masfufatun*

## Abstract

Nutrition has been recognized to play a regulatory role in human immune response and inflammation which may affect the pathogenesis of diseases. Current evidence suggests that the habitual dietary pattern therapeutical approach provides more synergistic beneficial action than the intervention of a single nutrient constituent. Several healthy dietary patterns are essential for the human immunity support against infectious diseases through alleviation of systemic inflammation. Long-term dietary patterns may affect the diversity of intestinal microbiota composition and lead to the decrease of pro-inflammatory cytokines from immune-related cells. Protease that may cause gut barrier breakdown (leaky gut) can be reduced either thus lessen translocation of endogenous bacterial endotoxin such as lipopolysaccharides (LPS) from the gut lumen to the bloodstream. In this review, we discuss the relationship between common healthy food-based dietary patterns with the protection of infectious diseases as a result of improvement in immune function and low-grade inflammatory indices. In contrary to the deleterious impact of the western diet, healthy eating habits (Mediterranean diet, dietary approaches to stop hypertension, plant-based diet, ketogenic diet) are associated with reduced susceptibility to infectious disease by the improvement of certain underlying metabolic comorbidities. Further studies are needed to determine suitable strategic implications of healthy dietary patterns on infectious disease mitigation in a particular context.

**Keywords:** nutrition, bioactive, dietary pattern, immunity, inflammation, oxidative stress, antioxidant, infectious disease

## 1. Introduction

The benefit of dietary patterns has appeared as a complementary and alternative approach to the study of the relation of diet and the risk of diseases. In contrast to a single substance or nutrient approach, an evaluation of whole dietary patterns may provide a more complete picture of a combination of foods and nutrients, such as synergistic and antagonist properties of the foods [1]. People do not eat isolated nutrients and rather consume foods that contain a variety of foods with complex interactive combinations of nutrients. Thus, a single active substance approach might be insufficient for considering complex interactions between food bioactive

components in the human study such as vitamin C improves Fe absorption [2]. Often, the high degree of intercorrelation between nutrients (e.g. magnesium and potassium) can be difficult for the evaluation of their separate effects in particular conditions [3]. Additionally, the cumulative effects of several nutrients are more likely detectable compared to the influence of a single substance. In the clinical trial setting, the dietary patterns approach has shown a positive health outcome in degenerative diseases [4]. Nutritional approach as dietary pattern intervention (e.g. Dietary Approaches to Stop Hypertension and Mediterranean Diet) as an integral part of disease management have been studied extensively on metabolic chronic diseases (cardiovascular diseases and diabetes) with beneficial clinical results [5, 6].

To what extend dietary patterns beneficial as an integral part of management and prevention strategy for communicable disease? The dietary pattern approach is more likely not only effective for non-communicable diseases but also infectious diseases [7]. Perhaps, this is a possible explanation that partial nutritional intervention exhibits lower than expected results in infectious diseases study settings. Partial nutritional interventions (macronutrients or micronutrients supplementation) as adjunctive treatment of standard antituberculosis agents among active tuberculosis patients is one of the examples. These nutritional interventions have shown no beneficial effects for main treatment outcomes. Even though the supplementation improves weight gain of the TB patients in some settings [8]. World Health Organization (WHO) has declared officially coronavirus diseases (COVID 19) as a global pandemic on 11 March 2020. Currently, there have been several attempts to recommend nutritional approaches for mitigation strategy the disease [9–14]. The dietary pattern plays important role in this communicable disease due to its severity is affected by a previous underlying disease. Comorbidities such as respiratory system diseases, chronic obstructive pulmonary diseases (COPD), diabetes, hypertension, cardiovascular/cerebrovascular disease have shown significant evidence of associations with the severity and prognosis of COVID-19 [15].

Intestinal dysbiosis (gut microbiota imbalance) recently has been proposed as a significant factor that is associated with several immune-related human diseases including infectious, inflammatory, neoplastic, metabolic, autoimmune diseases [7, 16, 17]. Within the gut lumen itself, the human gut microbiome will provide antigens and signals with the potential to interact with resident and systemic immune cells. The composition of the gut microbiome changes over the life course, in response to dietary components, infection, antibiotic exposure [18]. All of these may result in dysbiosis. During this condition, nutritional changes have been suggested as a suitable approach to restoring a healthy gut microbiota and host homeostasis [19]. Also, it has been proposed dietary patterns such as Mediterranean diet and low-fat diet possess the ability to restore partially microbiota dysbiosis [20]. Despite commonly studied single nutrient supplementation, this narrative review aimed to provide current perspectives on the association between the major dietary patterns and infectious disease susceptibility through immune response and systemic inflammation. Relevant articles (original articles, literature reviews, systematic reviews and meta-analyses articles) that identified major dietary patterns and related keywords (e.g., “infection”, “disease”, “immune system”, “inflammation”, and “gut microbiota”) were searched in Google Scholar, PubMed, MEDLINE, and Cochrane databases from the year 2010 to the year 2020 with exception for one article.

## 2. The role of bacteria homeostasis in gastrointestinal

Dietary patterns and quantity of food intake have been described to influence the microbiome in the gut [21]. *Bacteroidetes*, *Firmicutes*, *Actinobacteria*,

*Fusobacteria*, *Proteobacteria* and *Verrucomicrobium* are predominant phyla of microbiota in the human gastrointestinal tract [22]. Among these phyla, more than 90% of the microbiome colonies in the colon are *Bacteroidetes* (*Bacteroides*, *Prevotella*) and *Firmicutes* (*Eubacterium*, *Lactobacillus*) [23]. In Western countries, it has been shown that *Firmicutes* phylum becomes blooming and *Bacteroidetes* phylum population decrease due to prominent animal product consumption [24]. On the other hand, it has been demonstrated that high content fiber in the diet resulted in more *Bacteroidetes* phylum bacteria dominance and an increased amount of concentration of short-chain fatty acids (SCFAs) among children from Africa compared to children of European origin [25]. Short-chain fatty acids are fatty acids with fewer than six carbon atoms (acetate, propionate, and butyrate) derived from intestinal microbial fermentation of dietary fibers and resistant starch [26]. The concentration of short-chain fatty acids in the colon and systemic blood is crucial for immune response regulation. The fermentation of dietary fiber by gut microbes, resulting in the establishment of SCFAs, has been proposed to regulate anti-inflammatory pathways through numerous receptors such as G-protein coupled receptors [27]. Additionally, fermented foods and beverages are found to produce beneficial improvements in intestinal barrier function and permeability [28].

It has been suggested that vegan or vegetarian diets may stimulate intestinal microbiota that promotes anti-inflammatory response and lead to be more varied and steadier microbiota systems [29]. Contrary to this, particular food items such as red meat, gluten in wheat, and alcohol can induce dysbiosis which might cause a heightened pro-inflammatory response triggered by viral infections such as COVID-19 from underlying diet-derived chronic inflammation [21]. This intestinal mucosal chronic inflammation is characterized by the presence of cytokines (TNF- $\alpha$  and IFN- $\gamma$ ) which are produced by macrophages, T-cells and natural killer. Besides cytokines, various proteases are also released into the mucosa that has been reported to cause leaky gut due to degradation of tight junctions [30]. Thus, leaky gut allows translocation of microbial products such as lipopolysaccharides (LPS) from the gut into the blood circulation. This condition may transform the existing state of gut inflammation into chronic systemic inflammation during infections such as HIV [31]. This chronic inflammation may remain undetected as a predisposing risk factor and can develop any time into serious morbidity including infectious diseases [23].

Several studies have shown the association between the change of intestinal microbiomes with infectious diseases. It has been reported that intestinal bacterial diversity significantly decreases inversely associated with the severity in patients of chronic viral hepatitis C compared to healthy individuals. The gut microbiome could be a biological indicator and a novel potentially therapeutical approach to reduce the complications of chronic liver disease [32]. Another study has identified *Lachnospiraceae*, *Ruminococcaceae*, and butyrate-producing anaerobic bacteria can be significantly decreased in diarrhea caused by *Clostridium difficile* infection [33]. A short-term nutritional intervention study has reported the positive effect of the supplement on HIV-associated dysbiosis, which was most apparent among untreated individuals but less so in subjects with anti-retroviral therapy, whose gut microbiota was found more resilient [34].

