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Review

GUT MICROBIOTA AS RISK FACTOR CAUSING OBESITY IN CHILDREN

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Nowadays obesity resulting from abnormal or excessive fat deposits in a body has become a true epidemic. Risk factors that cause the disease include improper lifestyle, hereditary predisposition, as well as metabolic activity of gut microbiota. Research works performed over the last decades indicate that microbes that create colonies in human intestines play a significant role in maintaining proper metabolism. There is a correlation between disorders in gut microbiota structure and immune disorders, elevated susceptibility to infections, and obesity. There is more and more evidence that gut microbiota and its overall bacterial genome exert their influence on nutrients assimilation and regulate energy metabolism and fat accumulation.

Certain differences were detected in microbiota gut structure in children and adults with obesity and people with proper body mass index. Delivery and feeding are among key factors influencing gut microbiota formation in a child. Thus, research results indicate that natural birth, as opposed to cesarean section, can prevent obesity occurrence in a child. Breast-feeding also makes a substantial contribution into development of an infant since breast milk is balanced food that provides optimal metabolism in an infant's body and helps creating proper gut microbiota. At the same time, according to data obtained via numerous research works, artificial feeding can be related to obesity occurrence in future.

Ways to fight obesity include medication therapy, dietary nutrition, physical activity as well as bariatric surgery; the latter is nowadays considered to be the most efficient procedure on the matter. Reduction in body mass via influencing gut microbiota is a promising trend in research in the sphere. Despite there are objective data on benign effects produced by probiotics and prebiotics on gut microbiota, experts haven't been able to reach agreement on their efficiency yet.

Key words: *obesity, gut microbiota, obesity in children, probiotics, prebiotics, Akkermansia muciniphila, feeding, delivery, nutrition habits.*

Obesity is a multi-factor disorder that develops due to complicated interaction between genetic and environmental factors creating an imbalance between energy input and consumption [1]. The disease is among the most acute health problems in the 21st century. Obesity-related metabolic disorders do not only exert adverse effects on all organs and systems in a human body but also result in significant burden on a public healthcare system in any country [2, 3].

As per data collected in 2016, more than 1.9 billion people aged 18 and older had overweight and 600 million out of them suffered from obesity worldwide. Number of newborns and toddlers (aged from 0 to 5) who had overweight or obesity increased from 32 million in 1990 to 38 million in

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2019 all over the world. More than 60 % children who have overweight prior to pubescence enter their adult life still suffering from it [4]. Obesity both among children and adults is to a great extent related to risk factors that cause cardiovascular diseases, type II diabetes mellitus, immune pathologies, oncologic diseases, orthopedic problems, and mental disorders [5, 6].

Interaction between multiple factors that result in obesity occurrence has not been studied in depth [6]. Thus, for example, certain genes are known to take part in formation of predisposition to overweight. More and more reliable scientific studies confirm that gut microbiota plays a key role in obesity occurrence.

Microbiota is a cluster of all the microorganisms that are necessary for proper functioning of a human body [7]. More than 100 trillion (10^{14}) microcells are in symbiosis with a human body and make their contribution into maintaining metabolic health [8]. Bacteria in human guts perform several functions such as digestive, protective, immune-modulating, detoxifying, metabolic, etc. They play a significant role in maintaining carbohydrate, lipid, and protein metabolism. Given that, an issue related to a role played by microbiota in various diseases development becomes especially significant Thus, obesity as «21st century pandemic» is paid great attention by scientists all over the world.

The aim of this review was to assess a potential role gut microbiota plays in obesity pathogenesis in children.

Data and methods. To achieve our aim, we used data from papers mentioned in Scopus and NCBI Medline databases.

Results and discussion. ***Risk factors that cause obesity.*** There are multiple factors that can cause overweight and obesity. Some are non-modifiable such as age and sex, family history or hereditary predisposition. But other factors, for example, lifestyle, can be influenced. Should a person start to pursue a healthy lifestyle, it can reduce risks that overweight or obesity might occur [9].

