

THE INTERACTION BETWEEN THE DIETARY REGIME AND THE GUT MICROBIOTA: INVOLVEMENT FOR HEALTH AND DISORDERS: A REVIEW STUDY

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Abstract

Diet effects both positively and negatively in composition and diversity of gut microbiota that in turns has an impact on human health and relates to many health disorders. Human gut microbiome has a diverse ecosystem consisting of complex microbial communities that has a direct influence on disorders and issues related to health. The study of effects of diet on microbiota is compulsory as geographical location has impact on it. Dietary patterns like ketogenic diet, western diet, Mediterranean diet, high protein diet, plant-based diet and high fiber diet effects the formation and role of diverse microbial communities present in gut. There is a critical interaction of diet, immunity and microbiome. For developing precise nutrition and related therapies, understanding of the relation between host, dietary pattern and microbiota is necessary.

INTRODUCTION

Human gut microbiome has a diverse ecosystem consisting of complex microbial communities that has a direct influence on disorders and issues related to health (Del Pozo et al., 2022). Throughout, human life, this microbiota and its complex communities has a great influence in every physiological step related to growth and behavior. In the start of life, elements like a dietary regime, distribution of food, surroundings and nature make gut microbiome of a human. When time goes on and a child becomes adult, even the microbiota is quite normal and becomes stabilized yet its role and makeup is effected by some exogenous

elements especially dietary factor (Pasolli et al., 2017).

There is a critical interaction of diet, immunity and microbiome that regulates the levels of water and salts in our body, maintains the internal environment of body and fights against diseases and disease-causing agents(Heinken et al., 2023). Role and makeup of microbiome is changed when a particular diet is used for a short time or a long time that shows the importance of dietary regime (Johnson et al., 2019).

The latest research has specified the advancement in metagenomic sequencing and artificial intelligence. Thus, our knowledge

about diet and gut microbiome has extended that leads to microbiota targeted treatments and precise diet if a person has some diet related disease (Zampieri, Vijayakumar, Yaneske, & Angione, 2019).

Here is an example of the Mediterranean diet which shows a useful effect in combating health issues. But it can differ in two persons according to their health profile. The use of western diet and highly processed diet leads to cardiovascular disorders. A healthy person microbiota is due to different complex layouts (Armet et al., 2022; Wilson et al., 2020). There is a usually found bacteria *Prevotella copri* in microbiome that has some useful and some harmful role.

Nutrition And Its Effects on The Gut Microbiota:

Diet effects both positively and negatively, and now the below discussion shows different types of relations between diet and microbiome.

The Mediterranean Dietary Regime

This dietary regime contains unprocessed food and the natural food like vegetables, dairy products and a balanced quantity of meat, thus known as "gold standard". *Faecalibacterium prausnitzii* and *Roseburia* species are found in high quantity and shows a positive effect on health. As a result, short-chain fatty acids are increased while metabolas derivative are decreased (Bourdeau-Julien et al., 2023; Wang et al., 2021).

This dietary regime is related to 36 operational routes, particularly whole plant dietary regime showing positive role in SCFA ferment and roughage decomposition. If we use Mediterranean diet, it is useful for routes of D-fructuronate decomposition and mannan decomposition (Oliver et al., 2021).

It also shows a positive effect in lowering myocardial disorders. According to recent studies, 294 people that were overweight were more positively effected in terms of health as they were having the green Mediterranean diet that is an advanced variety of the Mediterranean diet (Abbas, Qadir, & Muhammad, 2020).

The Green Mediterranean diet includes use of polyphenol containing green tea and Mankai aquatic plant other than that already used the whole plant diet and less quantity of red meat. It showed even better results in terms of formation and range of gut microbiome. It was due to a huge presence of *Prevotella* species and branched chain amino acids degrading enzymes. There was also less presence of *Bifidobacterium* species (Alfonso Benítez-Páez et al., 2019; David et al., 2014).

The High-fiber Dietary Regime

Intake of diet having high fibers is compulsory for maintaining a healthy body because it decreases obesity even it is for a long time. People who take food having less fibers are more likely to type 2 diabetes and colon cancer. Food that is enriched with fibers changes the composition of microbiome in a healthy way (K. Afzal et al., 2017).

