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Review

New insight in severe acute respiratory syndrome coronavirus 2 consideration: Applied machine learning for nutrition quality, microbiome and microbial food poisoning concerns

Fatemeh Taslimi[1] , Seyedeh Elham Hosseini Ezabadi[2], Maed Jabbari[3], Erfan Ghanbarzadeh[4], Mandana Ashkan[5], Farhad Akbari Afkhami[6], Amir Rigi[4] , Mojtaba Hedayati Ch[7,*]

[1]*Faculty of Medicine, Mazandaran University of Medical Sciences, Sari, Iran*
[2]*Department of Nutrition, Faculty of Nutrition Sciences and Food Technology, Shahid Beheshti University of Medical Sciences, Tehran, Iran*
[3]*School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences, Tehran, Iran*
[4]*Microbial Toxins Physiology Group, Universal Scientific Education and Research Network, Rasht, Iran*
[5]*Student Research Committee, Guilan University of Medical Sciences, Rasht, Guilan, Iran*
[6]*Department of Chemistry and Biochemistry, University of Alabama, Tuscaloosa, Alabama 35487, United States*
[7]*Department of Microbiology, Virology and Microbial Toxins, School of Medicine, Guilan University of Medical Sciences, Rasht, Iran*

Abstract

Although almost two years have passed since the beginning of the coronavirus disease 2019 (COVID-19) pandemic in the world, there is still a threat to the health of people at risk and patients. Specialists in various sciences conduct various researches in order to eliminate or reduce the problems caused by this disease. Nutrition is one of the sciences that plays a very important supportive role in this regard. It is important for patients to pay attention to the potential of different diets in preventing or accelerating the healing process. The relationship between nutrition and microbiome regulation or the occurrence of food microbial poisoning is one of the factors that can directly or indirectly play a key role in the body's resilience to COVID-19. In this article, we introduce a link between nutrition, the microbiome, and the incidence of food microbial poisoning that may have great potential in preventing, treating COVID-19, or preventing deterioration in patients. In linking the components of this network, artificial intelligence (AI), machine learning (ML) and data mining (DM) can be important strategies and lead to the creation of a conceptual model called "Balance square", which we will introduce.

Keywords: COVID-19, Microbiome, Microbial toxins, Nutrition, Machine learning

1. Introduction

Todays, coronavirus disease 2019 (COVID-19), known as significant public health challenge and is the causal agent of severe acute coronavirus respiratory syndrome. Since December 2019, the COVID-19 outbreak has become a significant global epidemic threat for at risk people's health and patients [1]. In this pandemic situation, we are in constant struggle to stop virus infection or attenuate severity of disease every day [2]. Specialists in various fields of sciences try to do their best, attenuating or eliminating symptoms caused by disease. Recently, however, due to the more complex process of diagnosis and treatment, it seems that there is a need for multidisciplinary research and

[*]**Corresponding author:**
Mojtaba Hedayati Ch, Ph.D
Department of Microbiology, School of Medicine,
Guilan University of Medical Sciences, Rasht, Guilan, Iran
Tel/Fax: +98 13 33690099
Email: mhedayatich@gums.ac.ir
https://orcid.org/0000-0002-8277-9841

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performance based on system biology in the face of COVID-19.

We consider nutrition, microbiology, microbial toxins, and computer science-based research as a comprehensive diagnostic, prophylactic, and coping strategy against Covid-19. For this purpose, it is necessary to explain a series of concepts to understand the network relationship between these sciences, which we will describe below.

2. Correlations of nutrition, microbiome, microbial toxins and COVID-19

The determining role of nutrition, microbiome and food poisoning caused by microbial toxins in human health has long been demonstrated [3-5]. Different eating habits can play a role in the development of diseases by changing human microbiome ratio [6]. Eating habits, in turn, have a significant impact on the incidence of diseases such as obesity, diabetes and cardiovascular disease. Each of these diseases can cause different reactions of the body in the face of COVID-19 [7, 8]. Therefore, diets, need to observe with high accuracy in different human population from healthy to those who suffered disease. The type of nutritional value, cooking method and hours and amount of meals are other important and influential factors in the quality of food consumed by a person [9]. Consumption food groups can mainly include 9 groups of breads and cereals, fruits, vegetables, meats and meat products, legumes, nuts, fats, low-fat milk and dairy products, and high-fat milk and dairy products.