«Healthy lifestyle» as a concept includes eating patterns and habits, physical activity, emotional and mental health, and proper healthy sleep. Balanced nutrition that takes into account calories in consumed food depending on a person's age, sex, and physical activity should determine proper eating behavior [10]. Stress is another risk factor that can cause obesity since it exerts adverse impacts on the brain and induces stress hormones production. For instance, cortisol maintains control over hunger and energy balance [11].

Multiple research works have revealed that there is a correlation between lack of sleep and an increase in body mass index (BMI). It has been shown that sleep deprivation results in greater levels of hormones that make a person feel hunger and in lower levels of hormones that are responsible for satisfying this hunger; fatigue also increases thus leading to overall lower physical activity[12]. Additional hours during which a person is awake provide more opportunities for eating [12, 13].

Genetic studies reveal that predisposition to overweight can be inherited. Parental genes can influence amount of fat that is deposited in a human body as well as on the way of its distribution. FTO gene (fat mass and obesity associated) is one of such genes; it codes FTO protein that is involved into energy metabolism and influences metabolism as a whole [14].

Obesity can occur at any age, even among small children. As a person grows older, hormonal changes and less active lifestyle result in only greater risks of its occurrence. Besides, at an older age metabolism becomes less active, therefore, demand for calories goes down, and fighting against overweight becomes more difficult. Women have overweight more frequently than men [15].

Race and ethnic group can also determine body weight. For example, obesity among adults is more frequent in Negroids people and less frequent in Caucasians. At the same time, BMI among Asian men and

women is within physiological standards in most cases [16].

Pregnancy provokes body weight growth which is considered to be normal within certain limits. Some women face a serious problem when they try to lose weight after delivery due to slower metabolism and changes in their hormonal state [17].

All the above mentioned risk factors that can cause obesity are well-known. However, recently researchers have started to pay attention to gut microbiota. Bacteria participate directly in metabolic processes since they increase quantity of energy obtained from diet and regulate fat tissue formation [18]. Changes in gut microbiota structure are considered to be a risk factor [19]. Given that, a question arises: how does gut microbiota influence obesity development?

New developments in examining gut microbiota structure in people with obesity. Since researchers discovered a role played by gut microbiota in metabolism regulation in a host's body, scientists have been paying attention to two main bacteria phyla *Firmicutes* and *Bacteriodetes*. Their quantitative ratio distortion can underlie obesity pathogenesis. It was revealed that people suffering from obesity had *Bacteroidetes* bacteria in low quantity and *Firmicutes* bacteria in high quantity [20]. Later researchers found out that changes in microbiota composition occurring at lower taxonomic levels could also be related to this metabolic disorder. Therefore, changes in quantity of bacteria belonging to a specific genus or even species can be more reliable markers of dysbiosis that can result in obesity than a disproportion in *Firmicutes / Bacteroidetes* ratio [20].

Researchers are discussing various mechanisms that could provide an insight into a correlation between gut microbiota structure and obesity development [21]. One of them is gut microbes being able to derive energy from indigestible polysaccharides creating an additional source of calories for a host's body. Besides, gut microbiota bacteria are proven to be able to regulate lipopolysaccharides (LPS) content in blood and these substances induce moderate chronic systemic inflammation that creates favorable conditions for obesity and diabetes occurrence. The third mechanism is based on a fact that gut microbiota in a human body is able to regulate expression of genes in a host's body that are related to energy preservation and consumption [21].

Proteobacteria phylum is thought to be related to dysbiosis that can also result in such metabolic disorders as obesity [22]. It happens due to an increase in proteobacteria quantity correlating with lower mucus production that leads to damage to the gut protective barrier and non-specific inflammation [22, 23].

