

Journal of Advanced Zoology

ISSN: 0253-7214 Volume 44 Issue S-1 Year 2023 Page 310:316

Interpretation of The Relationship Between Caries Index and Body Mass Index in Infants by Literature Review

Adriana Katherine Quezada Quiñonez¹, Nancy Catalina Suárez Andrade², Sandra Nataly Rojas Rojas³

¹Universidad Regional Autónoma de los Andes (UNIANDES), Ecuador.

Email:<u>ui.adrianagg34@uniandes.edu.ec</u>

²Nancy Catalina Suárez Andrade. Universidad Regional Autónoma de los Andes (UNIANDES), Ecuador.

Email: ui.nancysa81@uniandes.edu.ec

³Sandra Nataly Rojas Rojas. Universidad Regional Autónoma de los Andes (UNIANDES), Ecuador.

Email: ui.sandrarr80@uniandes.edu.ec ORCID ID: https://orcid.org/0009-0002-3817-554x

*Corresponding author's E-mail: <u>ui.adrianagg34@uniandes.edu.ec</u>

Article History **Abstract** Introduction: The caries index is used to evaluate the prevalence and severity Received: 06 May 2023 of dental caries in a population; while the body mass index (BMI) is a Revised: 25 July 2023 measure used to evaluate the body weight of a person in relation to his or her Accepted: 28 July 2023 height. Both variables are related, and more studies are needed to study them in greater depth. Objective: The aim of the study was to interpret the relationship between caries index and body mass index in infants by means of a literature review. Methods: The study corresponded to the exploratory research level and was observational, cross-sectional, and retrospective. The search was carried out in the Pubmed and Scielo databases, including articles published between 2012 and 2023 that dealt with the relationship between caries index and BMI in infants. Results: It was found that the relationship between caries index and BMI in infants has been the subject of study in the scientific literature in recent years. Several studies have analyzed the possible association between both variables, finding contradictory results in some cases. Conclusions: It is important to explore the relationship of caries index with BMI in infants given that it is necessary to understand the factors that contribute to the development of dental caries and obesity in the child population. A more exhaustive literature review is recommended to provide an overview of the findings on the subject and to help identify possible areas for future research, on which they make some suggestions. **CC License Keywords:** Caries Index, Body Mass Index, Infants, Literature Review, CC-BY-NC-SA 4.0

1. Introduction

The caries index is a measure used to assess the prevalence and severity of dental caries in a given population. This measure can be useful for planning and evaluating dental caries prevention and treatment programs. The most widely used caries index in the scientific literature is the DMFT (Decayed, Missing, Filled Teeth) index of the World Health Organization (WHO). This index is based on the presence of dental caries (decayed teeth), missing teeth, and restored teeth. A 2022 study published in the journal Caries Research evaluates the validity and reliability of DMFT in detecting

Dentistry.

dental caries in children aged 6 to 12 years. The results show that it is a valid and reliable indicator (Walach, 2022). A study to be published in the journal Scientific Reports in 2021 evaluates the effectiveness of DMFT in detecting early caries in children. The authors conclude that the DMFT index has a low sensitivity for detecting incipient caries, suggesting the need to develop new indices or improve existing ones for early detection and more effective treatment of dental caries (Xu et al., 2022). On the other hand, body mass index (BMI) is a measure that is used to assess a person's body weight in relation to their height. Several studies highlight the usefulness of BMI in identifying people at risk for various health conditions, including type 2 diabetes, cardiovascular disease, and certain cancers. A recent study published in The Lancet Diabetes & Endocrinology shows that a high BMI is a major risk factor for premature mortality worldwide (Aaseth et al., 2022).

BMI is calculated by dividing weight in kilograms by the square of height in meters (kg/m2) (Neeland et al., 2018; Neeland et al., 2018; Lee et al., 2020). A BMI between 18.5 and 24.9 is considered normal, while a BMI above 25 is considered overweight and above 30 is considered obese. It is commonly used to assess obesity and associated health risks and is studied extensively, being validated as a useful tool for assessing obesity and associated health risks in various populations, including children, adults and the elderly. However, BMI is also criticized for its limitations, including its inability to differentiate between body fat and muscle mass and its potential to misclassify people with high muscle mass as overweight or obese (Neeland et al., 2019). In addition, some studies have suggested that alternative measures, such as waist circumference and body fat percentage, may be more accurate indicators of the health risks associated with excess body fat (Neeland et al., 2018). According to a study published in the journal Obesity Reviews in 2018, BMI is a useful measure for assessing obesity and the risk of obesity-related diseases, such as diabetes and cardiovascular disease. However, the authors note that BMI is not a perfect measure and that there may be limitations in its use, especially in certain populations such as athletes or older people (Lee et al., 2020).

