Baishideng Publishing Group

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: office@baishideng.com
https://www.wjgnet.com

Reviewer #1:
Scientific Quality: Grade B (Very good)
Language Quality: Grade B (Minor language polishing)
Conclusion: Minor revision
Specific Comments to Authors:
This manuscript presents a well-conducted study on the relationship between gut microbiota and childhood obesity. It utilizes 16S rRNA gene sequencing to identify differences in gut microbiota between obese and normal-weight children. The research topic is highly relevant and contributes valuable information to the field of pediatric obesity and microbiota. The inclusion of control and obese groups with careful matching is commendable, allowing for a more accurate comparison. The study's methodology and statistical analysis are thorough, contributing to the reliability of the results. I have just some minor comments.

1) The introduction could be expanded to provide a more detailed background on the mechanisms linking gut microbiota to obesity.

Thank you for your suggestion that we add a more detailed background on the mechanisms linking gut microbiota to obesity in the introduction section.

Page 5, line 166

In obesity, there is an increase in taxa within the Bacteroidales order, such as Lactobacillus spp., Bifidobacterium spp., Bacteroides spp., and Enterococcus spp., as well as an elevated ratio of Firmicutes to Bacteroidetes and Enterobacteriaceae, while taxa within the Clostridia class, including Clostridium leptum and Enterobacter spp., are decreased [1-3]. Numerous studies suggest that an increased Firmicutes to Bacteroidetes ratio at the phylum level is a notable feature of the gut microbiota in individuals with obesity. Families such as Christensenellaceae and orders like Methanobacteriales, as well as genera including Lactobacillus, Bifidobacteria, and Akkermansia, are commonly regarded as probiotics, and their relative abundance typically correlates negatively with obesity. The gut microbiota regulates obesity by modulating energy absorption, central appetite, fat storage, chronic inflammation, and circadian rhythms [4]. The composition of the gut microbiota profoundly influences nutrient acquisition and energy regulation in the body, thus playing a pivotal role in the onset and progression of obesity and associated conditions[5, 6]. Notably, the microbiota composition varies between infants and adults, as well as between obese and lean individuals. For instance, calorie-restricted diets can reduce the Firmicutes to Bacteroidetes ratio in the gut, while vegetarian diets have been found to increase Bacteroidetes and decrease Firmicutes, Bifidobacterium spp., Escherichia coli, Enterobacteriaceae, and Clostridia[7]. Consequently, targeting the gut microbiota presents a promising therapeutic avenue for addressing obesity[8].

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: office@baishideng.com
https://www.wjgnet.com

2) In terms of clinical applicability, suggestions on how these findings could influence treatment or prevention of childhood obesity would be valuable.

Incorporating the findings of the study on characteristic gut genera in obese and normal-weight children into clinical practice can indeed be valuable for the treatment and prevention of childhood obesity. Here are some suggestions on how these findings could influence treatment or prevention strategies:

BMI and Body Fat Percentage Differences: Significant differences in BMI and body-fat percentage were observed between obese and normal-weight children. This highlights the distinct physiological characteristics between the two groups.

Gut Microbiota Diversity: The Ace and Chao1 indices, which measure species richness, were significantly lower in the obese group compared to the normal-weight group. However, differences in the Shannon and Simpson indices, which assess species diversity, were not significant. This suggests that while obese children may have fewer microbial species, the diversity within those species is not significantly different from normal-weight children.

Differences in Gut Microbiota Composition: The study found significant differences in the gut microbiota composition between obese and normal-weight children. Prevotella and Firmicutes were more abundant in the obese group, whereas Bacteroides and Sanguibacteroides were more prevalent in the normal-weight group. These findings provide insight into the specific microbial taxa associated with obesity in children.

UniFrac Distances: Kruskal-Wallis tests indicated significant differences in both unweighted and weighted UniFrac distances between the gut microbiota of normal-weight and obese children ($P<0.01$). This suggests substantial disparities in both the presence and abundance of microbial taxa between the two groups.

Heatmap Results: The heatmap results further demonstrated significant differences in gut microbiota composition between obese and normal-weight children. This visual representation highlights the distinct microbial profiles associated with obesity status in children.

In light of these results, the clinical implications for the treatment and prevention of childhood obesity may include:

Targeted interventions aimed at modulating gut microbiota composition, such as probiotic supplementation or dietary modifications tailored to promote the growth of beneficial microbial taxa.

Individualized treatment approaches considering the specific gut microbiota profile of each child, which may involve personalized dietary recommendations and lifestyle interventions.

Longitudinal monitoring of gut microbiota composition alongside changes in BMI and

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: office@baishideng.com
https://www.wjgnet.com

body fat percentage to assess the effectiveness of interventions and inform adjustments to treatment plans over time.
Overall, these findings underscore the importance of considering gut microbiota composition in the management and prevention of childhood obesity and provide valuable insights for developing targeted interventions to improve metabolic health in children.

