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Human gut microbiome and obesity: A review

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Abstract
In today's society, obesity has become a major problem. It develops in healthy people as a result of genetic and environmental influences. Over the course of a year, this metabolic condition worsens. Recent research has made it clear that having a healthy gut flora reduces the complications associated with obesity. If people maintain a healthy lifestyle in addition to eating an adequate diet, their gut microbiome, a complex population, will be directly linked to eliminating all obesity symptoms. Different bacteria are urged to control obesity's symptoms. Probiotics such as *Lactobacillus* and *Bifidobacterium* have a direct impact on reducing obesity. The gut microbiota aids in digestion, controls hunger, reduces chronic inflammation, and regulates circadian rhythm. Therefore, the general gut microbiota directly influences the symptom of obesity. This review discusses the relationship between the gut microbiome and obesity.

Keywords: Gut microbiome, obesity, short chain fatty acids. energy absorption, manage appetite, reign fat content, circadian rhythm

Introduction

The link between human gut microbiome and obesity is a hotly debated subject. The most prevalent microbial population in the human host's gastrointestinal tract is called the gut microbiota. Numerous other organs, the host's gastrointestinal tract, saliva, and salivary glands all contain trillions of bacteria (Sender *et al.*, 2016) [38]. Gut microbiome or gut microbiota which helps in homeostasis at intestine, develop the immunity and decrease the activity of pathogen in host (Thursbyb & Juge, 2017) [43]. Gut microbiome is the composed of bacteria, yeast and virus. 1000 species or more are present in bacterial community which be in 6 phyla members like Firmicutes, Bacteroidetes, Actinobacteria, Proteobacteria, Fusobacteria, Verrucomicrobia. Firmicutes and Bacteroidetes are foremost phyla members of bacterial population that accounts 90% of gut microbiome (Rinninella *et al*., 2019) [35]. Authors have noted that, dissimilarities of gut microbiome have shown in every section of elementary tract and interchange along with time which is caused of ageing and other ecological attributes such as dietary intervention, life style modification, intake of antibiotics. Distinction about construction of microbiome in every single person along with variation ascribes to age, diet pattern, upgraded life style & also ethnicity (Rinninella *et al.*, 2019) [35]. Researchers have described that, in human host, gut microbiota is composed of 100 trillion microbes that encompasses 10 times the quantity of cells in the body. Gut microbiome depends on food remainder that is undigested food parts in the host body, excreted mucus through gut along with dead cells which are shack as nutrients to carry on it's high microbial population (Gentile & Weir, 2018) [11]. The host gut microbiota develops some substrates such as short chain fatty acids (SCFAs), vitamins along with some anti-inflammatory, analgesic, antioxidant components, apart from that, neurotoxin, carcinogen, immunotoxin like substances (Miyamoto *et al.*, 2019 [29]; Canfora *et al.*, 2019) [5]. These substances move to blood there after modulate gene expression in direct way and improve the immunity and also remove the metabolic distress. So that, gut microbiome is important for regulating metabolites and maintains the energy index. It is interpreted that, disproportion in gut microbiome may lead to metabolic distress and enhances appetite that's why appear obesity (Liu *et al.*, 2021) [22].

The most common metabolic disorder in the world is obesity. According to the WHO, obesity is defined as a BMI of 30.0 or more. Numerous surveys have revealed that half of the 2 billion persons who are considered to be adults in worldwide are fatty (Hoffman *et al*., 2020) [16]. Researchers have hypothesised that, the number of obese will outstretch to 1.12 billion in 2030. Authors have demonstrated that, in obese people modified the aspect of body development along with ascertained that, the disease of glucose and lipid metabolism, chronic infection, inflammation, oxidative damage aside from other disorders have grown like enhanced the complication of cardiovascular disorders (Tsung-Ru *et al.*, 2019) [45], diabetes (Hugo *et al*.,2020) [13], cancer, Non-alcoholic fatty liver disorders (NAFLD) (Tilg *et al.*,2020) [44], atherosclerosis (Mongraw-Chaffin *et al.*, 2018) [26]. Recently, clinical trials have revealed that, alteration the composition in gut microbiome can develop obesity (Gomes *et al.*,2018) [12].