It is important to interpret the relationship between DMFT and BMI in children because both tooth decay and obesity are major public health problems that can have a negative impact on overall health and quality of life. Several studies investigate the association between tooth decay and BMI in children. For example, a study published in the Journal of Dental Research finds that children with a higher BMI were more likely to have tooth decay than those with a lower BMI (Rugg et al., 2017). Another study published in the Journal of Dentistry suggests that children with a higher BMI and higher intake of sugary foods had a higher risk of tooth decay (Broomhead et al., 2021). Therefore, this study is current and important, but it is also relevant to the context of Ecuador (country of the authors of this bibliographic review), a nation that needs more studies on this topic, due to the contribution they would make from the clinical and academic point of view within the university career of dentistry (Ibarra et al., 2023; Quispe et al., 2023). However, there are some previous Ecuadorian studies on the subject (Lucero et al., 2022; Ibarra et al., 2023), which need to be expanded and continued. The objective of this study is to interpret the relationship between caries index and body mass index in infants through a literature review.

2. Materials And Methods

The study corresponded to the exploratory research level and was observational, cross-sectional and retrospective. The search was carried out in the *databases of Pubmed* and *Scielo*, including articles published between 2012 and 2023 that dealt with the relationship of caries index with body mass index in infants. The authors relied on hermeneutics to interpret the bibliographic review executed, since it is a methodology used to interpret and understand texts and discourses and in the context of this bibliographic review, it was useful to understand the meaning and implication of the findings obtained in the articles that were reviewed.

This literature review involved searching for and collecting a wealth of information from various sources, and hermeneutics was a useful tool to help authors analyze and synthesize the information, in order to identify common patterns or themes and clarify any ambiguities or conflicts in the findings. To achieve the stated objective, methods of the theoretical level of knowledge were especially used, such as Analytical-Synthetic, Inductive-Deductive, Historical-Logical and the systemic approach

(Ibarra et al., 2023; Villamarín et al., 2023; Monteiro et al., 2022; Jarrín et al., 2018; World Health Organization, 2011).

The search was executed in the *databases of Pubmed and Scielo*, including articles published between 2012 and 2023 that addressed the relationship of caries index with body mass index in infants. Articles that did not meet the criteria of being written in English or Spanish were excluded. The search focused on the interpretation of the caries index in infants, body mass index in this same study population, as well as the relationship of these two variables in infants. Descriptive records and matrices in Word format were used to compile the findings, particularizing aspects such as authors' names, journal names, main results and conclusions and bibliographic reference in Vancouver standards.

3. Results and Discussion

As results of the review, 34 articles that met the inclusion criteria were examined, of which a summary of the most significant findings is formalized in this article. Dental caries is one of the diseases with high prevalence in the world, it is currently represented as a frequent chronic disease of the human being that produces the loss of up to half of the teeth and it is estimated that 90 to 95% of the population is affected by this pathology (Carrión et al., 2009). Caries is considered as a dental pathology caused mainly by three factors that are: host, sugar time in the mouth and microorganisms, but there are multiple internal factors (microorganisms, amelodentinary structure, saliva, dental morphology); as external (cultural, socioeconomic, environmental, level of education on oral health and nutrition) that collaborate in the formation and spread of this disease. WHO has estimated that 60-90% of the world's children have caries lesions with obvious cavitation. The prevalence in Latin America is no less alarming, reaching values up to 90% (González, 2013).