It increases the presence of *Lactobacillus* species and *Bifidobacterium* species that are useful to gut microbiome (Masood, Qadir, Shirazi, & Khan, 2011). Different portions of high fibers have different effects on microbiota communities. For example, newborns that are on breastfeed have increased presence of *Bifidobacterium* species according to intake of human milk oligosaccharides (De Filippis et al., 2019).

As a result, Bacteroidetes and Firmicutes increase their number to digest other complicated polysaccharides. Whole wheat flour was added to the diet of 31 participants and as a result it enhanced the volume of some authentic bacteria like *Lactobacillus* and *Bifidobacterium* species (Alfonso Benítez-Páez et al., 2019).

It also shows a decrease in cholesterol levels. Oat bran reduces Firmicutes and enhances levels of Bacteroidetes. Small intestine digests easy saccharides, while the complicated ones go through colonic microbe related fermentation and produce SCFA which has a lot of benefits like signaling by G-protein coupled receptors (GPCRs). It also induces secretions from satiety hormones in endocrine cell lines (Costabile et al., 2008; Wang et al., 2021).

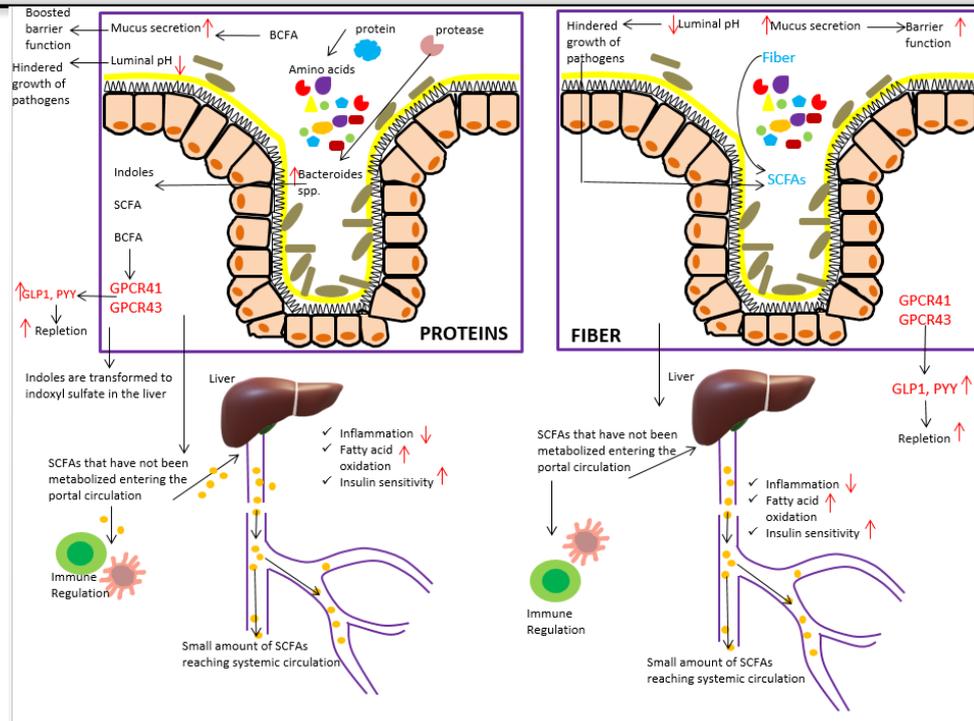


Figure 1: [Effects of proteins and dietary fibers on health of human.]

It has an effect on regulating hunger, in modulating the role of regulating T cells and regulation of water and salts in colon (S. Afzal et al., 2016). Butyrate becomes origin of strength for epithelial cells at colon line, has a role in mediation of inflammation reduction characteristics from intestinal cell lines that is macrophages and dendritic cells and increases the release of mucus that is important for regulation in intestine so that the absorbed nutrients are in optimized levels (Grzeskowiak et al., 2012). SCFA modulates intestinal microbiota thus reduces intestinal disorders like irritable bowel syndrome, co-rectal cancer, gastric cancer and constipation (Qadir & Faheem, 2017).