Different characteristics affect a person's resident or transient microbiome and the likelihood of food poisoning: age, level of education, economic status, height, weight, use of prebiotics, probiotics and synbiotic, multivitamin and mineral supplements, genetic disorders, health of drinking water, living in the city or village, cultural characteristics, lifestyle and occupation [10].

Studies have shown that the gut microbiota in people with a variety of diseases, including inflammatory bowel disease, type 1 and type 2 diabetes, celiac disease, autism, multiple sclerosis or COVID-19, can be different from healthy people [11]. As a result, the proper formation of the microbial population in life can, in a way, play an important role in a person's health in the future. It has even been observed that, the mother's microbiota is directly related to the baby's microbiota, and that the mother's diet during pregnancy can affect the microbial population of the baby's gut [12].

It seems that the effect of diet on many diseases can be explained by changes for example in intestinal microbiota. Different eating habits can play a role in the development of diseases by changing the microbiota [13]. Habits, food consumption cultures and environmental factors in different parts of the world are effective in the formation of intestinal microbiota in different forms. It is important to investigate the relationship between diet and microbiome and their toxins (such as lipopolysaccharide=LPS) or food poisoning in relation to Covid-19. Because it can have significant direct or indirect effects on the readiness and capacity of the immune system [14].

This association between microbiome and nutrition is important, even in relation to COVID-19 in pregnant mothers. In the past, it was thought that the baby's gut was sterile before birth and its microbial population formed only after birth, but now analysis of the baby's first stool, meconium, has shown that the mother's uterine environment is not sterile and contains a microbial population that was born before birth which the baby received through the placenta and amniotic fluid [15]. The origin of this microbial population can be from the mother's gastrointestinal tract, bacteria in the mother's oral cavity or from the urogenital area [16]. During pregnancy, gastrointestinal motility decreases and uterine pressure increases, especially late in this period. On the other hand, the effect of estrogen on mesenteric arteries and increasing pressure on these arteries by the fetus causes transient clogging of arteries. These factors, along with the weakening of intestinal barriers against bacterial growth, cause the transfer of bacteria from the intestine to other organs [17]. In addition, pregnancy can affect the thickness of the mucosal layer and the adhesion of enterocytes, causing bacteria to enter the blood and lymph vessels to reach other tissues, such as the placenta and amniotic fluid. This transmission is probably through dendritic cells and $CD18^{+}$ [18]. Surprisingly, by swallowing amniotic fluid, the germs enter the baby's gut and appear in meconium after birth [19]. The extent to which this microbiome is embedded can play a role in establishing or preventing mother-to-child reception of COVID-19.

Various studies have shown that human nutrition, even before birth, can affect the future human microbiome. For example, in a study in 2018, it was shown that mothers in the normal delivery group were associated with an increase in fruit consumption during pregnancy with an increase in the *Streptococcus/Clostridium* group population in the baby's stool. Interestingly, contrary to expectations, fruit consumption was inversely related to *Bifidobacterium* spp., which is known as a beneficial bacterium, and consumption of red meat and processed foods was directly related to the amount of this bacterium. In addition, maternal dairy consumption during pregnancy was associated with an increase in *Clostridium* in cesarean section infants. Consumption of fish and seafood also showed a positive relationship with *Streptococcus* bacteria in new born neonates [20]. Also, another study in 2018 that focused on maternal food intake in the third trimester of pregnancy showed that high consumption of vegetables and reduced consumption of processed meat and fried foods during pregnancy were inversely related to the amount of *Bacteroides* spp. and *Clostridium* spp. in infant feces [21].