It was evidenced that an excessive intake of non-nutritious foods such as sweets or saturated fats leads to imbalances in nutritional health, in the same way a low intake of healthy foods in the diet results in states of malnutrition such as malnutrition or overweight accompanied by sedentary lifestyle (JA et al., 2014). In the literature it is found that infant nutrition is important from the moment of conception through the mother and after childbirth, since it will be reflected as the years go by in the balance of health, both physical and mental. The nutritional status of the individual affects the development and maintenance of dental tissues and organs, because they are sensitive to nutritional deficiencies (Manohar et al., 2020). The WHO mentions that the period between zero and two years is a "critical time window" in terms of promoting optimal growth, health and development in humans (Carrión et al., 2009). It was found that feeding in children between the first and second years of life presents a modification in appetite, develops unregularly and an "undulating inappetence" is observed, which is when the child will eat little or a lot on different days. It is prepared to receive small and soft pieces of food with mature flavors. The use of bottles or teapots should be excluded from any type of beverage other than formulas, due to the delay in acquiring masticatory skills, language and nutritional habits; for which it is recommended to replace them with a glass from the year or earlier if the infant allows it (Cayo et al., 2021).

According to the WHO, children who are breastfeeding with a healthy state of health ingest all their macro and micronutrient requirements based on a varied diet, except for iron that due to growth there are low deposits; therefore, an iron-fortified supplement is essential to make up for this deficiency, just as it is advisable to administer vitamins B12 and folates to children of vegetarian mothers (Adriano et al., 2017). Children between the ages of 2 and 6 understand the preschool stage, this is where autonomy or independence is consolidated and they begin to express their whims in the tastes for food, rejecting the new foods that they want to introduce (Cayo et al., 2021). The calories needed at this stage decrease, since the speed of growth is reduced compared to the first year of life, but the activities that expend energy increase, so there must be a harmony between the consumption of caloric foods. Preschool is where healthy eating habits are created that will influence future years and will depend on the example of parents or relatives and the habits of friends and people around them, including advertising (Carrión et al., 2009).

Nutrition plays an important role in an individual's health, including oral health. An anthropological measurement provides information on the development and composition of the body that allows children to be categorized into underweight, normal weight, overweight and obesity (Aquino & Cuya, 2018). It was evidenced that dental caries differs from many infectious diseases, being shared vertically from the mother to the child. When the teeth erupt, the oral cavity becomes prone to the proliferation of bacteria by streptococcus mutans. The cariogenic potential caused by sweetened foods is mainly influenced by conditions such as: consistency, texture and adhesion; and the conditions under which they are ingested, rather than the amount of sugar they contain (Bitariho et al., 2020). Obesity is considered multifactorial etiology and one of the biggest problems that triggers it is sedentary lifestyle. Although the American Association of Pediatrics recommends not using television for more than two hours a day in children and adolescents, it is the sedentary behavior that most develops, when watching TV series or video games, due to the current ways of life that occur in homes (Revollar et., 2017).

Malnutrition is a contributor to the increased risk of caries due to abnormal enamel development and tooth erosion problems (Revollar et., 2017). It was found that the oral cavity has a constant microbial flora of its own that forms dental plaque in dental tissues. These bacteria use carbohydrates in the diet to produce acids that cause demineralization of dental tissue and consequently caries (Revollar et., 2017). In addition, the pH of the oral cavity has been modified when carbohydrates are consumed between meals, causing their increase and consequently alterations in the oral microbiota that reduce the remineralizing capacities of saliva (González, 2013). Studies conducted to look for the relationship of oral health problems with nutritional states in children have indicated that in nutritional alterations of overweight and obesity caries as a priority is dental disease, followed by alterations in occlusion (Cayo et al., 2021). Similar results from other studies have shown the high prevalence of caries in heavier children, both in temporary and permanent teeth (Manohar et al., 2020).

However, contrary to a study conducted in the city of Concepción in Chile on the oral health status of overweight preschoolers has found no significant relationship between ceo-d and overweight (Revollar et., 2017). In essence, BMI is a widely used and validated measure of obesity and related health risks, but it has limitations that need to be taken into account in certain populations. Researchers continue to explore alternative measures. Nutrition is the result of a balance between food intake and the amount of nutrients they have to maintain optimal health in the individual. Although there are other contributing factors in the appearance of caries, the diet is of great importance and indispensable to initiate a demineralization of dental tissues and consequently the appearance of caries, so poor nutrition significantly influences its development.

Tooth decay and obesity share common risk factors, such as a diet high in sugar and low in fiber, as well as poor oral hygiene. Therefore, interventions aimed at reducing the risk of dental caries, such as improving oral hygiene and reducing sugar consumption, may also have a positive impact on reducing the risk of obesity and related health problems. Hermeneutics was useful for understanding the context in which individual studies were conducted, as well as possible limitations or biases in their design or execution. By better understanding the context and limitations of the studies, the authors were able to provide a more accurate and meaningful interpretation of the findings.