It is worth noting that, 85 % hospitalised obese patients have needed mechanical ventilation among 62% patients are died from COVID19 (recent pandemic disorder) (Stefan *et* *al*.,2020) [39]. Among various treatment, to delete the complication of obesity, bariatric surgery is very much beneficial to improve the complication of obesity and co morbidities (Neff *et al*.,2017) [30]. Consumption of high calorie added foods along with less physical activity or sedentary life style are the principal cause of obesity that's outcome is the accumulation of increased energy in the body (Heymsfield & Wadden 2017) [15]. Much amount of lipid intake from excessive calorie dense foods therefore gathering lipid in subcutaneous and visceral adipose tissues that is caused of adipose tissue is incapable to preserve the energy as triglyceride resulting, overabundance of lipid goes to blood circulation. Increased systemic blood circulation and fat absorption in non-adipose tissues that may not involve into fatty acid oxidation however enhances fatty acid accumulation that's caused of ectopic fat storage (Bays *et al*.,2016) [4]. Researchers have described that, excess triglyceride in adipocytes promote the development proinflammatory cytokines, adipokines that develop insulin resistance, NAFLD, obesity including cancer (Rojas *et al*.,2019) [36]. In accordance with Abenavoli *et al*.,2019 [1] gut microbiome is directly linked with obesity by adiposity and disturbances in glucose metabolism. Literature review has discussed about diet is very much proficient subject to keep the adequate environment of gut microbiome. Here in, this review discusses about the adjunct relationship among human gut microbiome and obesity.

About gut microbiota

Microorganisms are found on every surface of the human body. These creatures are part of the dynamic microbiota, which is a community of bacteria, viruses, fungus, and archaea **(**Singh *et al*., 2017) [50].

The host elementary tract is very much intricate which is composed of variety of gut microbiota like 10^{14} bacterial cells are derived from 400 to 500 bacterial species per gramme of colonic content. Healthy person dock ~195 bacterial strains, among 101 species shows fecal microbiome. Elementary tract consists multiple composition and quantity of bacteria per gram content. For instance, stomach and duodenum consists 10-10^{13} cells, small intestine contains 10^4 to 10^7 cells, large intestine consists 10^{11} to 10^{12} cells. Gut microbiota develops the synergistic interconnection to the host (Liang *et al*.,2021 [21]; Tilg *et al*.,2020). In human host, gut microbiome is attributed by diversity along with firmness. In obesity, genera of *Bacteroidetes* for instance *Lactobacillus sp. Bifidobacterium sp. Bacteroides sp. Enterococcus sp.* besides the *Firmicutes* and *Bacteroidetes* proportion are stimulated whereas *Clostridia* like *Clostridium leptum, Enterobacter sp.* are decreased. Gut microbiome may influence the capability of human body to grab nutrients and synchronize the energy utilisation due to this, it shows crucial function in the emergence of obesity (Ding *et al.*, 2019 [9]; R´egnier *et al*.,2021) [34]. Authors have documented that, vegan diet stimulate the concentration of *Bacteroidetes sp*. as well as lesions the concentration of *Acteroides sp. Bifidobacterium sp. Escherichia coli*, besides *Enterobacteriaceae* and *Firmicutes*. Noteworthy, gut microbiota also improve the complication of obesity (Lee *et al*.,2019) [19]. The function of metagenomic, 16SRNA gene sequencing, the variation of gut microbiome has elaborately discussed in before literature review. The crucial application of gut microbiome of individuals are breakdown of polysaccharides, develop short chain fatty acid (SCFA), increase the concentration of SCFA, abundance of lipopolysaccharides, develop the vitamin and essential amino acid concentration (Lloyd-Price *et al*.,2016) [20]. Authors have reviewed that, healthy gut microbiome maintain vigorous symmetry that means, it's capacity to endure concernment and back to healthy life along with good metabolism like cure with antibiotic. On a similar note, alteration in structure and inadequate metabolism of gut microbiome modify physical mechanism like absorption of essential nutrients and metabolism of energy.