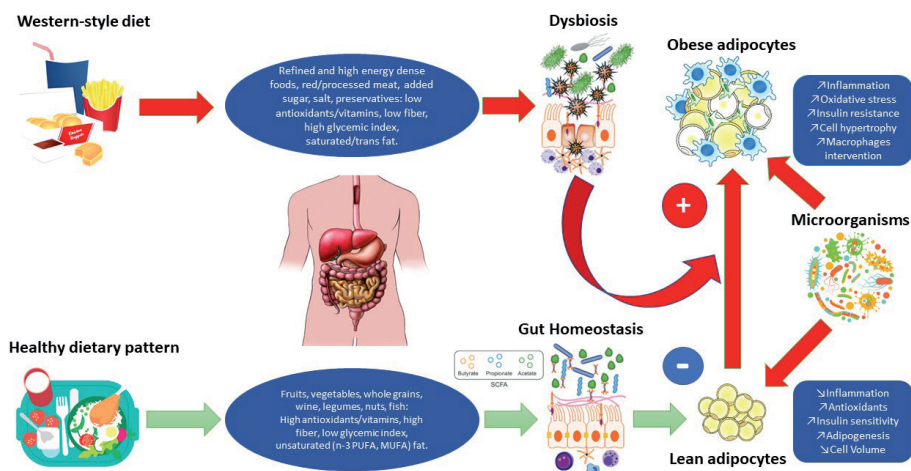
In contrast to short-term supplement intake, long-term dietary patterns and habitual diet are key factors that influence the composition of the gut microbiota. It reflects the potential for therapeutic dietary approaches to modulate microbiome variety, formation, and stability. Besides diet, the intestinal bacteria are formed by a composition of extrinsic (e.g., lifestyle and medication) and intrinsic (e.g., host genetics, immune and metabolic regulations) factors [35]. Changes in dietary patterns following the western diet, along with modifications in dietary components,

result in significant changes in the intestinal microbial configuration and function. As an example, changing from a low-fat, high-fiber diet to a high-fat, high-protein, low-fiber diet leads to reduced  $\alpha$ -diversity (intra-individual gut microbiota richness), increased  $\beta$ -diversity (inter-individual gut microbiota diversity) and deteriorated richness or even the extermination of *Prevotella* and *Treponema* species, with lower butyrate levels [36].

### 3. Western-style diet effect

From a current perspective, the western diet is defined as a modern diet that is primarily characterized by high consumption of red and processed meat, sugar-sweetened beverages, with a lower intake of cheese, wine, beer, cream, tea, vegetables and high-fiber foods [37]. This dietary pattern combined with a sedentary lifestyle can induce chronic systemic metabolic inflammation, termed as meta-inflammation. Systemic inflammation generates common prevalent modern non-communicable disease [38]. Western diet-induced obesity can result in gut dysbiosis then change lean adipocytes to obese adipocytes. **Figure 1** describes deleterious impact of the alteration to macrophages and adipocytes that lead to metabolic syndrome and diabetes. The western diet is closely associated to several degenerative or metabolic conditions such as obesity [40], metabolic syndrome [41], diabetes [42], cancer [43], hypertension [44], cardiovascular diseases [45], chronic kidney disease [46], and Alzheimer's disease [47].

Western diet pattern may also increase the risk of communicable diseases. It has been shown that women with the western diet might have a higher risk of Human Papilloma Virus infection compared to the Mediterranean-like diet [48]. People with obesity due to the western diet pattern may have a higher level of inflammatory cytokines, immunologic tolerance to inflammatory cytokines, reduced leukocyte number and function, and less control of infection [49]. Subsequently, obesity becomes a risk factor for increased morbidity and mortality of COVID-19 [50–53].



**Figure 1.** Unhealthy dietary pattern (western-style diet) along with sedentary life style and genetic predisposition may lead to dysbiosis and contribute toward obesity. Obesity may induce changes to adipocytes and macrophages lead to abnormal inflammation response, decrease insulin sensitivity, and low antioxidant capacity that may finally induce systemic inflammation, oxidative stress, and insulin resistance [39]. On the other hand, healthy dietary pattern provides fiber derived short chain fatty acids (SCFAs) that regulate intestinal barrier and immune system through protein G-coupled receptors signaling. Preservation of gut homeostasis may prevent leaky gut thus reduce inflammation during infection by microorganisms through several mechanisms.

Body mass index (BMI) has been proposed as a prognostic score since higher BMI (BMI  $\geq 30$  kg/m<sup>2</sup>) more likely results in poor outcome in COVID-19 patients [50, 53]. Body mass index  $\geq 30$  kg/m<sup>2</sup> is more likely associated with lower oxygen saturation of blood by weakened ventilation at the base of the lungs. Furthermore, systemic low-grade inflammation due to obesity may occur, such as higher levels of pro-inflammatory cytokines may result in compromised immunity [54]. Therefore, obese COVID-19 patients should receive special attention for their treatment.

Similarly, other non-communicable diseases strongly associated with western diet patterns are also comorbidities for COVID-19. Some comorbidities have been extensively investigated such as diabetes, hypertension, cardiovascular diseases, cerebrovascular diseases, chronic respiratory system diseases, chronic kidney disease [54–57]. Since SARS CoV-2 invades the host cell via ACE-2 receptor on the surface of the cell, certain comorbidities have a strong association with ACE-2 receptor upregulation and impaired immune response that may give rise to susceptibility for viral invasion into the host cells [54]. The infection of SARS-CoV-2 among individuals with these comorbidities can be harmful and might end up with acute respiratory distress syndrome, multiple organ failure, shock, arrhythmias, heart failure, renal failure, and, eventually, mortality [58].

## 4. Healthy dietary patterns

### 4.1 Mediterranean diet

Mediterranean diet is a dietary pattern traditionally applied by people who live near Mediterranean Sea, particularly in the region where olive trees are cultivated. It describes the frequent consumption of vegetables, fruits, legumes, nuts, and olive oil as a primary fat source. Additionally, this eating habit is characterized by moderate consumption of fish, poultry, dairy products, wine, and limited intake of red meat [59]. The dietary pattern is one of the most frequently studied for the protective effect of non-communicable diseases such as cardiovascular disease and coronary heart disease [60–62], diabetes [63–65], cognitive disorders [66–68], and malignancies [69–71]. It might be due to the effect of reduced inflammation through changes of C-reactive protein level [72], myeloperoxidase and 8-hydroxy-2-deoxyguanosine [73], white blood cell count and fibrinogen [74], methylation in inflammation-related genes [75]. Additionally, the diet habit also demonstrates modulation of the gut microbiome that results in a reduction of metabolic endotoxemia and subsequently lower systemic inflammation [73, 76, 77].

More likely these positive effects of Mediterranean may produce also protection for infectious diseases. Among communicable diseases, this dietary approach has been proposed for COVID-19 to reduce the mortality rate through the suppression of cytokines [78]. The Mediterranean diet might describe a possible dietary approach to mitigate both short - and long - term complications related to COVID-19 infection. It may decrease the severity and improve mortality and improve the overall well-being of affected populations [79]. **Table 1** shows several studies related to beneficial effects of Mediterranean diet among individuals with diseases caused by virus. A viral infection disease such as chronic hepatitis C and B viruses has shown an inverse correlation to the Mediterranean diet adherence [81]. Cervical cancer that caused by human papillomavirus also has described the same tendency in relation to this dietary pattern and opposite results can be caused by unhealthy diet habit [83]. Mediterranean diet has been found to be beneficial on metabolic indices in human immunodeficiency virus (HIV) patients with the highly active antiretroviral therapy [80]. Perhaps, parasitic infections could be also mitigated by the Mediterranean diet