The Plant-based Dietary regime

This diet majorly consists of food that is made up of plants includes vegetables, fruits, nuts, seeds, legumes and whole grains. It is not be considered as a vegetarian dietary regime because it also includes beef, eggs, fish, chicken and milk-based products but the major component of your diet is based on a plant-based diet. It makes different kind of microbial ecosystem as it includes polyphenols, digestible

and indigestible carbohydrates that includes pre and post biotic impacts (Wagenaar et al., 2021). Higher levels of Bacteroidetes and *Prevotella* species are found in the gut than omnivores. Some species are in comparing amounts which causes a tense environment in microbial communities when there is a sudden change in dietary regimes like, healthy to an unhealthy version of diet (Aziz et al., 2021). Polyphenols are secondary metabolites that are digested in the small intestine in less amounts. Then aglycones are transformed within enterocytes and later on within hepatocytes which then go towards kidneys and liver through the circulatory system and then excretion through urine (David et al., 2014).

Bifidobacterium and Lactobacillus are found in large quantities that is why they serve anti-inflammatory effect and protects from cardiovascular disorders (Selinger et al., 2023). An experiment was done on 20,000 participants that showed that if they were supplemented with cocoa extract that contains high levels of polyphenols, it makes a reduction in death rate due to cardiovascular issues (Corrêa, Rogero, Hassimotto, & Lajolo, 2019).

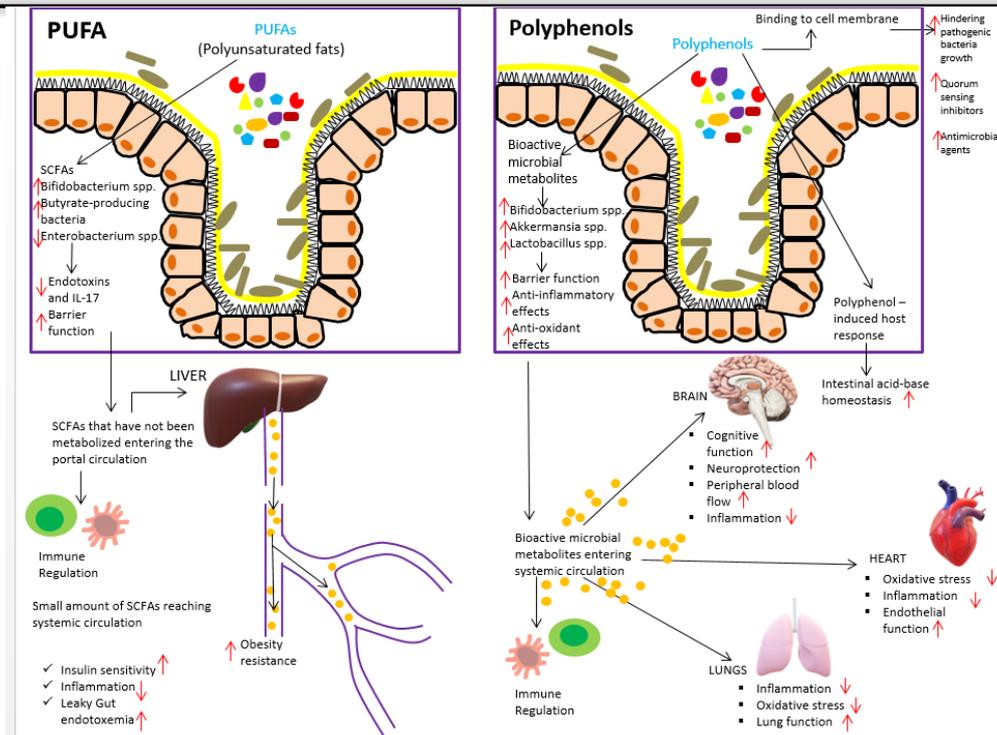


Figure 2: [Effects of diet related polyunsaturated fatty acids and polyphenols on health of human.]

Latest studies tell us that if active microbe related byproducts are taken as food, they show positive impact on body, for example, urolithin- A addition to diet improves health of cell and mitochondria (A Benítez-Páez, 2019).

Polyphenols regulate SCFA, dopamine, lipopolysaccharides and acids of bile that as a result changes the constitution and functions of microbial communities. Modification in gut microbiome using polyphenols shows that it helps in regulating homeostasis of lungs and CNS functions and it maintains integration in intestinal barrier (Costabile et al., 2008; Del Pozo et al., 2022).

Different types of lipids and proteins have variations from both sources that are plants and animals causing imbalances in the constitution of gut microbiome and as a result in metabolites, for example, the animal based dietary regime causes an increase in bacterial species (for bile tolerance like *Bilophila* and *Alistipes*) (Dehingia et al., 2015).