In this respect it is interesting to look at *Faecalibacterium prausnitzii* bacteria that belong to *Firmicutes* phylum, *Clostridia* class in *Ruminococcaceae* family and are leading butyrate producers in the guts [24, 25]. Butyrate is a short-chain fatty acid (SCFA). It is a main energy source for colonocytes and produces protective effects regarding colorectal cancer and inflammatory gut diseases. This SCFA is able to reduce inflammatory reactions in the gut mucosa due to its ability to inhibit activation of NF-κB transcription factor (a universal transcription factor that controls expression of genes related to immune response, apoptosis, and cellular cycle), as well as due to PPARγactivation and IFN-γ inhibition. *F. prausnitzii* bacteria have additional anti-inflammatory properties due to their ability to maintain a cytokine profile with very low secretion of IL-12, IFN-γanti-inflammatory cytokines and high secretion of IL-10 anti-inflammatory cytokine [25]. Therefore, we can conclude that *F. Prausnitzii* bacteria are able to produce anti-inflammatory effects on the gastrointestinal tract due to producing butyrate in great quantity and being able to maintain a certain cytokine profile; so, a decrease in their quantity in children's gut microbiota can be indirectly related to biological obesity. Moreover, these bacteria were offered as a biomarker to be used in gut diseases diagnostics [25, 26].

Lactobacilli (*Firmicutes* phylum) are gram-positive, acidogenic, and aciduric bacteria; their content in a body is greatly influenced by a person's eating habits [21]. Impacts exerted by Lactobacilli on body weight growing are considered to be depending on their species. For example, high *L. reuteri* content correlates with high BMI [27] whereas such phyla as *L. paracasei* and *L. plantarum* can protect from body weight growing due to their ability to produce bacteriocins that prevent an increase in contents of dysbiosis-inducing pathogens [6, 22, 28].

Bacteria from *Fusobacterium* genus are opportunistic pathogenic and their content can be elevated in people who suffer from obesity [22].

Akkermansia muciniphila bacterium is the only one cultivated gut bacterium belonging to *Verrucomicrobia* phylum [29]. Akkermansia are mucin-degrading bacteria and they influence metabolic processes in a host's body. They participate in maintaining the gut barrier integrity and keep gut microbiota structure in eubyosis that makes for normal body weight preservation [6, 22, 30]. It is interesting to note that lower *A. Muciniphila* content was detected in patients with gut inflammations (predominately, ulcerous colitis) and metabolic disorders; it allows assuming that these bacteria can have certain anti-inflammatory properties [30].

Clostridium leptum, together with fecal bacteria, belongs to Clostridium IV cluster; this bacterium ferments unabsorbed sugar and dietary fiber and produces SCFA [21]. SCFA (butyrate, propionate, and acetate) can serve as an energy source both for other bacteria and a host's body as a whole (approximately 10 % of all the energy) as well as participate in maintaining proper functioning of gut epithelium [20].

Another representative from this cluster, *Eubacterium hallii*, is able to utilize dextrose and such intermediate fermentation products as acetate and lactate thus creating butyrate and hydrogen. Lactate accumulation is thought to be related to some gut diseases and malabsorption syndrome [31].

Methanobrevibacter smithii is a one-celled microorganism that belongs to Archaea domain and makes for carbon and hydrogen turning into methane; it also produces SCFA [32]. Researchers think that a basic role *M. Smithii* plays in a body is maintaining balanced hydrogen contents in the guts. Changes in *M. Smithii* concentration in the guts are assumed to create higher risks of obesity and inflammatory diseases in the gastrointestinal tract such as irritable gut syndrome, colorectal cancer, or diverticular disease [32].

Microbiota in children with obesity. It is highlighted in scientific works that child obesity is a multi-factor disease that can be caused by non-optimal microelements content in nutrition rations together with low physical activity. The disease might also be caused by genetic, endocrine, and psychoemotional factors. Besides, recent clinical studies indicate that there are significant differences in gut microbiota structure in children with obesity and those with normal body weight.