The authors of this review consider that the studies that are consulted demonstrate the direct relationship of caries with the type of diet that children have, since, as there is a higher intake of carbohydrates, the microorganisms of the oral cavity have more elements to generate acids that are the cause in the beginning of the decalcification of the enamel and then of the caries. It is also interpreted that children with low weight or height for their age have a high prevalence of caries, because the nutrients necessary for optimal development of dental tissues are scarce or absent, which makes the tooth more susceptible to demineralization and consequently to the formation of carious disease. Studies conducted in China and Italy conclude that obesity is another factor associated with a high prevalence of caries in children and adults, because its main etiology is possibly a high intake of sugars and their consumption between meals, which are the main generators of acids that produce caries (JA et al., 2014; Adriano et al., 2017). While another study conducted in Valencia shows that

Interpretation of The Relationship Between Caries Index and Body Mass Index in Infants by Literature Review

the association between obesity and caries is not clear, since it is thought that the two coexist over time due to the etiology they have in common and the similar factors that produce.

The authors interpret nutrition and oral health as showing a strong relationship; When there is protein-caloric malnutrition, problems of development and time of eruption of the teeth can occur, due to a lack of vitamins (A, D), calcium and phosphorus. In developing countries with this malnutrition, a reduction of immunoglobulin A in saliva is observed, which predisposes the oral cavity and periodontal tissues to infections, but the most significant effect is a development of the bacterial flora that causes dental caries (JA et al., 2014). It should be borne in mind that the consumption of sugars in the diet not only generates a greater susceptibility to caries, but also contributes to the development of obesity and consequently in adulthood to suffer major diseases such as diabetes, cardiovascular, respiratory and liver diseases (Aquino et al., 2018). Dental caries is a progressive disorder, which is related to various factors in which diet and host susceptibility play a fundamental role. It is a common disease, especially in children and has a direct relationship with nutrition since nutrients prevent its appearance and carbohydrates increase it (Aquino et al., 2018).

It is mentioned in several studies, a considerable incidence of caries between the five years, since it is when children present a considerable openness to the consumption of sweets and by the beginning of the eruption of permanent teeth there are discomforts that hinder good oral hygiene, in addition to parents leave toothbrushing to their responsibility to give more autonomy to the child (Manohar et al., 2020). It can be said that in this study there is a significant prevalence of nutrition problems, both obesity and overweight, which draws attention and calls for action on the matter to reduce future morbidity rates. The issue of the relationship of obesity with dental caries is controversial, but the most recent studies indicate that overweight states are not considered as predisposing factors for the appearance of caries, although those children with high weight may have alterations in their saliva due to high carbohydrate intake.

The presence of caries in children's oral cavity is more associated with oral hygiene, socioeconomic and cultural factors, parental education level, and access to dental health services (JA et al., 2014). Based on the results obtained in the bibliographic review that is developed here, the authors propose several possible studies to continue, in the short term, deepening this line of research. Here are the suggestions: Longitudinal study: A longitudinal study following children from an early age through adolescence could be conducted to look at how caries index and body mass index change over time and how they relate to each other. Intervention study: An intervention study could be conducted in which measures to reduce children's body mass index are implemented and how this affects the rate of dental caries is evaluated. Follow-up study: A follow-up study may be conducted to evaluate the long-term outcomes of dental or weight loss treatments in overweight or obese children who have dental caries. Study with fuzzy logic: fuzzy logic could be incorporated into data analysis to take into account uncertainty and imprecision in the measurements of caries and body mass indices. Comparative study: A comparative study could be conducted between different populations or geographic regions to analyze differences in the relationship between caries index and body mass index in infants and explore possible factors that may influence these differences.

4. Conclusion

In the present study, the relationship of caries index with BMI in infants was interpreted through a literature review. BMI is a measure that relates a person's weight to their height squared (kg/m^2) and is commonly used to assess obesity and associated health risks. It has been widely studied and validated as a useful tool for assessing obesity and associated health risks in various populations, including children, adults, and older people. The caries index is used to assess the prevalence and severity of dental caries in a given population. Interpreting the relationship between tooth decay and BMI in infants can help identify common risk factors and inform preventive measures for both tooth decay and obesity. Hermeneutics was useful for the authors of this literature review to better understand the meaning and implication of the findings presented in the reviewed articles and to analyze and synthesize information gathered from various sources.