It also reduces the amount of Firmicute species, results in a reduced amount of BCAA and increased amounts of SCFA. Carotenoids and terpenes have a positive effect on human health. Using metabolic typing for analyzing polyphenolic compounds can be a very useful step towards deep and advanced knowledge for

understanding of microbial diversity and metabolic compounds in individuals (F. Ross et al., 2024).

High-protein dietary regime

If utilization of protein in diet exceeds than 1.5g/kg in a day then it is known as a diet having high protein. Sportsmen or obese people generally use this diet. Even host proteases break down the proteins in our diet, yet some quantity (12-18g) of proteins go through our large intestine where their metabolism occurs by our microbiota. There are many types of complicated proteins having distinct stages of consumability (Wang et al., 2021).

Some species of bacteria have a proteolytic role and present in abundance in our gut microbiome including *Bacillus*, *Streptococcus*, *Clostridium*, *Fusobacterium* and *Bacteroides* species (Wilson et al., 2020). These bacterial species make short peptides or free amino acids by using different types of exogenic proteases (includes for example, serine, glutamic, aspartic), peptidases and endopeptidases. Short chain fatty acids are produced as a result of fermentation of many amino acids and fermentation of BCAA produces BCFA's like

iso-butyrate and isovalerate (Bourdeau-Julien et al., 2023; Oliver et al., 2021).

There are some other things that are fermented includes indoles, ammonia, gases, phenolic products and organic acids that have sometimes a potential role in health disorder. Indoles are converted into a very harmful product known as indoxyl sulfate. It is toxic for kidneys and disturbs endothelial functions (Gómez-Pérez et al., 2023; F. Ross et al., 2024).

The Ketogenic Dietary Regime

Diet that includes a very less amount of carbohydrates, a balanced amount of proteins and a dietary model of high fat is known as a ketogenic dietary regime (Qadir & Ahmed, 2017). Its metabolic results are same as the metabolic results during fasting that increases ketone molecules. Ratio is kept as 4:1 (fats: proteins + carbohydrate) (Bashir & Qadir, 2017). For treating epilepsy, this dietary regime is used as a medication.

Recent studies shows that ketogenic dietary regime has great results for medication of other diseases like cancer, Alzheimer and obesity. High fat dietary pattern increases Firmicutes and decreases Bacteroidetes, but it can also cause different results (Martínez et al., 2015).

Recently a research was done on 17 people that were obese, medication was done for 4 weeks and it resulted a decrease in Actinobacteria in human microbiota. 19 bacterial species that were good for health were reduced. Then a research was done on 12 children having epilepsy (Mancabelli et al., 2017). They were supplemented with ketonic dietary regime and it reduced bacterial species that were promoting health and digesting fibers, for example, Bifidobacterium spp. Then it increased the amount of Escherichia coli (David et al., 2014; Wilson et al., 2020).

Some studies also showed that ketogenic dietary routine modified the constitution of gut microbiota increasing *Akkermansia*, *Lactobacillus*, *Roseburia* and *Shigella* species. The recent study tells that if faecal microbiome from person consuming ketogenic dietary regime is transported to axenic mouse, it shows alterations in T helper 17 cell collection in intestine. More research is still needed for understanding this ketogenic diet (Janbaz, Qadir, Jan, & Gilani, 2013; Miao et al., 2022).

Western Dietary Regime

Diet having very high amount of calories, red meat, fats (saturated) and highly processed diet including improper quantities of fruit, vegetable and fibers is known as western dietary regime (Bisanz, Upadhyay, Turnbaugh, Ly, & Turnbaugh, 2019). Due to this diet, gut is more diverse than other dietary patterns and has an abundance of Bacteroides. Due to low fiber content, a very less amount of short chain fatty acids is produced. Choline from animal protein converts into trimethylamine which then further converts into TMAO when it reaches liver that is related to long term disorders (Shanahan, Ghosh, & O'Toole, 2021).

Artificial sweet inducers include saccharin and aspartame cause chronic effects on formation and variety of microbiota. Additives that are present in the ultra-processed diet cause burning effects in the gut and disturb the mucus layering. Artificial food colors mostly present in bakery items affects regulations of salts and water in the human body. This diet is totally related to long term disorders (Armet et al., 2022; Oliver et al., 2021).

The Effect of a Dietary Regime on Microbiome Related Health Disorders

Diet directly or indirectly effects health and gut. The remaining portion is based on the discussions that how dietary regime leads to diseases related to our microbiota.