Author and year	Dietary pattern	Study design (n) and assessment	Population	Outcomes
Tsiodras, S., et al. 2009 [80]	Mediterranean dietary pattern	Cross-sectional study (n = 227). Food frequency questionnaire (FFQ), and Mediterranean Diet Score (MedDietScore).	Human immunodeficiency virus (HIV) positive adult patients with the highly active antiretroviral therapy (HAART) in Israel.	Adherence to a Mediterranean dietary pattern was favorably related to cardiovascular risk factors such as insulin resistance, high density lipoprotein level, and circulating triglyceride level.
Turati, F., et al. 2014, [81]	Traditional Mediterranean diet.	Case-control study (n = 518 vs. n = 772). MedDietScore.	Adult hepatocellular carcinoma (HCC) patients, chronic infection with hepatitis B and/or C viruses in Italy and Greece	Adherence to the Mediterranean diet demonstrates protective effect against HCC. Potential benefits from adhering to the dietary pattern for individuals with chronic infection of hepatitis viruses.
Policarpo, S., et al. 2017 [82]	Mediterranean diet	Cross-sectional (n = 571). MedDietScore	Adult HIV positive adults in Portugal	A higher adherence was associated to individuals with a BMI $\geq 25$ kg/m <sup>2</sup> , to subjects with metabolic syndrome and to patients with moderate to high cardiovascular risk.
Barchitta, M., et al., 2018 [83]	Mediterranean diet, prudent dietary pattern, western style diet	Cross-sectional study (n = 539). FFQ and MedDietScore.	Adult women with high-risk human papillomavirus (hrHPV) infection and the risk of high-grade cervical intraepithelial neoplasia (CIN2+) in Italy	Inverse association of Mediterranean-like dietary patterns with hrHPV infection and cervical cancer. The outcomes discourage unhealthy eating habits.

**Table 1.** General characteristics of studies examining the role of Mediterranean diet on mitigation of communicable diseases caused by virus.

via the positive effects of omega-3 and omega-9 from olive oil and fish intake. These fatty acids modulate intracellular pathways and transcription factor activation, as well as metabolic and immune regulatory effects [84].

Polyphenols, monounsaturated and polyunsaturated fatty acids, or fiber are more likely bioactive ingredients of the Mediterranean diet [85]. Olive oil is one of the main components of the Mediterranean Diet which has a high profile of fatty acids and phenolics. Oleic acid, a predominant monosaturated fatty acid component in olive oil that can prevent inflammation and insulin resistance induced by palmitic acid in skeletal muscle, adipose tissue, pancreas, and liver. This preventing effect might be due to a reduction in palmitic acid-mediated adenosine monophosphate-activated protein kinase activity which is similar to Metformin [86].

Several minor constituents of Olive oil demonstrate possible synergic effects to counter inflammation. Oleocanthal is known as a minor ingredient of olive oil with significant anti-inflammatory properties that may have therapeutic potential [87]. It has been shown that Oleocanthal has a natural anti-inflammatory property by inhibition of cyclooxygenase enzymes [88]. Hydroxytyrosol is another salient minor phenolic compound of Olive oil that exhibits potential nutraceutical through immunomodulatory and nutrigenomic mechanisms [89].

The immune system is closely correlated with inflammatory processes and oxidative stress [90]. The precise mechanism of oxidative stress during infection is not fully understood, but free radicals have played an important role to defend against micro-organism's invasion [34]. Persistent oxidative stress may happen during chronic viral infections and has been associated with a weakened immune system due to long-lasting inflammation activation [90]. The anti-inflammatory effect of the Mediterranean diet may stop a vicious circle in which chronic oxidative stress and inflammation feed each other. Therefore, the Mediterranean diet might prevent further consequences such as impaired immune response. Additionally, The Mediterranean diet which rich in unsaturated fats and fiber may reduce the circulating level of endotoxin from gastrointestinal bacteria that has been proposed as a cause of inflammation [76]. In other words, The Mediterranean dietary patterns possess the ability to restore the gut to normal microbiota homeostasis through its anti-inflammatory effect [91]. Since gut microbial communities are involved in the modulation of the host innate and adaptive immune response so that this approach will play an important role in future therapeutic development for major global infectious diseases [92].

#### **4.2 Dietary approaches to stop hypertension (DASH)**

The Dietary Approach to Stop Hypertension (DASH) was designed as a non-pharmacological treatment for lowering blood pressure among adults. The dietary pattern consists of a higher intake of fruits, vegetables, whole grains, fish, poultry but less consumption of saturated fats, meat, and sugar. As result, DASH diet is high in calcium, potassium, magnesium, fiber, and protein. It is not a restricted sodium diet but its effect can be improved by less sodium consumption [93]. Adoption of this dietary pattern is effective not only in reducing blood pressure but also results in lower body weight so that it might be suitable for bodyweight management in overweight or obese individuals [94, 95]. Besides, the diet has shown an association with a lower incidence of cardiovascular diseases, coronary heart disease, stroke, and diabetes. The evidence of cardiometabolic beneficial effects is not only among diabetes patients but also people without diabetes [96]. It has been demonstrated that DASH can control glucose level, infant birth weight and decrease gestational preeclampsia risk among pregnant women [97, 98]. DASH approach is also associated with lower mortality from different cancer types [99, 100]. It means this dietary pattern is suggested as an effective treatment approach for various non-communicable diseases with long-lasting effect [101].

Since hypertension, diabetes and cardiovascular diseases are well-known comorbidities for viral infection COVID-19 [15, 102, 103], so that DASH might be helpful to mitigate the severity and fatality of the disease. The foods in the dietary pattern are rich in bioactive compounds that exhibit potent modulation of pro-inflammatory pathways and may support the immune response to reduce the morbidity and mortality of an infectious disease [104]. Furthermore, the improvement of the antioxidant defense of the body and decrease oxidative stress can be achieved by adherence to DASH diet. These effects might be due to lower malondialdehyde and glutathione levels mechanism [105]. It is suggested that oxidative stress plays a dual role during infections. Reactive species (e.g., nicotinamide adenine dinucleotide

phosphate oxidase, myeloperoxidase, and nitric oxide synthase) can induce cell apoptosis or destroy invading microorganisms as a defense mechanism. However, they can also cause tissue injury and resulting inflammation [106]. It has been proposed that the immune system plays important role in the etiology of hypertension. The DASH may promote the expansion of protective microbes that release gut metabolites such as short-chain fatty acids which are protective for the immune system and blood pressure [107]. Eventually, a healthy eating habit supports the immune system that protects against the invasion of microorganisms or viruses and produces antibodies to eradicate pathogens.

### **4.3 Plant-based diet**

The plant-based diet generally consists of two dietary patterns: vegetarian diets and vegan diets. Vegetarian diets are characterized by reduced or eliminated animal products intake but may include dairy products and/or eggs, while vegan diets contain only plant foods. Both vegetarian and vegan are dietary patterns that emphasize the consumption of vegetables, fruits, grains, legumes, and nuts [108]. Several potential beneficial effects of a plant-based diet are ameliorating insulin resistance, including preservation of healthy body weight, higher intake in fiber and phytonutrients, promoting food-microbiome interactions. The adoption of a plant diet decreases levels of advanced glycation end products, saturated fat, heme iron, and nitrosamines [109]. Several studies have shown plant-based diet efficacy for the prevention and treatment of diabetes [109–112]. The plant-based diet has also demonstrated a significant positive impact on cardiovascular diseases, coronary heart diseases, hypertension, and hypercholesterolemia [113–118].

In contrast to the western diet which consists of red meat, wheat and alcohol consumption, the plant-based diet has suggested having the ability to maintain symbiosis and prevent dysbiosis of the microbiome and results in lower morbidity and mortality during an infection such as COVID 19 [23]. The implementation of plant-based diets could improve the diversity of nutrients for the host by the gut microbiome. The undigested plant cell walls components are not absorbed by gastro intestinal tract and lead to microbiota-derived nutrients such as peptides and lipids. These substances can promote the development and function of the host immune system [119]. There might be situations in which immune cells of the gut-associated lymphoid tissue come into direct contact with nutrients or gut microbiome, such as in the circumstance of increased epithelial permeability (leaky gut) occurred in both acute and chronic gut inflammation [120]. Numerous plant-based biologically active compounds exhibit antibacterial [121], antifungal [122], and antiviral activity [123]. Moreover, China and India predominantly rely on plant-based medications under different domain names like Chinese Traditional Medicines and Ayurveda but the plant-based therapeutical approach remains largely unexplored [123]. Therefore, a more likely plant-based dietary pattern has protective effects against infection due to its anti-inflammatory and immune response modulation properties that come from plant bioactive molecules. Plant-based food has been recommended also as a nutritional approach treatment for COVID-19. The dietary pattern improves the gut beneficial bacteria and rich in plant bioactive compounds, vitamins C, D, E, magnesium, and zinc [124].