Consortium of obesity and gut microbiome

Research findings have confirmed about the interconnection among gut microbiome and obesity in mice which is germ free. Transfer the gut microbiome from conventional mice to germ deleted mice enhanced the transplants' fat accumulation along with upregulate the insulin resistance apart from that fallen down food consumption which proposed that, gut microbiota escalate the cumulation of adipose tissues in host body. Moreover, 16SRNA gene sequence pattern has possessed that, obesity is directly inter connected with phyla of bacterial member- *Firmicutes* and *Bacteroidetes*. In this context, in obese mice 50% lower the *Bacteroidetes* as well as enhance the concentration of *Firmicutes*. On a similar note, in case of obese patient, proportion of *Firmicutes* and *Bacteroidetes* are surged with enhanced BMI (Koliada *et al*.,2017) [17]. Simultaneously, another experiment has reviewed that, affluence of *Bacteroidetes* concentration is not remarkable for obese and even in normal person. A study has conducted about the gut microbiome of obese and normal healthy person on the basis of database and also intestinal programme in the US which manifest that, gut microbiome of 1655 in fit and fine people and 898 in obese adult people have the proportion of *Firmicutes* and *Bacteroidetes* in obese are fallen down. Findings have shown that, *Christensenellaceae* and genera *Methanobacteriales*, *Lactobacillus, Bifidobacteria and Akkermansia* these bacteria are specifically concerned to develop obesity. *Christensenellaceae* is involved for losing weight however plenty of this type bacteria are conversely linked with BMI in host (Waters & Ley,2019 [46]). *Akkermansia muciniphila* is directly associated for burning the weight. Augmentation with *A. muciniphila* upgrade the clinical symptoms of overweight and obese (Depommier *et al*.,2019) [10]. Many studies have revealed that, *Lactobacillus* and *Bifidobacterium* are important probiotics which convey equilibrium of microbiome in the gut. According to Crovesy *et al*.,2017 [8], *Lactobacillus* plays a very particular function in case of overweight. Specifically, *L. paracasei* is negatively interlinked with obesity simultaneously, opulence *of L. reuteri* and *L. gasseri* are corresponded with obesity. Authors have pointed that, increased quantity of *Bifidobacterium* which resist obesity. Animal model has verified that, *Bifidobacterium* incorporate into diet influenced obesity resulting in beneficial effect is fully depended on *Bifidobacterium* strain. Even though decreased quantity of *Bifidobacterium* can show the complication of obesity in gut. *M. smithii* and *B. animalis* are corresponded to normal weight however *L. reuteri* is connected to mature obesity (Million *et al*.,2012) [27].

Subcutaneous and visceral obesity are the two types of obesity. The hallmark microbiome for obesity is a proportion of firmicutes and bacteroidetes. Brown adipocytes at subcutaneous adipose tissue are connected with an increased number of Firmicutes in cases of morbid obesity. The visceral adipose tissues, however, are not **(**Moreno-Navarrete *et al.,*2018) [28]. Based on positive Research outcome, browning in white adipose tissue prolong a good phenotype of obesity recommends that increased quantity of *Firmicutes* can be advantageous for subcutaneous obesity. A clinical trial has recommended that, low calorie consist diet shows weight reduction in postmenopausal woman who is obese, decrease the concentration of *Roseburia* and escalate the *Christensenellaceae* which is corresponded along with gene expression avenues like protein-amino acid N-glycation at subcutaneous adipose tissues (Alemán *et al*., 2018) [3]. Importantly, probiotic conveys a pragmatic function in visceral obesity affected mice who consume excessive amount of sugar or fat. The probiotic or live microorganisms are *L. acidophilus, L. rhamnosus, L. paracasei*, *Pediococcus pentosaceus, B. lactis, B. breve* recurrently decrease BMI along with lesion intrahepatic fat concentration in case of NAFLD patients at post administration of 12 wk. Excluding *L. paracasei* the increased quantity of another 5 probiotic strains is very much beneficial in human gut (Ahn *et al.*, 2019) [2]. Authors have illuminated that, *Christensenellaceae*, *Porphyromonadaceae* and *Rikenellaceae* are very much beneficial in gut microbiome population of adult which decrease the visceral adipose tissue (Tavella *et al*.,2021) [41]. The heterogenicity of gut microbiota in human gastrointestinal tract is a crucial subject which is interlinked with obesity. In accordance with Ciobârcă *et al.,*2020 [7]; Heiss & Olofsson, 2018 [14]; adequate gut microbiota environment may decrease the symptoms of obesity. α diversity of obese are decreased than a fit person however no crucial mechanism of β diversity has shown in gut microbiome (Ma *et al*.,2019) [25]. Numerous Research have examined that, obesity is known as a flora associated disorder without pathogen viability can be associated with dysbiosis.

Mechanism of obesity instigate by gut microbiome

Absorption of energy

Obese mice consume protein and carbohydrates, and the gut microbiota then transmits the energy index to the human host. Clinical trial has possessed that, there is no distinction among diet and weight of mice, more over the body fat of germ-free mice colonised with the help of ‘obese gut microbiota’ enhanced apparently in comparison with those are colonised through ‘lean gut microbiota’. This experiment has possessed that obese gut microbiome enhances the capability for energy absorption from diet Multiomics has proposed that, enhances absorption of lipid in host. Apart from that, colonisation of *Clostridium* in germ free mice decreases the gene regulation which monitor the adequate lipid metabolism (Petersen *et al.,*2019) [32]. Ultimately, it can be said that, gut microbiome involves to ferment the carbohydrate components into short chain fatty acids simultaneously absorbed by gut and expelled by faeces. SCFAs are very much important for homeostasis of energy (Cani *et al.,*2019) [6].