Over recently ears multiple papers have been disproving a theory on the intrauterine medium being sterile since microbe traces are discovered in placenta and amniotic fluid [5, 33, 34]. Studies on infants' meconium have revealed bacteria in it, mostly enterococci and staphylococci [33, 34]. Multiple theories are now being discussed on how microbiota is being transferred from a mother to a child during pregnancy, and during the first months after birth it is still not very diverse [5]. It was discovered that significant changes in gut microbiota occurred in children aged from 9 to 18 months, especially when breastfeeding was gradually replaced with baby food [21]. Approximately at the age of 3, a child's gut microbiota is relatively similar to that in adult people [5]. Therefore, childhood can provide a unique opportunity to interfere with gut microbiota in order to improve a child's health and to prevent certain diseases, obesity included [35].

Thousand bacteria belonging to *Firmicutes* phylum can be involved into body weight growing. Thus, for example, it was

shown that increased quantities of *C. leptum* and *E. hallii* species together with a decrease in quantity of *F. prausnitzii* and *C. difficile* was related to obesity and overweight in infants, pre-school children and schoolchildren as well [36–39].

Bacteroidetes phylum mostly consists of gram-negative bacteria as opposed to predominantly gram-positive microorganisms of *Firmicutes* phylum. Three studies revealed a positive correlation between *B. fragilis* and obesity in children with high and moderate evidence. The research work performed by Vael et al. focused on a correlation between gut microbiota structure and BMI during the first three years of life [40]. It was shown that high *B. fragilis* concentrations in a three-week old infant highly correlated with high BMI during the first three years of life. This data was also confirmed in research works by Scheepers et al. and Ignacio et al. [40, 41].

Besides, several research works revealed that people with obesity tended to have lower quantity of bacteria from *Bacteroides / Prevotella* genera (gram-negative bacteria belonging to *Bacteroidetes* phylum) [21]. Bacteria from these two genera are representatives of standard gut microbiota; however, their excessive quantities are also related to gut inflammation that is mediated with anti-inflammatory cytokines released by Th17. It is necessary to accomplish further studies on certain bacteria species in order to explain this contradiction. But at the same time, studies that focused on the whole *Bacteroidetes* phylum revealed that their quantities and, consequently, *Bacteroidetes/Firmicutes* ratio were substantially lower in children with obesity against children with normal body weight; it probably can be considered a specific marker. It is important to note that such species / families as *M. smithii*, *A. muciniphila*, *Bifidobacteriaceae* which belonged to other bacteria phyla were also related to low BMI.

We should note that gut microbiota in an adult is predominantly represented by such phyla as *Firmicutes*, *Bacteroidetes*, *Proteobacteria*, *Actinobacteria* and *Verrucomicrobia* [22]. And *Firmicutes* and *Bacteroidetes* account for approximately 90 % of all bacteria in gut microbiota of a healthy person. To compare microbiota parameters in children that are described above, let us draw your attention to Table that contains data on a gut microbe profile for a person with obesity taken from [22].

Content of various bacteria in people suffering from obesity [22]

Bacteria	Content in adults with obesity
Firmicutes	Elevated
Bacteroidetes	Decreased
Firmicutes/Bacteroidetesratio	Elevated
Akkermansia muciniphila	Decreased
Proteobacteria	Elevated
Faecalibacteriumprausnitzii	Decreased
Fusobacterium	Elevated
Methanobrevibactersmithii	Decreased
Lactobacillus reuteri	Elevated

Influence exerted by delivery type on obesity occurrence and development in children. Delivery type is a factor that determines gut microbiota in newborns. Gut microbiota in infants who were born via cesarean section (CS) differs significantly from that in children who were born naturally [5, 42]. During natural delivery microorganisms that occur in a woman's birth canal, guts, and perineum create their colonies in an infant's gut. For example, such vaginal bacteria as *Lactobacillus spp.* and *Prevotella spp.* participate in creating infants' gut microbiota. And on the contrary, children born via CS are colonized with microbes from the environment (mother's skin, medical personnel, medical equipment, and other children) [42].