### **4.4 Ketogenic diet**

Ketogenic diet (KD) is a dietary pattern that promotes a low carbohydrate intake (usually to <50 g/day), adequate proportions of protein and higher percentages of fat [125]. Since the diet provides lower carbohydrates intake, glucose reserves



become insufficient both for Krebs cycle and for the central nervous system (CNS). Thus, after several days of carbohydrate restriction, the CNS is forced to find an alternative source of energy. This alternative source of energy is ketones and there are two types of ketone bodies produced in the liver: acetoacetate and  $\beta$ -hydroxybutyrate [125]. Ketosis is a physiological mechanism and it reflects the breakdown of fats in order to compensate for a low level of glucose. The ketogenic diet originally was introduced for epilepsy treatment and the current evidence suggests that KD could help children with drug-resistant epilepsy [126]. Despite its therapeutic application for a neurological disorder such as Alzheimer, malignant glioma and adult epilepsy have shown potential benefits [127], but this may lead to further lowering of consumed essential nutrients by elderly persons with neurodegenerative diseases [128]. Recent findings suggest that even though not all types of cancers give a positive response but KD as an adjuvant treatment, it may give beneficial effect for body composition and quality of life among cancer patients [129]. However, controversies remain on the implementation of the KD especially for diabetes and obesity since the risks, benefits, and applicability of the diet to avoid unnecessary harm and costs to patients [130]. Additionally, the improvements in some cardiovascular risk factors (obesity, type 2 diabetes and high-density lipoprotein (HDL) cholesterol level) are usually not long-lasting and the development of insulin resistance might occur [131]. The international ketogenic diet study group has suggested that constant nutritional monitoring is needed for ketogenic diet therapy to ensure its effectiveness and to reduce potential adverse effects [132]. Perhaps, the sequential method in a biphasic combination of two dietary patterns such as ketogenic diet and Mediterranean diet may provide an effective strategy against obesity-related inflammation with higher compliance of consumers [133].

On the other hand, the short-term ketogenic diet therapy has been applied for COVID-19 patients in order to perform a rapid reduction of comorbidities. These comorbidities (obesity, type 2 diabetes and hypertension) are well known as modifiable risk factors for COVID-19 patients [134]. The rationale behind this approach is the induction of ketosis may reduce hyperglycemia and eucaloric ketogenic diet could affect macrophage phenotype M1 limiting cytokine storm syndrome. Furthermore, SARS-CoV-2 replication could be inhibited by the antiglycolytic action of eucaloric ketogenic diet [135]. It has been suggested that therapies that increase levels of (R)- $\beta$ -hydroxybutyrate, such as the ketogenic diet or consuming exogenous ketones, should restore altered energy metabolism and redox state in patients with COVID-19. This approach is marked at the molecular level by reduced energy metabolism, modulate redox state, decreased oxidative stress, and cell death lead to blunt cytokine storms caused by Human SARS-CoV-2 infection [136].

Social distancing, quarantine, and isolation for prevention of COVID-19 spread may lead to a sedentary lifestyle, one of the factors for overfat that can affect negatively immune function [137]. The pandemic may aggravate depression due to social distancing and isolation, and thus unhealthy eating habits are used to compensate [138]. These Societal interventions against the COVID-19 pandemic might induce a sequence of psychobiological mechanisms that stimulate obesity incidence and raise the risk of comorbidities [139]. Perhaps, an alternative combination of dietary patterns between the ketogenic diet and a low-calorie diet may provide a safe, rapid and long-lasting approach for body weight as well as fat mass reduction. Very-low-calorie ketogenic (VLCK) diets are a dietary pattern that imitates fasting by limiting carbohydrates and fat intake with a relative increase in protein consumption [140]. Very-low-calorie ketogenic diet is able to reduce body weight especially in a relatively short time at the expense of fat mass and visceral mass; muscle mass and strength were preserved [141]. This effect can be long-lasting up to one year among patients that lose more than 10% of their initial weight without any impact

on the muscle mass [142]. It has been shown that the VLCK diet also induced more weight reduction compared to the low-calorie diet until 24 months follow-up and decreased the individual burden of disease among obese patients [143]. The modified ketogenic dietary patterns may exhibit a more suitable and safer solution for a longer effect to mitigate obesity-linked comorbidities.

## **5. The health implication aspects of dietary patterns**

Several factors can be differentially contributed to the implication of major dietary patterns such as meal-specific patterns which are identified as one of these factors [144] besides dietary composition [145]. An unhealthy meal pattern may have an association with dietary quality and diversity and it has been shown that lower dietary diversity scores increase the probability of metabolic syndrome [146]. A low dietary diversity score might be predisposed to nutrients deficiency such as iron deficiency anemia among adolescent girls [147]. Nutrients deficiency is considered a significant factor for infection susceptibility due to immune response impairment if left untreated in some settings [148, 149]. Furthermore, age category might affect the dietary pattern preference for example adults, their common dietary pattern is a western diet-like style and it may increase the risk of metabolic syndrome, obesity, hypertension and cardiovascular disease [150, 151]. Older people are more likely to consume fruits and vegetables and less likely to consume red meat, whole milk, and other fatty foods compared to younger people. However, older individuals tend to consume less calorie intake and a reduction in the quantity of food due to a decrease in physical activity as well as muscle mass [152]. Diet alone may not be sufficient to prevent micronutrient deficiency during aging and this situation can compromise immune function and increase infection risk [153]. Food insecurity is also an essential factor that associated with the unhealthy dietary pattern and it may refer to the limited ability to acquire nutritious food in socially acceptable ways [154]. Therefore, food insecurity may affect negatively infectious diseases susceptibility such as viral suppression of HIV/AIDS [155], COVID 19 spread [156, 157] TB treatment failure and mortality [158], and Malaria [159].

## **6. Conclusions**

Healthy dietary patterns might be protective against inflammation triggered by oxidative stress which is an important determinant of chronic diseases. The proposed mechanisms include preservation of gut microbiome homeostasis and integrity of the epithelial lining of the gastrointestinal tract. These conditions could alleviate lipopolysaccharide-induced inflammatory response and endotoxemia due to leaky gut. Additionally, short-chain fatty acids from fermented dietary fiber as common component of the dietary patterns exhibit anti-inflammatory properties. Therefore, healthy dietary patterns may improve metabolic indices, certain medical conditions and pre-existing comorbidities in infectious disease. In a nutshell, the healthy dietary pattern might be suggested as an alternative for prevention or an integral part of infectious disease management that can be adjusted to local settings.

## **Acknowledgements**

The author received no financial support for the research, authorship, and/or publication of this article.

## **Conflict of interest**

The authors declare no conflict of interest.

## **Other declarations**

We gratefully thank Brahma Putra Marijadi, MD., MPH., Ph.D. for his suggestion as a valuable contribution to this work.

## **Author details**

Budhi Setiawan<sup>1\*</sup> and Masfufatun Masfufatun<sup>2</sup>


1 Department of Pharmacology, Medical Faculty University of Wijaya Kusuma Surabaya, Surabaya, Indonesia

2 Department of Biochemistry, Medical Faculty University of Wijaya Kusuma Surabaya, Surabaya, Indonesia

\*Address all correspondence to: [budhisetiawan@uwks.ac.id](mailto:budhisetiawan@uwks.ac.id)

## **IntechOpen**

---

© 2021 The Author(s). Licensee IntechOpen. This chapter is distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/3.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. 