It is concluded that it is important to explore the relationship of caries index with BMI in infants since it is necessary to understand the factors that contribute to the development of dental caries and obesity in children. At the end of this review of the research articles, according to the results obtained, it can be concluded that the alterations in the nutritional status of infants are increasingly evident, especially obesity that occurs due to the sedentary lifestyle of children. Although this condition causes several health problems in general, it can also have a significant effect on the prevalence of tooth decay.

Acknowledgements:

The authors recommend a more exhaustive bibliographic review of the published studies, using a systematic review with the PRISMA 2020 methodology and a meta-analysis in other databases such as SCOPUS or the *Web of Science*, which is a limitation of this study. In this way, an overview of the findings in the field could be provided and help identify possible areas of future research, on which some suggestions are already made here.

Conflict of interest:

The authors show that they have no conflicts of interest related to the present study.

References:

- Aaseth, J., Javorac, D., Djordjevic, A. B., Bulat, Z., Skalny, A. V., Zaitseva, I. P., ... & Tinkov, A. A. (2022). The role of persistent organic pollutants in obesity: a review of laboratory and epidemiological studies. *Toxics*, 10(2), 65. http://dx.doi.org/10.1016/S2213-8587(20)30371-2.
- Adriano-Anaya, M. D. P., Caudillo-Joya, T., & Caudillo-Adriano, P. A. (2017). Caries Dental su Asociación con el Índice de Masa Corporal en una Población Joven Adulta. *International journal of odontostomatology*, 11(4), 437-442. http://dx.doi.org/10.4067/S0718-381X2017000400437.
- Aquino-Canchari, C., & Cuya-Salvatierra, G. N. (2018). Body mass index and its relation with the prevalence of dental caries on schoolchildren of Huando, Huancavelica, Perú, 2016. *CES Odontología*, 31(1), 3-10. https://doi.org/10.21615/cesodon.31.1.1.
- Bitariho, R., Blundo, C., Carilla, J., Grau, R., Malizia, A., Malizia, L., ... & Bradford, M. (2020). Taking the pulse of earth's tropical forests using networks of highly distributed plots.
- Broomhead, T., Ballas, D., & Baker, S. R. (2021). Neighbourhoods and oral health: Agent-based modelling of tooth decay. *Health & place*, 71, 102657.
- Carrión, J. S., González-Sampériz, P., López Sáez, J. A., López García, P., & Dupré, M. (2009). Quaternary pollen analysis in the Iberian Peninsula: the value of negative results.
- Cayo-Rojas, C. F., Santillán-Espadín, K. D. R., Nicho-Valladares, M. K., Ladera-Castañeda, M. I., Aliaga-Mariñas, A. S., & Cervantes-Ganoza, L. A. (2021). Knowledge about oral health, salivary PH, body mass index and its relationship with dental caries in preschool children. *Revista de la Facultad de Medicina*, 69(4).
- González de Dios, J. (2013). Systematic review about dental caries in children and adolescents with obesity and/or overweight. *Nutricion hospitalaria*, 28(5), 1372-1383.
- Ibarra, J. C. P., Noroña, R. F. D., & Naranjo, G. R. M. (2023a). Description of the Psychological State of a Pregnant Women with Fetal Death Attended at Hospital General Ambato Iess in Ecuador. *Journal for ReAttach Therapy and Developmental Diversities*, 6(9s (2)), 387-395.
- Ibarra, J. C. P., Noroña, R. F. D., & Naranjo, G. R. M. (2023b). Description of the Psychological State of a Pregnant Women with Fetal Death Attended at Hospital General Ambato Iess in Ecuador. *Journal for ReAttach Therapy and Developmental Diversities*, 6(9s (2)), 387-395.
- Ibarra, J. C. P., Noroña, R. F. D., & Naranjo, G. R. M. (2023c). Description of the Psychological State of a Pregnant Women with Fetal Death Attended at Hospital General Ambato Iess in Ecuador. *Journal for ReAttach Therapy and Developmental Diversities*, 6(9s (2)), 387-395.
- JA, M. N., SS, G. V., JE, C. B., Meneses-Echávez, J. F., & Gonzalez-Jimenez, E. (2014). Effectiveness of educational interventions conducted in latin america for the prevention of overweight and obesity in scholar children from 6-17 years old; a systematic review. *Nutricion Hospitalaria*, 31(1), 102-114.
- Jarrín-Peñafiel, M. J., Toalombo-Puma, O. V., Carrera-Robalino, A. E., Quintana-Carrillo, E. A., Ribadeneira-Morales, L. A., & Armas-Vega, A. D. C. (2018). Riesgo cariogénico y su relación con el factor socio económico, en niños de 8-10 años de una zona agrícola del Ecuador. *Revista Científica Odontológica*, 14(1 http://dx.doi.org/10.1016/J.PEDn.2019.02.011.
- Lee, J. M., Park, Y. M., Yun, J. S., Ahn, Y. B., Lee, K. M., Kim, D. B., ... & Ko, S. H. (2020). The association between nonalcoholic fatty liver disease and esophageal, stomach, or colorectal cancer: National population-based cohort study. *PLoS One*, *15*(1), e0226351.