Various research works have shown that children born via CS have less diverse gut microbiota and their guts are less frequently colonized with such microorganisms as *Bifidobacterium spp.* and *Bacteroides spp.* but they tend to have *C. difficile* more frequently [42]. At the same time it is well known that bifidobacteria

and bacteroids prevail in gut microbiota of children who were born naturally [43]. These bacteria make for immunity formation in infant children. Bifidobacteria prevent from obesity occurrence via different mechanisms; one of them is their ability to degrade human milk oligosaccharides (HMOs) into SCFA. Therefore, we can assume that CS-birth is related to risks of obesity occurrence in future.

Natural birth was shown to produce protective effects regarding various diseases; in its turn, CS can have remote consequences for health (obesity, bronchial asthma, allergy, and type I diabetes mellitus) [42]. Three meta-analyses revealed that children born via CS ran 33 % higher risks of child obesity occurrence [44–46].

Some researchers think that low bifidobacteria quantities and high clostridia contents in children born via CS are caused by antibiotics intake since mothers have to take them prior to and after delivery in order to provide selective decontamination [47]. Besides, delivery via CS can be a reason that there is no lactation during the first hours after a child has been born as well as shorter breastfeeding period; it can lead to metabolic disorders in a child [47, 48].

There is an interesting procedure when children born via CS are exposed to their mothers' microflora. To do that, a swabbed sponge is used to transfer mother's vaginal liquids onto infant's mouth, face, and body directly after CS. The procedure is assumed to make for an infant's guts being colonized with «healthy» bacteria from a mother's body and prevent obesity occurrence in future. Several research works proved that oral, skin, and gut microbiota in CS-born children who underwent this procedure was similar to that in children who were born naturally [49].

Influence exerted by infant feeding on risks of obesity occurrence. There was a cohort study accomplished by Wallby et al. [50]; it focused on a role of breastfeeding in obesity and overweight prevention. 18 children were observed starting from birth and till they reached 4 years of age; their BMI and subcutaneous fat percentage were estimated in dynamics. Infants were distributed into two groups; the first one were infants who were breastfed for less than 3 months since birth and the second one was made up of children who received breastfeeding for longer than 3 months since birth. BMI and subcutaneous fat percentage were identical in both groups. By an age of 3 months, infants form the first group had significantly higher values of both examined criteria against children from the second one; starting from the age of 6 months, BMI and subcutaneous fat percentage in the first group became higher than their physiological standard in most children in this group. By 3–4 years, obesity prevalence among children from the first group grew up by 3 times whereas there were only slight changes in the parameter in the second group (the difference between two groups was determined as statistically significant) [50]. Additional analysis revealed that «mother-related» factors exerted their influence on obesity risks in their children; these factors included mother's BMI being higher than 27, smoking and alcohol intake during pregnancy. Therefore, we can conclude that an early weaning combined with mother's overweight, bad habits, and low social status, are risks factors that can cause overweight and obesity in her children who were younger than 4 years old.

From pathophysiological point of view, breastfeeding determines dynamics of growth in a child's height and weight [51, 52]. Research revealed that children who were breastfed had flatter curves showing their height and weight against children who were fed artificially. Breastfeeding is assumed to be a protective factor regarding obesity at older age [53]. Difference in height and weight dynamics is justified by elevation of insulin like growth factor (IGF-1) in blood plasma of children who receive artificial feeding [54]. It can possibly be caused by endocrine modulation that results from differences in the structure of biologically active substances in human milk as compared with artificial feeding mixes. In particular, breast milk has lower energy value and

contains less protein but more fat in comparison with most feeding mixes based on milk substitutes [15]. Besides, it was established that breast milk contained bifidobacteria that could modulate an infant's microbiota thus producing a preventive effect regarding obesity occurrence.