The Contribution of the Maternal Dietary Regime in adult Health Consequences

Breast milk has a great impact on the gut health of an infant as it consists of many bioactive products mainly immunoglobulins (G), miRNA, HMOs and immune cells. Breastfeed causes an increase in inflammatory indicators like faecal calprotectin, as a result reduction of pro-inflammatory serum cytokine makes immune system mature. Many bacterial species like Bifidobacterium breve, B. longum, B. fidum and B. infantis use HMO and as a result they make their abundance in gut of children that are on breastfeeding, and they can change relation between microbes and their products (De Filippo et al., 2010).

HMO used as prebiotics and that is how they protect the infants from any infection, helps in developing the brain and reduces permeability

in intestine. Host uses short chain fatty acids as a source of power which is produced as a result of HMO consumption. Children that are not on breastfeeding and consume formula-based milk have higher levels of Streptococcus, Clostridioides and Enterococcus (Del Pozo et al., 2022).

HMO has many health benefits. It protects from obesity and allergy. Recently a study showed if mice are given a low fiber diet during pregnancy, it disturbs the regulating T cells in an infant and causes severe respiratory infection. Fermented diet has positive effect on offspring health as it reduces colonic inflammation and develops gut microbiome (Singh et al., 2017).

A Dietary Routine, Gut Microbiota and Metabolic and Intestinal Diseases

Our microbiome regulates metabolic system in body and makes some changes in composition of microbiota. It also decreases the diversity of some microbes that cause diseases in metabolic system. Scientists used models of axenic rodents to find a relationship between obesity and gut microbiome. These axenic rodents

were colonized with gut microbiome from the rodents that were obese and it followed by insulin resistant and overweight. But when they were supplemented with western dietary pattern, it resulted in no obesity (F. C. Ross et al., 2024).

In gut microbiome, there is abundance of Bacteroidetes spp. and Firmicutes, their abundance relates to increase in obesity and thus as a result variability in microbial environment reduces. Some disorders that are related to bulkiness are hypertension, diabetes type 2 and cardiovascular disorders (Ho et al., 2018).

People that are obese and have diabetes type 2, have reduced amount of butyrate producers. Research was done in mice and it showed that some microbial species like Bacteroides, Akkermansia and Bifidobacterium have a negative role in people having type 2 diabetes. A commonly used treatment for diabetes type 2 is Metformin which supports the antidiabetic activity by changing homeostatic function for glucose and in producing short chain fatty acids (Gul, Abbas, & Qadir, 2015).

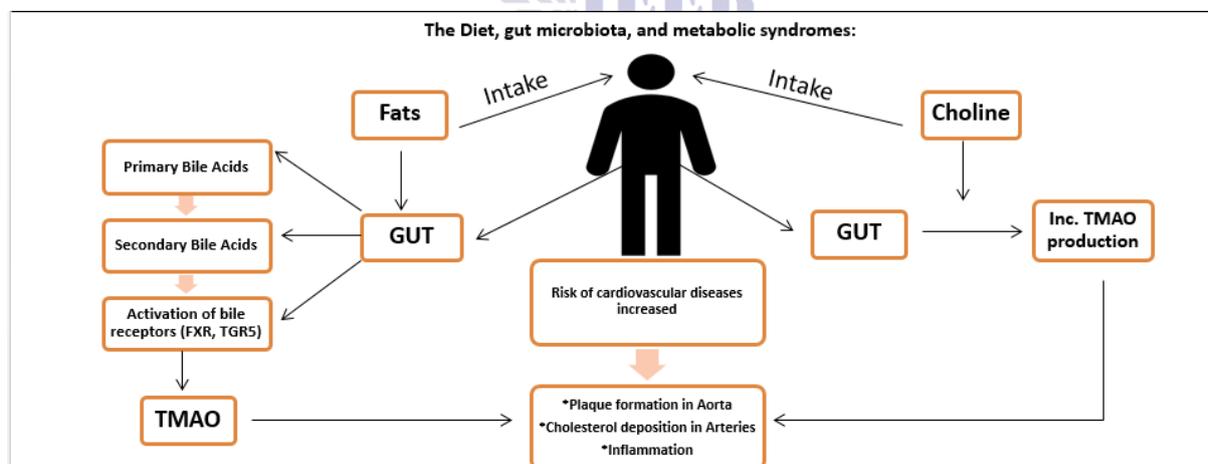


Figure 3[Relation between gut, diet and metabolic disorders]