We summarize the above and supplement this section on page 10, line 353
The study revealed significant differences between obese and normal-weight children, including higher BMI and body-fat percentage in obese children. While the Ace and Chao1 indices indicated lower species richness in the obese group, the Shannon and Simpson indices showed no significant diversity differences. Moreover, Kruskal-Wallis tests highlighted significant dissimilarities in both unweighted and weighted UniFrac distances between the gut microbiota of normal-weight and obese children ($P<0.01$). Prevotella and Firmicutes were more abundant in obese children, while Bacteroides and Sanguibacteroides were prevalent in normal-weight children, as evidenced by heatmap results. These findings suggest distinct microbial profiles associated with obesity in children, implicating the potential for targeted interventions to modulate gut microbiota composition and inform individualized treatment strategies for childhood obesity. Longitudinal monitoring of gut microbiota alongside BMI changes may offer insights into intervention effectiveness and guide adjustments to treatment plans over time.

3) The manuscript would benefit from a discussion on potential limitations of the study.

Thanks for your suggestion, we have supplemented this part on page 11, line 365
Although the study made some important findings in comparing the gut microbiota of obese and normal-weight children, there are several limitations. Firstly, the sample size of the study was relatively small, including only 30 obese children and 30 normal-weight children, which may limit the generalizability and statistical significance of the results. Secondly, the study only utilized 16S rDNA sequencing technology for microbial composition analysis, which may restrict the understanding of microbial functions and metabolic activities. Additionally, the study did not comprehensively control for children's dietary habits, lifestyles, and environmental factors, which could influence the composition and abundance of the gut microbiota. Furthermore, the study did not explore the causal relationship between gut microbiota and childhood obesity, making it unclear whether changes in gut microbiota are the cause or the result of obesity. Therefore, future research needs larger sample sizes, more in-depth methods, and

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: office@baishideng.com
https://www.wjgnet.com

comprehensive controls to validate and expand these findings, thus enhancing our understanding of the relationship between childhood obesity and gut microbiota.

4) In Text page 10 line 16, Figure 2C, 2D should be Figure1C, 1D. I recommend acceptance of this manuscript for publication after minor editing. Sincerely
Thank you for reminding us. We have a writing error and will correct it now.

Reviewer #2:
Scientific Quality: Grade B (Very good)
Language Quality: Grade B (Minor language polishing)
Conclusion: Minor revision
Specific Comments to Authors:
The study aims to explore the association between childhood obesity and gut microbiota using 16S rRNA gene sequencing. It provides insights into the characteristic gut genera in obese and normal-weight children, potentially contributing to understanding the mechanisms and prevention strategies of childhood obesity. The study addresses a significant and timely topic, linking childhood obesity with gut microbiota. The methodology, especially the use of 16S rRNA gene sequencing, is robust and appropriate for the study's aims. The data analysis is comprehensive, with a clear presentation of findings, including differences in gut microbiota composition between obese and normal-weight children. Despite these commendable aspects, there is room for improvement in certain areas to elevate the manuscript's overall impact.

1. The discussion could benefit from a deeper exploration of how these findings translate into practical prevention strategies for childhood obesity.

Thank you for your suggestion. This question is exactly the same as the question 2 of reviewer 1. We have made a detailed explanation and supplemented it in the discussion section.

2. While the sample size is adequate, a more diverse demographic might provide broader applicability of the findings.
We appreciate the reviewer's important point regarding the diversity of the sample and its potential impact on the applicability of our findings. We acknowledge the crucial role that sample diversity plays in the robustness of research outcomes. In our study, we made efforts to ensure the sample's representativeness, considering various demographic factors during participant recruitment and inclusion. However, we

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: office@baishideng.com
https://www.wjgnet.com

recognize that in future research, a more extensive and diverse sample could enhance the generalizability of our findings. Therefore, we are committed to expanding the diversity of our sample in future studies, and we welcome the reviewer's suggestions to help refine the design and implementation of our future research endeavors.

3. The study could be strengthened by longitudinal follow-up to assess changes in gut microbiota over time in relation to obesity development. Thanks

We appreciate the reviewer's insightful suggestion regarding the potential benefits of longitudinal follow-up to evaluate changes in gut microbiota over time in relation to obesity development. We agree that longitudinal studies offer valuable insights into the dynamic relationship between gut microbiota composition and obesity progression. While our current study provides important cross-sectional data, we recognize the importance of longitudinal assessments to capture temporal changes and causal relationships.

In future research endeavors, we plan to incorporate longitudinal follow-up to track changes in gut microbiota composition and obesity status over time. By conducting longitudinal analyses, we aim to elucidate the temporal associations between shifts in gut microbiota and the development or resolution of obesity. We believe that longitudinal studies will enhance our understanding of the complex interplay between gut microbiota dynamics and obesity outcomes, and we appreciate the reviewer's suggestion as a valuable direction for future investigations.