When supplemental feeding is introduced into nutrition, overall energy consumption grows by 15–23 % in children aged from 3 to 18 months who receive artificial feeding [55]. Besides, children who are fed with formulas consume by 20–30 % more food each time they eat. They also tend to consume more food when they grow older [56]. And on the contrary, breast milk satisfies demands for energy better than artificial one; breast milk consumption goes down after solid food has been added into a ration as supplemental feeding [55]. Therefore, different feeding can influence a child's body weight: each additional 100 kilocalories per day that were consumed during 4 months were related to higher probability of overweight in 46 % cases among 3-year old children [57].

We should note that formulas are usually made as per recipes that prescribe higher protein contents; usually this contents are by 50–80 % higher than in breast milk [57]. This discrepancy is assumed to be a major cause of height and weight differences between naturally fed children and artificially fed ones [58]. According to «early protein hypothesis», when protein is introduced with food in high quantities into a child's body, it produces significant effects on a child's growth thus increasing a probability that obesity might occur in future [59]. There was a multi-centered study on child obesity when healthy children who were artificially fed got only cow milk during their first year and then a mix with low or high protein contents accordingly. A share of children with greater body weight was higher in a group where children got food with higher protein contents [60].

As opposed to proteins, fat contents are higher in breast milk than in baby formulas [61]. Besides, breast milk contains long-chain polyunsaturated fatty acids in higher concentrations [62]. However, no researcher has yet been able to reveal a correlation between fat consumption in infancy and early childhood and body weight growth at older ages.

Apart from all these crucial differences in nutritional substrates between breast milk and baby formulas, we should also remember that breast milk structure changes dynamically over lactation period. Therefore, there is a close connection via feeding «from a mother to a child». Due to this connection a child's energy demands can be regulated, for example, via changing frequency and duration of feeding and it influences weight dynamics [50]. It is assumed that a choice of breast feeding results in more efficient self-regulation of consumed food quantity by a newborn [62].

Besides, breast milk contains hormones that impose certain limitations on energy metabolism and food consumption by an infant. For example, such hormones as leptin, insulin, adiponectin, and obestatin can activate mechanisms that regulate hunger depending on energy demands via epigenetic processes [63]. Besides, positive effects produced by breast feeding on obesity prevention can be partially due to healthier gut microbiome structure being induced by certain components contained in breast milk, for example, oligosaccharides [64].

Human milk oligosaccharides (HMOs) hold the third rank place among various components in breast milk as per prevalence after lactose and lipids; they play a key role in creating and maintaining healthy gut microbiota of an infant via supporting growth of such benign bacteria genera as *Bifidobacterium*, *Lactobacillus* and *Akkermansia* [29, 65]. HMOs profile is unique in each woman and it provides each infant with a unique gut microbiota [65]. Researchers point out that *A. muciniphila* and *B. longum bv. Infantis* are able to decompose HMOs into simple sugars releasing SCFA in the process that make for maintaining proper functioning of the gut barrier and pro-

vide a host's body with energy; it makes the most significant contribution into supporting healthy metabolic state.

However, SCFA do not only act as energetic substrates for their host but also as signal molecules that influence energy consumption and metabolism. SCFA are ligands for at least two receptors, free fatty acid receptors 2 and 3 (FFAR2 and FFAR3) [6]. These receptors are expressed by gut epithelium cells and APUD-system cells. An increase in SCFA contents in the guts is thought to be related to a proportionate increase in pancreatic polypeptide, glucagon-like peptide, and leptin that suppress appetite; hence, FFAR2 and FFAR3 modulate host's energy balance via effects related to gut microbiota [6]. These examples allow us to conclude that SCFA are able to tune metabolism in a host's body via regulating energy metabolism, appetite, and fat accumulation.