Appetite control

The gut-brain axis strongly links the gut bacteria to the central neurological system. The gut microbiome's shape and composition are influenced by the central nervous system. Gut bacteria influences food intake through regulating brain activity with the aid of neuromodulators like serotonin that regulate basic activities. Lactate is generated by *Lactobacillus* and *Bifidobacterium* that is functioned as substrate for neuron may elongate the satiety after meal intake. Authors have enumerated that; gut microbiome engages in gut brain axis through promotion of hormones present in gut. Which is excreted by enteroendocrine cells. Peptide YY, pancreatic polypeptide is anorexia hormone excreted by human gastrointestinal tract. GLP-1 lesion glucagon content, therefore unhurried gastric emptying, activate the synthesis of insulin, decreases the food consumption (Wu *et al*.,2019 [47]; Salehi & Purnell,2019 [37]). Authors have delivered that, in case of obese people peptide YY and GLP-1 are dwindled.

Repository of fat

Gut microbiome enhances the glucose absorption in intestine of human host along with glucose contented in serum therefore enhances the pronouncement of two transcription factors like ChREBP (Carbohydrate response element binding protein) and SREBP-1 (Sterol regulatory element binding protein) these introduce the accumulation of fat in liver. Furthermore, *L. paracasei* controlled ANGPTL4 which is involved into regulation of fat deposition. *L. paracasei* instigate the pronouncement of ANGPTL4 by peroxisomal proliferator activated receptors α and γ. It is widely recognised that, ANGPTL4 stop the activity of lipoprotein lipase (LPL) resulting in inhibit the gathering of fat. *L. paracasei* repel excessive diet introduced obesity (Tazi *et al*.,2018) [42].

Circadian rhythm

According to literature review, the interference of circadian rhythm can develop the manifestations of obesity (Rácz *et al*.,2018) [33]. Gut microbiome controls the consumption of lipid and therefore accumulation of fat with the help of adjust the circadian transcription factor NFIL3. Authors have demonstrated that, ILC3-STAT-3 signalling avenue is involved in the interconnection among microbiome and circadian clock. Gut microbiome regulates rhythmic histone acetylation by HDAC3 (Histone deacetylase -3) communicate epithelial cells of intestine. Therefore, Cd36 which is lipid carrying gene that encourage the absorption of lipid and obesity (Kuang *et al*.,2019) [18]. The introduction of histone modifiers to chromatin is the essential mechanism for development of circadian rhythm by HDCA3. It is important to note that, rhythms in feeding are the adequate controller of circadian rhythm and community of gut microbiome. Time cramped feeding decrease bad outcome of fat dense foods through controlling the circadian rhythm of gut microbiome (Ye *et al*.,2020 [48]; Zeb *et al*.,2020) [49]. Substrate of gut microbiome influence the circadian rhythm. Bile is directly attached in rhythmic mechanism among human host and gut microbiome. Furthermore, microbial bile salt breakdown and controlled the circadian clock and develop lipid metabolism associated genes. *Lachnospiraceae, Clostridiaceae, Ruminococcaceae, Lactobacillus, Bacteroides*, *Bifidobacterium* involves into bile salt biotransformation (Parkar *et al*.,2019) [31]. SCFA monitor the pronouncement of clock genes in liver. SCFA such as acetate and butyrate modulate the proclamation of clock genes Per2 and Bmal1 in liver accompanied with serum shock. Moreover, SCFA introduce ordinance of circadian clock as alter the no steps in peripheral circadian clock is recognised in fibrosis and cultured slice of liver hepatic cells **(**Tahara *et al*.,2018) [40].

Conclusion

The gastrointestinal tract's gut microbiome colony serves a necessary function. Dysbiosis is the root cause of obesity. For the development of an obesity-related problem, many microorganisms are interconnected. Inadequate gut microbiota composition may worsen obesity symptoms by increasing the amount of energy absorbed, escalating appetite, increasing fat storage, developing chronic inflammations, and regulating circadian rhythm. We need to talk more about obesity since the gut microbiome has a complex regulatory system. The gut microbiome's composition affects homoeostasis. Metabolites are produced by the gut microbiome, modified biochemically by the gut microbiota, and formed by the host, but they are also produced from dietary components by bacterial colonies, which play a significant role in the manifestation of obesity. Probiotics are the most effective live microorganism for treating obesity complications because they increase intestinal microbe quantity and control in obese people. In order to fully understand the delicate link between the gut microbiome and obesity, more research is specifically required.

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