## References

- [1] Tucker, K.L., *Dietary patterns, approaches, and multicultural perspective*. Applied physiology, nutrition, and metabolism, 2010. **35**(2): p. 211-218.
- [2] Abdullah, M., R.T. Jamil, and F.N. Attia, *Vitamin C (ascorbic acid)*. StatPearls [Internet], 2020.
- [3] Guerrero-Romero, F. and M. Rodríguez-Morán, *The ratio potassium-to-magnesium intake and high blood pressure*. European Journal of Clinical Investigation, 2019. **49**(6): p. e13093.
- [4] van den Brink, A.C., et al., *The Mediterranean, Dietary Approaches to Stop Hypertension (DASH), and Mediterranean-DASH Intervention for Neurodegenerative Delay (MIND) diets are associated with less cognitive decline and a lower risk of Alzheimer's disease—a review*. Advances in Nutrition, 2019. **10**(6): p. 1040-1065.
- [5] Siervo, M., et al., *Effects of the Dietary Approach to Stop Hypertension (DASH) diet on cardiovascular risk factors: a systematic review and meta-analysis*. British Journal of Nutrition, 2015. **113**(1): p. 1-15.
- [6] Esposito, K., et al., *A journey into a Mediterranean diet and type 2 diabetes: a systematic review with meta-analyses*. BMJ open, 2015. **5**(8).
- [7] Harris, E.V., J.C. de Roode, and N.M. Gerardo, *Diet-microbiome-disease: Investigating diet's influence on infectious disease resistance through alteration of the gut microbiome*. PLoS pathogens, 2019. **15**(10): p. e1007891.
- [8] Grobler, L., et al., *Nutritional supplements for people being treated for active tuberculosis*. The Cochrane database of systematic reviews, 2016(6): p. CD006086-CD006086.
- [9] Muscogiuri, G., et al., *Nutritional recommendations for CoVID-19 quarantine*. European Journal of Clinical Nutrition, 2020: p. 1-2.
- [10] Thibault, R., et al., *Nutrition of the COVID-19 patient in the intensive care unit (ICU): a practical guidance*. Critical Care, 2020. **24**(1): p. 447.
- [11] Naja, F. and R. Hamadeh, *Nutrition amid the COVID-19 pandemic: a multi-level framework for action*. European Journal of Clinical Nutrition, 2020: p. 1-5.
- [12] Butler, M.J. and R.M. Barrientos, *The impact of nutrition on COVID-19 susceptibility and long-term consequences*. Brain, Behavior, and Immunity, 2020.
- [13] de Faria Coelho-Ravagnani, C., et al., *Dietary recommendations during the COVID-19 pandemic*. Nutrition Reviews, 2020.
- [14] Headey, D.D. and M.T. Ruel, *The COVID-19 nutrition crisis: What to expect and how to protect*. IFPRI book chapters, 2020: p. 38-41.
- [15] Fang, X., et al., *Epidemiological, comorbidity factors with severity and prognosis of COVID-19: a systematic review and meta-analysis*. Aging (Albany NY), 2020. **12**(13): p. 12493-12503.
- [16] Levy, M., et al., *Dysbiosis and the immune system*. Nature Reviews Immunology, 2017. **17**(4): p. 219-232.
- [17] Weiss, G.A. and T. Hennet, *Mechanisms and consequences of intestinal dysbiosis*. Cell Mol Life Sci, 2017. **74**(16): p. 2959-2977.
- [18] Childs, C.E., P.C. Calder, and E.A. Miles, *Diet and Immune Function*. Nutrients, 2019. **11**(8).
- [19] Zeng, M.Y., N. Inohara, and G. Nuñez, *Mechanisms of inflammation-driven bacterial dysbiosis in the gut*.

Mucosal Immunology, 2017. **10**(1): p. 18-26.

[20] Haro, C., et al., *Consumption of Two Healthy Dietary Patterns Restored Microbiota Dysbiosis in Obese Patients with Metabolic Dysfunction*. Mol Nutr Food Res, 2017. **61**(12).

[21] Luthra-Guptasarma, M. and P. Guptasarma, *Inflammation begets hyper-inflammation in Covid-19 : Diet-derived chronic inflammation promotes runaway acute inflammation resulting in cytokine storms*. 2020.

[22] Kedia, S., et al., *Gut microbiome diversity in acute infective and chronic inflammatory gastrointestinal diseases in North India*. Journal of gastroenterology, 2016. **51**(7): p. 660-671.

[23] Rishi, P., et al., *Diet, Gut Microbiota and COVID-19*. Indian Journal of Microbiology, 2020. **60**(4): p. 420-429.

[24] Senghor, B., et al., *Gut microbiota diversity according to dietary habits and geographical provenance*. Human Microbiome Journal, 2018. 7: p. 1-9.

[25] De Filippo, C., et al., *Diet, environments, and gut microbiota. A preliminary investigation in children living in rural and urban Burkina Faso and Italy*. Frontiers in microbiology, 2017. **8**: p. 1979.

[26] Canfora, E.E., J.W. Jocken, and E.E. Blaak, *Short-chain fatty acids in control of body weight and insulin sensitivity*. Nature Reviews Endocrinology, 2015. **11**(10): p. 577-591.

[27] Maslowski, K.M. and C.R. Mackay, *Diet, gut microbiota and immune responses*. Nature immunology, 2011. **12**(1): p. 5-9.

[28] Bell, V., et al., *One health, fermented foods, and gut microbiota*. Foods, 2018. 7(12): p. 195.

[29] Tomova, A., et al., *The Effects of Vegetarian and Vegan Diets on Gut Microbiota*. Frontiers in Nutrition, 2019. **6**(47).

[30] Van Spaendonk, H., et al., *Regulation of intestinal permeability: The role of proteases*. World journal of gastroenterology, 2017. **23**(12): p. 2106-2123.

[31] Storm-Larsen, C., et al., *Microbial translocation revisited: targeting the endotoxic potential of gut microbes in HIV-infected individuals*. AIDS, 2019. **33**(4): p. 645-653.

[32] Inoue, T., et al., *Gut Dysbiosis Associated With Hepatitis C Virus Infection*. Clinical Infectious Diseases, 2018. **67**(6): p. 869-877.

[33] Antharam, V.C., et al., *Intestinal Dysbiosis and Depletion of Butyrogenic Bacteria Clostridium difficile Infection and Nosocomial Diarrhea*. Journal of Clinical Microbiology, 2013. **51**(9): p. 2884-2892.

[34] Serrano-Villar, S., et al., *The effects of prebiotics on microbial dysbiosis, butyrate production and immunity in HIV-infected subjects*. Mucosal Immunology, 2017. **10**(5): p. 1279-1293.

[35] Leeming, E.R., et al., *Effect of Diet on the Gut Microbiota: Rethinking Intervention Duration*. Nutrients, 2019. **11**(12).

[36] Kolodziejczyk, A.A., D. Zheng, and E. Elinav, *Diet-microbiota interactions and personalized nutrition*. Nature Reviews Microbiology, 2019. **17**(12): p. 742-753.

[37] Drake, I., et al., *A Western dietary pattern is prospectively associated with cardio-metabolic traits and incidence of the metabolic syndrome*. British Journal of Nutrition, 2018. **119**(10): p. 1168-1176.