Therefore, breast milk is optimal and best-balanced nutrition for an infant that can provide proper development. It has been proven that lactation period being longer than 6 months produces beneficial effects on gut microbiota formation in a child [66, 67]. Given all the above-mentioned facts, we can state that feeding provided for infants makes a substantial contribution into their growth and development. A period starting from conception and up to a child reaching 4 years of age is considered to be the most significant for induction of such pathophysiological disorders that ultimately result in child obesity and in future in adult one.

Ways to treat obesity in childhood. Nowadays, a conventional way to treat obesity is to combine physical activity, proper diet, and medications as well as bariatric surgery. In developed countries specific eating habits are widely spread and very popular; these eating habits involve elevated consumption of saturated fats, animal proteins, refined carbohydrates and low consumption of fiber [68]. Some researchers state that such dietary patterns result in overall decrease in quantity of gut microbiota bacteria and serious deviations in a ratio between prevailing bacteria phyla *Bacteriodetes* and *Firmicutes* [69, 70]. De Fillippo et al. compared microbiota samples taken from children who lived in rural areas in Burkina-Faso and children from urban areas in Italy [71]. African children consumed mostly fiber and vegetable polysaccharides but Italian children predominantly ate animal proteins, carbohydrates, and fats. As a result, the authors established an authentic discrepancy between 4 genera in gut microbiota, where *Actinobacteria* and *Bacteriodetes* prevailed in children from Burkina-Faso and *Firmicutes* and *Proteobacteria* were prevailing bacteria in Italian children. There is data on an association between balanced nutrition with high fiber consumption and greater bacteria variety [71, 72]. Keeping to the Mediterranean diet also produces positive effects on gut microbiota [73]. People who follow this diet usually have decreased *Firmicutes* contents and an increase in overall SCFA contents [74].

Surgery is the most radical way to fight obesity [75]. Bariatric surgery started to appear as an independent surgical sub-specialty in 1950-s and has been constantly developed ever since [76]. These surgeries basically aim to efficiently reduce weight, to cause as few postoperative complications as it is only possible and to improve patients' life quality. Sleeve gastrectomy and gastric bypass hold the leading places among all possible surgical operations performed all over the world [75]. Apart from direct beneficial effects produced on weight reduction, bariatric surgeries also have positive influence on metabolism and comorbidity. Experts revealed a correlation between gastric bypass and a decrease in dextrose contents as well as glycated hemoglobin in patients suffering from type II diabetes mellitus. There are also data on changes in gut microbiota with growing *Bacteriodetes* and *A. Muciniphila* prevalence in such patients [77]. However, it still seems rather a controversial issue whether such a radical approach as surgical operation is to be applied when it comes to treating obesity in children.

Global obesity pandemic is spreading too rapidly and it requires new treatment procedures. Weight loss associated with various impacts exerted on gut microbiota is a promising trend in this research. Thus, Hibberd et al. established that intake of a *Bifidobacteriumlactis*-based probiotic was associated with control over body weight in patients with obesity [78]. Microbiota samples were examined profoundly and the examination revealed an increase in contents of lactobacilli and akkermansia indicating that a balance in microbiota typical for healthy people was reached. When *Bifidobacteriumlactis* were taken together with polydextrose, it resulted in growing quantities of bacteria belonging to *Akkermansia* and *Christensenellaceae (Firmicutes)* genera and *Methanobrevibacter* genus Archae and there was also a reduction in *Paraprevotella (Bacteriodetes)* quantity [78]. L. Payahoo et al. examined potential oleoylethanolamide (OEA, natural fatty acids amide) intake as a medication for weight loss. It was established that oleoylethanolamide intake by patients who suffered from obesity resulted in growing *A. muciniphila* contents in gut microbiota structure [79].

However, despite there are multiple data on beneficial effects produced by probiotics and prebiotics on gut microbiota, experts have not yet reached a common opinion on their efficiency. When such treatment is prescribed, it can cause certain risks that are not examined enough; there will also be no personalized treatment approach, and research is likely to yield controversial results.

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