Interpretation of The Relationship Between Caries Index and Body Mass Index in Infants by Literature Review

- Lucero Tapia, M. P., Noroña Salcedo, D. R., & Vega Falconi, V. (2022). Burnout y depresión en médicos de medicina interna y unidad de cuidados intensivos en Riobamba, Ecuador. *Revista Cubana de Reumatología*, 24(1).
- Manohar, N., Hayen, A., Fahey, P., & Arora, A. (2020). Obesity and dental caries in early childhood: A systematic review and meta-analyses. *Obesity Reviews*, 21(3), e12960. doi: http://dx.doi.org/10.1111/obr.12960.
- Monteiro Fonseca, S., Faria, S., Cunha, S., Silva, M., Ramos, M. J., Azevedo, G., ... & Queirós, C. (2022). Mental health patterns during COVID-19 in emergency medical services (EMS). *International Journal of Emergency Services*, 11(2), 193-206. http://dx.doi.org/10.35381/S.V.V612.2048.
- Neeland, I. J., Poirier, P., & Després, J. P. (2018). Cardiovascular and metabolic heterogeneity of obesity: clinical challenges and implications for management. *Circulation*, *137*(13), 1391-1406. http://dx.doi.org/10.2337/DC19-0309.
- Neeland, I. J., Ross, R., Després, J. P., Matsuzawa, Y., Yamashita, S., Shai, I., ... & Eckel, R. H. (2019). Visceral and ectopic fat, atherosclerosis, and cardiometabolic disease: a position statement. *The lancet Diabetes & endocrinology*, 7(9), 715-725. http://dx.doi.org/10.1016/S2213-8587(19)30192-3.
- Quispe, S. M. S., Sucuzhañay, B. I. Q., Armijos, M., & López, A. G. S. (2023). Descripción de la ansiedad en estudiantes de segundo semestre de odontología de UNIANDES. *Revista Cubana de Investigaciones Biomédicas*, 42(2).
- Revollar, S., Vega, P., Vilanova, R., & Francisco, M. (2017). Optimal control of wastewater treatment plants using economic-oriented model predictive dynamic strategies. *Applied Sciences*, 7(8), 813.
- Rugg-Gunn, A., Durward, C., Ungchusak, C., & Khitdee, C. (2017). Early childhood caries—a major public health problem. *Thai Dental Public Health Journal*, 22(พิเศษ), 1-2. http://dx.doi.org/10.4103/1735-3327.245824.
- Villamarín, S. M. G., Moreta, J. F. A., Andrade, P. A. M., & Benavides, A. L. M. (2023). Consideraciones sobre el bruxismo. *Revista Cubana de Investigaciones Biomédicas*, 42(2).
- Walach, H. (2022). Understanding and treating Cancer holistically. Integrative Strategies for a new Way of dealing with Cancer. http://dx.doi.org/10.1159/000522586.
- World Health Organization. (2011). World Health Organization Obesity and Overweight.
- Xu, H., Tian, B., Shi, W., Tian, J., Zhang, X., Zeng, J., & Qin, M. (2022). A correlation study of the microbiota between oral cavity and tonsils in children with tonsillar hypertrophy. *Frontiers in Cellular and Infection Microbiology*, 11, 724142 http://dx.doi.org/10.1038/s41598-021-96805-9.