Another study conducted in 2017 showed that maternal fat intake during pregnancy, including saturated fatty acid (SFA) and monounsaturated fatty acids (MUFA), was associated with an increase in the order *Firmicutes* and a decrease in some groups, such as the *Proteobacteria* order. A number of vitamins (A, D, E, B_2, B_1, B_3, B_3, B_9, B_{12}, B_6, C, carotenoids, retinoic acid), plant protein and fiber negatively associated with *Coprococcus*, *Blautia*, *Roseburia* and several bacterial family reflected *Ruminococcaceae* and *Lachnospiraceae*. Most of these species were more abundant and positively associated with maternal fat intake, MUFA, animal protein and especially significant association with SFA. Total maternal fat intake during pregnancy was negatively related to *Escherichia* and *Shigella* genera and positively related to *Firmicutes* genus including *Blautia*, *Roseburia*, *Rombustia* and *Faecalibacterium* genera. These groups also had a negative relationship with fiber and animal protein source. Total carbohydrates, plant proteins, and fiber were inversely related to the order *Firmicutes*. In neonates born by cesarean section, maternal fiber intake was positively associated with *Proteobacteria*. They also reported that polyunsaturated fatty acids (PUFAs) levels were positively associated with *Proteobacteriaceae* and negatively associated with *Firmicutes* [22].

It is found that intestine microbiome changes found in COVID-19 hospitalized patients. This suggests that changes in the intestinal microbiome may play a role in increasing the intensity of COVID-19 [23]. As a matter of fact, gut microbiota as a dark side of life in human body set metabolic homeostasis of mankind and its imbalance could turn pathogenesis of COVID-19 more complex. For this reason, various studies have been performed in which foods containing polyphenols and dietary supplements such as probiotics and vitamins such as vitamin D have been shown to be effective in preventing or reducing the severity of COVID-19 [24, 25].

3. Application of computer sciences and programming: Promising strategies

As described before, nutritional portions and types is capable to lead to microbiome dysbiosis and eventually leads to immune imbalance which is critical in order to COVID-19 management [26]. For instance, it is possible to observe simultaneous penetration of microbial toxic metabolites like bacterial LPS, into intrauterine space in pregnant mothers and other human intracellular fluids and organs. LPS as a potent cytokine storm inducer then might lead to immune imbalances in neonates, which are predictable. Such an outcome can also be seen as a result of receiving foods that carry microbial toxins or bacteria that produce microbial toxins (staphylococcal superantigens and bacillus enterotoxins).

So far, various methods have been used to increase the effectiveness of drug compounds, identify microbial toxins, different pathogens identification in different patients and make optimal use of environmental and food capacities [27]. Still, there is a need for a multidisciplinary perspective to evaluate the data obtained. In linking the components of nutrition science, microbiology, microbial toxins and COVID-19 network, artificial intelligence (AI), machine learning (ML) and data mining (DM) can be important strategies and lead to the creation of a conceptual model called "Balance square", which we will introduce.

In short, AI deals with automated methods of reasoning and inference by computers. ML is a subset of AI. This field converts data into information and

makes decisions based on it. Some of its important algorithms are: classification, clustering, feature selection and prediction. DM is about extracting information from a large amount of data or the big data. Data mining is not a technical discipline but uses different algorithms related to natural language processing (NLP), ML and AI. Search programs, text summaries, and question-and-answer systems are examples of data mining applications [28]. These new sciences help machines to behave like an intelligent human being and to be able to perform various tasks. AI does not have the power to learn and analyze events, but it does program the information needed to solve potential problems and provides it to the system, then uses these data and calculations to begin solving problems and issues [29]. AI is closely related to ML; in essence, a pre-written program tells the system to learn new knowledge over time from past outputs and performance to improve future performance and decision making. ML has the ability to generalize information from large amounts of data and can use algorithms to identify relationships and patterns between the results of DM, obtain useful results, and take new actions [30]. DM, AI, and ML are three sciences that, in addition to their differences, are also directly related to each other. The use of AI made it smarter [31].