- [38] Christ, A., M. Lauterbach, and E. Latz, *Western diet and the immune system: an inflammatory connection*. Immunity, 2019. **51**(5): p. 794-811.
- [39] Thomas, D. and C. Apovian, *Macrophage functions in lean and obese adipose tissue*. Metabolism, 2017. **72**: p. 120-143.
- [40] Kopp, W., *How Western Diet And Lifestyle Drive The Pandemic Of Obesity And Civilization Diseases*. Diabetes, metabolic syndrome and obesity: targets and therapy, 2019. **12**: p. 2221-2236.
- [41] Hosseini, Z., S.J. Whiting, and H. Vatanparast, *Current evidence on the association of the metabolic syndrome and dietary patterns in a global perspective*. Nutrition Research Reviews, 2016. **29**(2): p. 152-162.
- [42] Walsh, E.I., et al., *Midlife susceptibility to the effects of poor diet on diabetes risk*. European Journal of Clinical Nutrition, 2020.
- [43] Mehta, R.S., et al., *Dietary patterns and risk of colorectal cancer: analysis by tumor location and molecular subtypes*. Gastroenterology, 2017. **152**(8): p. 1944-1953. e1.
- [44] Alexander, S., et al., *A plant-based diet and hypertension*. Journal of Geriatric Cardiology: JGC, 2017. **14**(5): p. 327.
- [45] Fanelli Kuczmarski, M., et al., *Dietary patterns associated with lower 10-year atherosclerotic cardiovascular disease risk among urban African-American and white adults consuming western diets*. Nutrients, 2018. **10**(2): p. 158.
- [46] Kramer, H., *Diet and Chronic Kidney Disease*. Advances in Nutrition, 2019. **10**(Supplement\_4): p. S367-S379.
- [47] Sullivan, P.M., *Influence of Western diet and APOE genotype on Alzheimer's disease risk*. Neurobiol Dis, 2020. **138**: p. 104790.
- [48] Barchitta, M., et al., *The Association of Dietary Patterns with High-Risk Human Papillomavirus Infection and Cervical Cancer: A Cross-Sectional Study in Italy*. Nutrients, 2018. **10**(4).
- [49] Myles, I., *Fast food fever: Reviewing the impacts of the Western diet on immunity*. Nutrition journal, 2014. **13**: p. 61.
- [50] Földi, M., et al., *Obesity is a risk factor for developing critical condition in COVID-19 patients: A systematic review and meta-analysis*. Obesity Reviews, 2020. **21**(10): p. e13095.
- [51] Hussain, A., et al., *Obesity and mortality of COVID-19. Meta-analysis*. Obesity research & clinical practice, 2020.
- [52] Malik, P., et al., *Obesity a predictor of outcomes of COVID-19 hospitalized patients-A systematic review and meta-analysis*. J Med Virol, 2020.
- [53] Soeroto, A.Y., et al., *Effect of increased BMI and obesity on the outcome of COVID-19 adult patients: A systematic review and meta-analysis*. Diabetes & Metabolic Syndrome: Clinical Research & Reviews, 2020. **14**(6): p. 1897-1904.
- [54] Ejaz, H., et al., *COVID-19 and comorbidities: Deleterious impact on infected patients*. Journal of Infection and Public Health, 2020. **13**(12): p. 1833-1839.
- [55] Yang, J., et al., *Prevalence of comorbidities in the novel Wuhan coronavirus (COVID-19) infection: a systematic review and meta-analysis*. International journal of infectious diseases, 2020.
- [56] Baradaran, A., et al., *Prevalence of Comorbidities in COVID-19 Patients: A Systematic Review and Meta-Analysis*. The archives of bone and joint surgery, 2020. **8**(Suppl 1): p. 247-255.

- [57] Qiu, P., et al., *Clinical characteristics, laboratory outcome characteristics, comorbidities, and complications of related COVID-19 deceased: a systematic review and meta-analysis*. *Aging Clinical and Experimental Research*, 2020. **32**(9): p. 1869-1878.
- [58] Zaim, S., et al., *COVID-19 and multi-organ response*. *Current Problems in Cardiology*, 2020: p. 100618.
- [59] López-Olivares, M., et al., *Mediterranean Diet and the Emotional Well-Being of Students of the Campus of Melilla (University of Granada)*. *Nutrients*, 2020. **12**(6).
- [60] Rosato, V., et al., *Mediterranean diet and cardiovascular disease: a systematic review and meta-analysis of observational studies*. *European journal of nutrition*, 2019. **58**(1): p. 173-191.
- [61] Salas-Salvado, J., et al., *Mediterranean diet and cardiovascular disease prevention: what do we know?* *Progress in cardiovascular diseases*, 2018. **61**(1): p. 62-67.
- [62] Martínez-González, M.A., A. Gea, and M. Ruiz-Canela, *The Mediterranean diet and cardiovascular health: A critical review*. *Circulation research*, 2019. **124**(5): p. 779-798.
- [63] Becerra-Tomás, N., et al., *Mediterranean diet, cardiovascular disease and mortality in diabetes: A systematic review and meta-analysis of prospective cohort studies and randomized clinical trials*. *Critical reviews in food science and nutrition*, 2020. **60**(7): p. 1207-1227.
- [64] Guasch-Ferré, M., et al., *Dietary polyphenols, Mediterranean diet, prediabetes, and type 2 diabetes: a narrative review of the evidence*. *Oxidative Medicine and Cellular Longevity*, 2017. **2017**.
- [65] Esposito, K., et al., *Mediterranean diet for type 2 diabetes: cardiometabolic benefits*. *Endocrine*, 2017. **56**(1): p. 27-32.
- [66] Petersson, S.D. and E. Philippou, *Mediterranean diet, cognitive function, and dementia: a systematic review of the evidence*. *Advances in Nutrition*, 2016. **7**(5): p. 889-904.
- [67] Berti, V., et al., *Mediterranean diet and 3-year Alzheimer brain biomarker changes in middle-aged adults*. *Neurology*, 2018. **90**(20): p. e1789-e1798.
- [68] Limongi, F., et al., *The effect of adherence to the Mediterranean Diet on late-life cognitive disorders: A systematic review*. *Journal of the American Medical Directors Association*, 2020. **21**(10): p. 1402-1409.
- [69] Farinetti, A., et al., *Mediterranean diet and colorectal cancer: A systematic review*. *Nutrition*, 2017. **43**: p. 83-88.
- [70] Schwingshackl, L., et al., *Adherence to Mediterranean diet and risk of cancer: an updated systematic review and meta-analysis*. *Nutrients*, 2017. **9**(10): p. 1063.
- [71] Morze, J., et al., *An updated systematic review and meta-analysis on adherence to mediterranean diet and risk of cancer*. *Eur J Nutr*, 2020.
- [72] Wu, P.-Y., K.-M. Chen, and W.-C. Tsai, *The Mediterranean Dietary Pattern and Inflammation in Older Adults: A Systematic Review and Meta-analysis*. *Advances in Nutrition*, 2020.
- [73] Luisi, M.L.E., et al., *Effect of Mediterranean Diet enriched in High Quality Extra Virgin Olive Oil on oxidative stress, inflammation and gut microbiota in obese and normal weight adult subjects*. *Frontiers in Pharmacology*, 2019. **10**: p. 1366.
- [74] Park, Y.-M., et al., *Obesity Mediates the Association between Mediterranean Diet Consumption and Insulin Resistance and Inflammation in US Adults*. *The Journal of Nutrition*, 2017. **147**(4): p. 563-571.

- [75] Arpón, A., et al., *Adherence to Mediterranean diet is associated with methylation changes in inflammation-related genes in peripheral blood cells*. Journal of Physiology and Biochemistry, 2016. **73**(3): p. 445-455.
- [76] Bailey, M.A. and H.D. Holscher, *Microbiome-Mediated Effects of the Mediterranean Diet on Inflammation*. Advances in Nutrition, 2018. **9**(3): p. 193-206.
- [77] Ghosh, T.S., et al., *Mediterranean diet intervention alters the gut microbiome in older people reducing frailty and improving health status: the NU-AGE 1-year dietary intervention across five European countries*. Gut, 2020. **69**(7): p. 1218.
- [78] Eiser, A.R., *Could Dietary Factors Reduce COVID-19 Mortality Rates? Moderating the Inflammatory State*. The Journal of Alternative and Complementary Medicine, 2020.
- [79] Angelidi, A.M., et al., *Mediterranean diet as a nutritional approach for COVID-19*. Metabolism-Clinical and Experimental, 2020.
- [80] Tsiodras, S., et al., *Adherence to Mediterranean diet is favorably associated with metabolic parameters in HIV-positive patients with the highly active antiretroviral therapy-induced metabolic syndrome and lipodystrophy*. Metabolism: clinical and experimental, 2009. **58**(6): p. 854-859.
- [81] Turati, F., et al., *Mediterranean diet and hepatocellular carcinoma*. J Hepatol, 2014. **60**(3): p. 606-11.
- [82] Policarpo, S., et al., *Adherence to Mediterranean diet in HIV infected patients: Relation with nutritional status and cardiovascular risk*. Clinical Nutrition ESPEN, 2017. **18**: p. 31-36.
- [83] Barchitta, M., et al., *The association of dietary patterns with high-risk human papillomavirus infection and cervical cancer: a cross-sectional study in Italy*. Nutrients, 2018. **10**(4): p. 469.
- [84] Silva, A.R., B.P.T. Moraes, and C.F. Gonçalves-de-Albuquerque, *Mediterranean Diet: Lipids, Inflammation, and Malaria Infection*. Int J Mol Sci, 2020. **21**(12).
- [85] Schwingshackl, L., J. Morze, and G. Hoffmann, *Mediterranean diet and health status: Active ingredients and pharmacological mechanisms*. British Journal of Pharmacology, 2020. **177**(6): p. 1241-1257.
- [86] Palomer, X., et al., *Palmitic and Oleic Acid: The Yin and Yang of Fatty Acids in Type 2 Diabetes Mellitus*. Trends in Endocrinology & Metabolism, 2018. **29**(3): p. 178-190.
- [87] Pang, K.-L. and K.-Y. Chin, *The biological activities of oleocanthal from a molecular perspective*. Nutrients, 2018. **10**(5): p. 570.
- [88] Beauchamp, G.K., et al., *Ibuprofen-like activity in extra-virgin olive oil*. Nature, 2005. **437**(7055): p. 45-46.
- [89] Wani, T.A., et al., *Olive oil and its principal bioactive compound: Hydroxytyrosol—A review of the recent literature*. Trends in Food Science & Technology, 2018. **77**: p. 77-90.
- [90] Liguori, I., et al., *Oxidative stress, aging, and diseases*. Clinical interventions in aging, 2018. **13**: p. 757.
- [91] Tsigalou, C., et al., *Interplay between Mediterranean Diet and Gut Microbiota in the Interface of Autoimmunity: An Overview*. 2020.
- [92] Waldman, A.J. and E.P. Balskus, *The Human Microbiota, Infectious Disease, and Global Health: Challenges and Opportunities*. ACS Infectious Diseases, 2018. **4**(1): p. 14-26.