Diet also effects our intestinal functions and can also lead to some diseases like inflammatory bowel syndrome and cancerous colon. Different factors are related to irritable bowel disease like oversensitivity, multiple food allergy, microbiome structure, mild mucositis and permeability in intestine. People having this syndrome have reduction in Bacteroidetes and increase in levels of Firmicutes. They have

less genes that are involved in metabolic functions for carbohydrates and amino acids. Inflammatory bowel diseases are due to increased proportions of diet like dairy, red meat, unsaturated fatty acids and lots of carbohydrates (Trefflich et al., 2020).

Due to their incomplete metabolism, some dangerous byproducts are produced like hydrogen gas and phenol stopping butyrate

production and increasing pathogenicity for this disease. Diet is also involved in colon cancer (David et al., 2014). Using fatty foods and low fiber foods increase the abundance of *Fusobacterium* spp. that causes changes in

phenotype due to epigenetic, changing tumor microenvironment and activates E-cadherin-beta-catenin signaling mechanism (Ghosh et al., 2020).

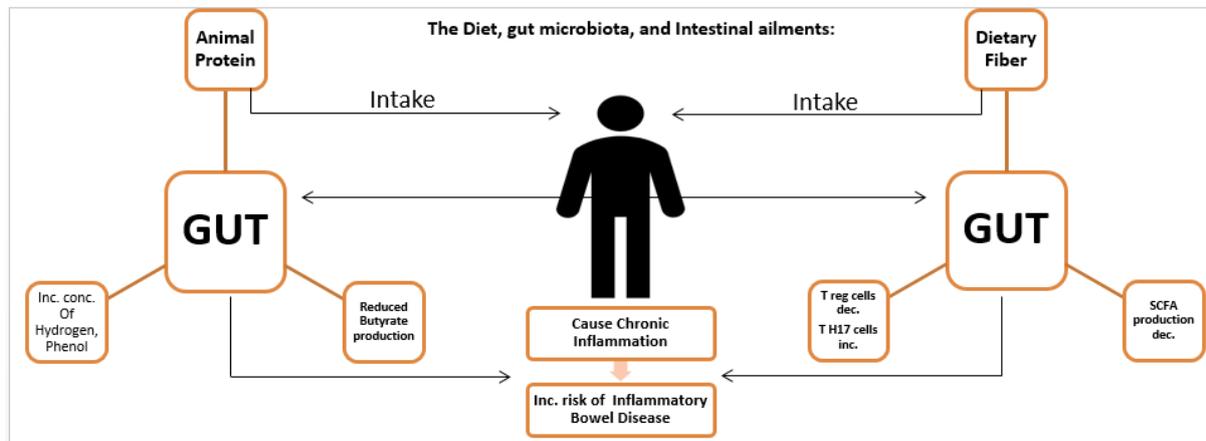


Figure 4[Relation between gut, diet and intestinal disorders.]

Precise Nutrition Directing Gut Microbiome

Precise nutrition is an advanced field in which diet is recommended to a person according to his/her special characters relating to microbiota in health and disorders. Role and makeup of microbiota is analyzed to find inadequate amounts of some basic nutrients according to specific structure. Right choice of prebiotics and probiotics is also necessary for a balanced gut microbiome (Meslier et al., 2020). Using precision nutrition helps to reduce the risk of diet related diseases. Precise medication can be similar to precise nutrition if effects positively on gut health. Trials should be conducted on a large scale for deep understanding of the effects of dietary patterns on gut microbiome (Oliver et al., 2021; F. Ross et al., 2024).

Conclusion

To conclude complex association between gut microbiota, nutrition and related disease, some integrated techniques that are metagenomics, meta-proteomics, meta-transcriptomics and metabolomics have become compulsory. For ensuring reproducible results in different localities, it is compulsory to verify the results by different platforms. There are still many questions for explaining association between diet, diseases and microbiome. Thus, study of individual microbiota and its historical display is necessary for understanding the changing

makeup and function of microbes due to environmental factors. Differences in components of food that are utilized on a global level and effect of additives like antibiotics and also pesticides should be examined. Low-income countries should be considered globally where malnutrition is the major problem. This needs large scale collaborations between different research centers in the world.

Conflict of interest:

The authors declare no competing interests.

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