Modern medicine produces large volumes of data in various fields. This is clearly seen in relation to the vast amount of data obtained from COVID-19. Data mining has the ability to analyze large raw or multidimensional data of COVID-19 that is stored in medical and clinical databases or collected from medical centers and hospitals. This knowledge has the ability to discover regular patterns involved in disease development, proposing correlations between different characteristics such as patients' personal data, disease symptoms or even predictions. One of the important aspects of data mining in accurate diagnosis of diseases and choosing the appropriate

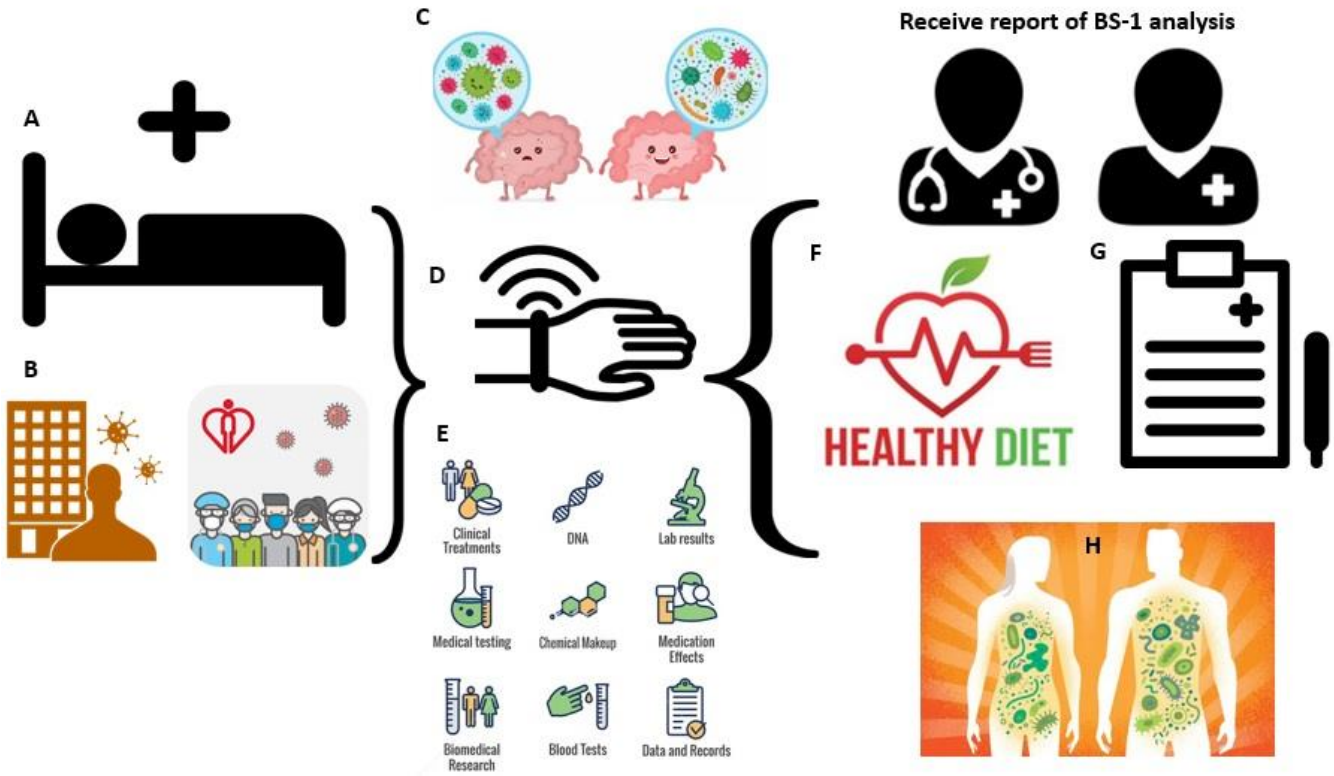

Figure 1. BS-1 Conceptual Model. This model introduces the best model of nutrition ingredient, portion size, or diet for Covid-19 patients (A) or people at high risk of getting sick (B), based on AI, ML, and DM assistance. Information data of individual microbiome (C) is provided to BS-1 software through user interfaces such as a wearable gadget (D) or laboratory-recorded information (E). The best diet (F) or prescription (G) is then given to the user to create a golden ratio of microbiome (H) or to avoid microbial poisoning which can worsen the disease. The information obtained can provide health care providers with more accurate decision-making power.