- [93] Steinberg, D., G.G. Bennett, and L. Svetkey, *The DASH diet, 20 years later*. *Jama*, 2017. **317**(15): p. 1529-1530.
- [94] Bricarello, L.P., et al., *Effects of the dietary approach to stop hypertension (DASH) diet on blood pressure, overweight and obesity in adolescents: a systematic review*. *Clinical Nutrition ESPEN*, 2018. **28**: p. 1-11.
- [95] Soltani, S., et al., *The effect of dietary approaches to stop hypertension (DASH) diet on weight and body composition in adults: a systematic review and meta-analysis of randomized controlled clinical trials*. *Obes Rev*, 2016. **17**(5): p. 442-54.
- [96] Chiavaroli, L., et al., *DASH dietary pattern and cardiometabolic outcomes: An umbrella review of systematic reviews and meta-analyses*. *Nutrients*, 2019. **11**(2): p. 338.
- [97] Li, S., et al., *Effects of the Dietary Approaches to Stop Hypertension (DASH) on Pregnancy/Neonatal Outcomes and Maternal Glycemic Control: A Systematic Review and Meta-analysis of Randomized Clinical Trials*. *Complementary Therapies in Medicine*, 2020: p. 102551.
- [98] Yamamoto, J.M., et al., *Gestational diabetes mellitus and diet: a systematic review and meta-analysis of randomized controlled trials examining the impact of modified dietary interventions on maternal glucose control and neonatal birth weight*. *Diabetes Care*, 2018. **41**(7): p. 1346-1361.
- [99] Ali Mohsenpour, M., et al., *Adherence to Dietary Approaches to Stop Hypertension (DASH)-style diet and the risk of cancer: A systematic review and meta-analysis of cohort studies*. *Journal of the American College of Nutrition*, 2019. **38**(6): p. 513-525.
- [100] Milajerdi, A., et al., *The association of dietary quality indices and cancer mortality: A systematic review and meta-analysis of cohort studies*. *Nutrition and cancer*, 2018. **70**(7): p. 1091-1105.
- [101] Suri, S., et al., *DASH dietary pattern: A treatment for non-communicable diseases*. *Current hypertension reviews*, 2020. **16**(2): p. 108-114.
- [102] Gold, M.S., et al., *COVID-19 and comorbidities: a systematic review and meta-analysis*. *Postgraduate medicine*, 2020: p. 1-7.
- [103] Nandy, K., et al., *Coronavirus disease (COVID-19): A systematic review and meta-analysis to evaluate the impact of various comorbidities on serious events*. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews*, 2020. **14**(5): p. 1017-1025.
- [104] Tsoupras, A., R. Lordan, and I. Zabetakis, *Thrombosis and COVID-19: The Potential Role of Nutrition*. *Frontiers in Nutrition*, 2020. **7**: p. 177.
- [105] Pirozeh, R., et al., *Effect of DASH diet on oxidative stress parameters: A systematic review and meta-analysis of randomized clinical trials*. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews*, 2020.
- [106] Pohanka, M., *Role of oxidative stress in infectious diseases. A review*. *Folia Microbiologica*, 2013. **58**(6): p. 503-513.
- [107] Jama, H.A., et al., *The effect of diet on hypertensive pathology: is there a link via gut microbiota-driven immunometabolism?* *Cardiovascular Research*, 2019. **115**(9): p. 1435-1447.
- [108] Alwarith, J., et al., *Nutrition Interventions in Rheumatoid Arthritis: The Potential Use of Plant-Based Diets. A Review*. *Frontiers in Nutrition*, 2019. **6**(141).
- [109] McMacken, M. and S. Shah, *A plant-based diet for the prevention and treatment of type 2 diabetes*. *Journal of geriatric cardiology : JGC*, 2017. **14**(5): p. 342-354.



- [110] Chowdhury, B.R., *Diabetes reversal by plant-based diet*. J Metabol Synd, 2017.
- [111] Satija, A., et al., *Plant-Based Dietary Patterns and Incidence of Type 2 Diabetes in US Men and Women: Results from Three Prospective Cohort Studies*. PLoS Med, 2016. **13**(6): p. e1002039.
- [112] Rinaldi, S., et al., *A Comprehensive Review of the Literature Supporting Recommendations From the Canadian Diabetes Association for the Use of a Plant-Based Diet for Management of Type 2 Diabetes*. Canadian Journal of Diabetes, 2016. **40**(5): p. 471-477.
- [113] Hemler, E.C. and F.B. Hu, *Plant-based diets for cardiovascular disease prevention: all plant foods are not created equal*. Current atherosclerosis reports, 2019. **21**(5): p. 18.
- [114] Patel, H., et al., *Plant-based nutrition: An essential component of cardiovascular disease prevention and management*. Current cardiology reports, 2017. **19**(10): p. 104.
- [115] Kim, H., et al., *Plant-Based diets are associated with a lower risk of incident cardiovascular disease, cardiovascular disease mortality, and All-Cause mortality in a general population of Middle-Aged adults*. Journal of the American Heart Association, 2019. **8**(16): p. e012865.
- [116] Satija, A. and F.B. Hu, *Plant-based diets and cardiovascular health*. Trends in cardiovascular medicine, 2018. **28**(7): p. 437-441.
- [117] Esselstyn, C.B., *A plant-based diet and coronary artery disease: a mandate for effective therapy*. Journal of geriatric cardiology : JGC, 2017. **14**(5): p. 317-320.
- [118] Najjar, R.S., C.E. Moore, and B.D. Montgomery, *A defined, plant-based diet utilized in an outpatient cardiovascular clinic effectively treats hypercholesterolemia and hypertension and reduces medications*. Clin Cardiol, 2018. **41**(3): p. 307-313.
- [119] Hansen, N.W. and A. Sams, *The Microbiotic Highway to Health—New Perspective on Food Structure, Gut Microbiota, and Host Inflammation*. Nutrients, 2018. **10**(11): p. 1590.
- [120] Bischoff, S.C., et al., *Intestinal permeability—a new target for disease prevention and therapy*. BMC gastroenterology, 2014. **14**(1): p. 189.
- [121] Salas, C.E., et al., *Biologically active and antimicrobial peptides from plants*. BioMed research international, 2015. **2015**.
- [122] Arif, T., et al., *Natural products—antifungal agents derived from plants*. Journal of Asian natural products research, 2009. **11**(7): p. 621-638.
- [123] Prasad, A., M. Muthamilarasan, and M. Prasad, *Synergistic antiviral effects against SARS-CoV-2 by plant-based molecules*. Plant Cell Reports, 2020. **39**(9): p. 1109-1114.
- [124] Arshad, M.S., et al., *Coronavirus Disease (COVID-19) and Immunity Booster Green Foods: A Mini Review*. Food Sci Nutr, 2020. **8**(8): p. 3971-6.
- [125] Shilpa, J. and V. Mohan, *Ketogenic diets: Boon or bane? The Indian journal of medical research*, 2018. **148**(3): p. 251-253.
- [126] Martin-McGill, K.J., et al., *Ketogenic diets for drug-resistant epilepsy*. Cochrane Database of Systematic Reviews, 2020(6).
- [127] McDonald, T.J.W. and M.C. Cervenka, *The Expanding Role of Ketogenic Diets in Adult Neurological Disorders*. Brain Sci, 2018. **8**(8).
- [128] Włodarek, D., *Role of Ketogenic Diets in Neurodegenerative Diseases (Alzheimer's Disease and Parkinson's Disease)*. Nutrients, 2019. **11**(1).