treatment for COVID-19 patients can be used is the prognosis of the disease, which is of great importance in medicine. Prognosis discovery improves the quality of medical decisions, minimizes medical errors, and reduces the cost and time of diagnosis, or even rescues and satisfies patients [32]. Radiologists use ML image segmentation algorithms to find any emergencies in patient's radio/X-Images. They also applied ML-based software's to assist younger radiologists for educational manner and training. ML is also helpful to prevent any misdiagnosis. Radiologists usually use it in rapid lesions identification and confirm their diagnosis [33]. Gender determination from hand image, automatic detection of grandiose epilepsy and recognition of normal actions in video by combining machine vision (MV) techniques and ML, selection of effective features in breast cancer diagnosis using parametric ML models, detection of mitotic cells in images Breast biopsy with the help of fast learning machines, diagnostic screening of pulmonary tuberculosis using AI, heart problems and disorders prediction, helping to identify and progress neurological diseases such as MS and Parkinson's and many other health problems are examples of AI, ML and DM applications in the medical sciences [34].

In the "Balance square number-1 (BS-1) model (Figure 1), we propose to evaluate the golden ratio of microbiome, nutrition portion and type, and microbial toxins for COVID-19 patients. After analyzing the results, each person should be prescribed a golden diet related to their own systems biology. This diet, along with medication and lifestyle changes, can provide an important diagnostic, preventive, or therapeutic role for the individual.

Probiotics play a key role in the battle against foreign germs, causing inhibition and adhesion of the intestines in direct opposition to bacteria and viruses by inhibiting the mucosal barrier of the body. They also boost alveolar macrophage activity and are useful against lung disorders. They also enhance the immune system with their by-products [35].

Another study focused on the impact of probiotics, vitamin D, and omega-3 fatty acids on intestinal issues in COVID-19 illness [36].

One of the most important applications of machine models and analysis will undoubtedly be to aid in the sequencing of microbial genes and to promote microbial analysis [37].

Microbial resistance and the creation of harsher toxins can also result from poor dietary habits, necessitating the development of new medications [38].

4. Comprehensive conclusion

The BS-1 model is able to examine large amounts of data about individuals before or after COVID-19 infection. If the laboratory information is abnormal, suggest appropriate warnings and precautions for each individual after logical mathematical reasoning. BS-1 helps physicians understand what the best diet is or diet limitations for COVID-19 patients or people at high risk for the disease? What compounds are inflammatory or suppress the immune system? What behaviors lead to person's microbiome dysbiosis?

So far, there has been no study conducted to test validation of such model (BS-1) according to correlation of microbiome-microbiota toxic metabolites like bacterial LPS and nutrition in COVID-19 positive patients. We suggest to AI, ML and DM scientist to produce BS-1 software as an effective tool for better Covid-19 management. Arrays of different wearable gadgets could develop for each person to record and report individuals' data to BS-1. This data can ultimately help the doctor or other specialists make better decisions or help them diagnose the best time to visit and assess the patient's condition. Unfortunately there are also some limitations according clear application of "Balance square" concept as follows: weakness in multidisciplinary insights for scientific teams, complexity of concept's systems biology, poor connection between basic and medical sciences. We proposed more interdisciplinary collaboration to overcome and fill in present gaps.

Authors' contributions

FT, SEH: Collecting and summarizing nutrition-related articles. MJ, MA: Collecting and summarizing both nutrition and microbiome-related articles. EGH: EndNote library preparation and drafting manuscript. FA: Native language editing. AR: Drafting and critical revision. MH: Suggesting the idea of article, writing first draft of article, scientific editing.

Conflict of interests

None to declare.

Ethical declarations

Not applicable.

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