- [129] Klement, R.J., *The emerging role of ketogenic diets in cancer treatment*. *Current Opinion in Clinical Nutrition & Metabolic Care*, 2019. **22**(2): p. 129-134.
- [130] Joshi, S., R.J. Ostfeld, and M. McMacken, *The Ketogenic Diet for Obesity and Diabetes—Enthusiasm Outpaces Evidence*. *JAMA Internal Medicine*, 2019. **179**(9): p. 1163-1164.
- [131] Kosinski, C. and F.R. Jornayvaz, *Effects of Ketogenic Diets on Cardiovascular Risk Factors: Evidence from Animal and Human Studies*. *Nutrients*, 2017. **9**(5).
- [132] Kossoff, E.H., et al., *Optimal clinical management of children receiving dietary therapies for epilepsy: Updated recommendations of the International Ketogenic Diet Study Group*. *Epilepsia Open*, 2018. **3**(2): p. 175-192.
- [133] Paoli, A., et al., *Long term successful weight loss with a combination biphasic ketogenic Mediterranean diet and Mediterranean diet maintenance protocol*. *Nutrients*, 2013. **5**(12): p. 5205-5217.
- [134] Paoli, A., S. Gorini, and M. Caprio, *The dark side of the spoon - glucose, ketones and COVID-19: a possible role for ketogenic diet?* *Journal of Translational Medicine*, 2020. **18**(1): p. 441.
- [135] Sukkar, S.G. and M. Bassetti, *Induction of ketosis as a potential therapeutic option to limit hyperglycemia and prevent cytokine storm in COVID-19*. *Nutrition*, 2020. **79-80**: p. 110967.
- [136] Bradshaw, P.C., et al., *COVID-19: Proposing a Ketone-Based Metabolic Therapy as a Treatment to Blunt the Cytokine Storm*. *Oxidative Medicine and Cellular Longevity*, 2020. **2020**: p. 6401341.
- [137] Maffetone, P.B. and P.B. Laursen, *The Perfect Storm: Coronavirus (Covid-19) Pandemic Meets Overfat Pandemic*. *Front Public Health*, 2020. **8**: p. 135.
- [138] Mason, T.B., J. Barrington-Trimis, and A.M. Leventhal, *Eating to Cope With the COVID-19 Pandemic and Body Weight Change in Young Adults*. *Journal of Adolescent Health*, 2020.
- [139] Clemmensen, C., M.B. Petersen, and T.I.A. Sørensen, *Will the COVID-19 pandemic worsen the obesity epidemic?* *Nature Reviews Endocrinology*, 2020. **16**(9): p. 469-470.
- [140] Paoli, A., *Ketogenic diet for obesity: friend or foe?* *International journal of environmental research and public health*, 2014. **11**(2): p. 2092-2107.
- [141] Gomez-Arbelaez, D., et al., *Body Composition Changes After Very-Low-Calorie Ketogenic Diet in Obesity Evaluated by 3 Standardized Methods*. *The Journal of Clinical Endocrinology & Metabolism*, 2016. **102**(2): p. 488-498.
- [142] Moreno, B., et al., *Comparison of a very low-calorie-ketogenic diet with a standard low-calorie diet in the treatment of obesity*. *Endocrine*, 2014. **47**(3): p. 793-805.
- [143] Moreno, B., et al., *Obesity treatment by very low-calorie-ketogenic diet at two years: reduction in visceral fat and on the burden of disease*. *Endocrine*, 2016. **54**(3): p. 681-690.
- [144] Murakami, K., M.B.E. Livingstone, and S. Sasaki, *Meal-specific dietary patterns and their contribution to overall dietary patterns in the Japanese context: Findings from the 2012 National Health and Nutrition Survey, Japan*. *Nutrition*, 2019. **59**: p. 108-115.
- [145] Michels, K.B. and M.B. Schulze, *Can dietary patterns help us detect diet-disease associations?* *Nutrition Research Reviews*, 2007. **18**(2): p. 241-248.
- [146] Gholizadeh, F., et al., *The relation of Dietary diversity score and food insecurity to metabolic syndrome features*

and glucose level among pre-diabetes subjects. Primary care diabetes, 2018. **12**(4): p. 338-344.

[147] Olumakaiye, M.F., *Adolescent Girls With Low Dietary Diversity Score Are Predisposed to Iron Deficiency in Southwestern Nigeria*. ICAN: Infant, Child, & Adolescent Nutrition, 2013. **5**(2): p. 85-91.

[148] Pereira, M., et al., *Vitamin D deficiency aggravates COVID-19: systematic review and meta-analysis*. Critical reviews in food science and nutrition, 2020: p. 1-9.

[149] Zhu, X., G. Herrera, and J.B. Ochoa, *Immunosuppression and infection after major surgery: a nutritional deficiency*. Crit Care Clin, 2010. **26**(3): p. 491-500, ix.

[150] Sun, J., N.J. Buys, and A.P. Hills, *Dietary Pattern and Its Association with the Prevalence of Obesity, Hypertension and Other Cardiovascular Risk Factors among Chinese Older Adults*. International Journal of Environmental Research and Public Health, 2014. **11**(4): p. 3956-3971.

[151] Aekplakorn, W., et al., *Dietary Pattern and Metabolic Syndrome in Thai Adults*. Journal of Nutrition and Metabolism, 2015. **2015**: p. 468759.

[152] Wakimoto, P. and G. Block, *Dietary Intake, Dietary Patterns, and Changes With Age: An Epidemiological Perspective*. The Journals of Gerontology: Series A, 2001. **56**(suppl\_2): p. 65-80.

[153] Maggini, S., A. Pierre, and P.C. Calder, *Immune Function and Micronutrient Requirements Change over the Life Course*. Nutrients, 2018. **10**(10).

[154] Morales, M.E. and S.A. Berkowitz, *The Relationship Between Food Insecurity, Dietary Patterns, and Obesity*. Current Nutrition Reports, 2016. **5**(1): p. 54-60.

[155] Aibibula, W., et al., *Association Between Food Insecurity and HIV Viral Suppression: A Systematic Review and Meta-Analysis*. AIDS and Behavior, 2017. **21**(3): p. 754-765.

[156] Laborde, D., W. Martin, and R. Vos, *Poverty and food insecurity could grow dramatically as COVID-19 spreads*. International Food Policy Research Institute (IFPRI), Washington, DC, 2020.

[157] Pereira, M. and A.M. Oliveira, *Poverty and food insecurity may increase as the threat of COVID-19 spreads*. Public Health Nutrition, 2020. **23**(17): p. 3236-3240.

[158] Balinda, I.G., D.D. Sugrue, and L.C. Ivers, *More Than Malnutrition: A Review of the Relationship Between Food Insecurity and Tuberculosis*. Open Forum Infectious Diseases, 2019. **6**(4).

[159] Uscátegui Peñuela, R.M., et al., *Relationship between malaria, malnutrition, food insecurity and low socio-economica conditions in children of Turbo, Colombia*. Perspectivas en Nutricion Humana, 2009. **11**(2): p. 153-164.