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Childhood obesity is associated with a high degree of metabolic disturbance in children from Brazilian semi-arid region

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Projected to impact 310 million children by the next decade, childhood obesity is linked to serious health issues like metabolic disturbance and cardiovascular diseases. This study introduces a novel approach for the integrated assessment of inflammatory, glycemic and lipid disorders in obese children in resources-limited settings and also identifies key factors contributing to these changes. Conducting a cross-sectional analysis of 231 children aged 5–12 years from public schools in Brazil's semi-arid region, the research involved collecting medical history, anthropometric measurements, and blood samples to analyze glycemic and lipid profiles, along with C-reactive protein levels. We used an adapted the Molecular Degree of Perturbation model to analyze deviations in metabolic markers from a healthy control group. Statistical analyses included Mann–Whitney and Fisher exact tests, backward logistic regression, and hierarchical cluster analysis. The study identified a direct and independent association between elevated Metabolic Disturbance Degree and both overweight and obesity in children, with significant differences in CRP, Triglycerides, and HDL levels noted between obese and healthy-weight groups. The findings highlight the critical need for early detection and comprehensive understanding of obesity-related changes to mitigate the severe health risks associated with childhood obesity.

Childhood obesity has emerged as an important global health challenge. In 2020, an estimated 175 million children were diagnosed as obese, a figure projected to alarmingly escalate to 310 million by the end of the next decade¹. It is well established, in the literature, a deep-seated connection between obesity and metabolic disturbances across all age groups². Beyond alterations in blood glycemic and lipid profiles, obesity exacerbates adipocyte enlargement, which fosters a chronic low-grade inflammatory state. This is characterized by elevated levels of inflammatory cytokines and markers such as C-Reactive Protein (CRP). All these metabolic disturbances are related to a spectrum of health complications, including atherosclerotic diseases³. Disturbingly, research indicates the emergence of early signs of these arterial lesions in children as young as the first decade of life⁴.

Sedentary lifestyle, excessive use of electronic devices and poor nutrition are factors related to the widespread of this health problem across different nations, age groups and social classes⁵. Thus, screening for obesity is recommended for all children 6 years and older using age- and sex-adjusted Body Mass Index (BMI)⁶. However, it is important to note that BMI should not be used as the sole method for identifying obesity⁷. Additional measures, such as waist circumference, have been recognized as a valuable and accessible tool for evaluating pediatric nutritional status and overall body composition^{8–10}. In Brazil, a 2021 systematic review revealed a childhood obesity rate of 12.2%, with a slightly higher prevalence in boys (12.3%) compared to girls (10.8%)¹¹.

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A comprehensive understanding and early detection of obesity-related changes are imperative for effective intervention planning. A large study showed a 2.6% prevalence of metabolic syndrome among Brazilian adolescents, reaching 21.3% among those obese individuals¹². Despite the existence of over 40 definitions of metabolic syndrome in the pediatric population, the evaluation of inflammatory markers is absent (14,15). Research on the inclusion of CRP in assessing metabolic alterations in children has yielded inconsistent results^{13,14}. Moreover, the investigation into the presence of altered inflammatory markers, alongside other metabolic profile components remains poorly investigated between children from vulnerable regions of Brazil.

The semi-arid region in Bahia comprises 258 municipalities, covering an area of 388,274 km², which is 70% of the state's area, with a population of 6,316,846 inhabitants. This region represents 68% of Bahia's territory and 48% of its population. The climate is characterized by high temperatures, low annual temperature range, low relative air humidity, and long periods without rain, leading to socioeconomic indicators lower than the state average. Conducting this study in a semi-arid city is particularly important due to these unique socio-economic and environmental factors that influence health outcomes. The semi-arid regions often face limited access to healthcare, lower socio-economic status, and distinct dietary patterns, exacerbating the risk factors associated with obesity and metabolic disturbances.

To our knowledge, this is the first study to analyze nutritional and metabolic aspects in children and adolescents from this region. Therefore, this study endeavors to introduce an innovative methodology for a thorough assessment of metabolic disturbances in children from Brazil's semi-arid region. It also aims to identify and analyze the factors contributing to heightened metabolic disturbance scores. Through this research, we aspire to enhance the understanding of pediatric metabolic health and aid in the development of more effective strategies to address these critical conditions.

Materials and methods

Ethics statement

The project was approved by the institutional review board of the Fundação Bahiana para Desenvolvimento das Ciências, Salvador, Brazil, where the study was performed (CAAE: 35038914.3.0000.5544). All children consented to participate after meetings to explain the study, and written informed consent was obtained from each parent or guardian. All clinical investigations were conducted according to the principles expressed in the Declaration of Helsinki.

Study design

This is a cross sectional study that evaluated school-aged children, based on public schools in the municipalities of Serrinha, Biritinga, Barrocas and Teofilândia, in the state of Bahia, Brazil, in 2019. Students between 5 and 12 years old, with a minimum school attendance of 70%, were randomly included from different schools in each municipality, maintaining the proportion between rural and urban areas. The students were excluded if (I) they had taken antibiotics or anti-inflammatory medications, (II) those who had experienced acute infections within the 30 days prior to sample collection; (III) individuals who were previously diagnosed with chronic diseases.

Data collection

Two pediatricians and two nutritionists obtained a brief medical history using a standardized questionnaire. All of them were trained before the study started. Height was measured to the nearest millimeter with a wall-mounted stadiometer (Altura Exata[®], Brazil), graduated every 10 cm, with a limit of 2.13 m. All students were instructed to stand in an upright position, feet together and barefoot. Weight was measured with an analytical anthropometric balance that was regularly calibrated by the accredited technical assistance provided by the National Institute of Metrology, Standardization and Industrial Quality (INMETRO) to the nearest 0.1 kg. Body mass index (BMI; in kg/m²) was calculated. Waist circumference (cm) was measured at the level of an imaginary horizontal line in the intermediate region between the margin of the lowest rib and the iliac crest. All anthropometric data were measured in triplicate.

BMI was classified according to the Z-score (BMI-for-Age) from the World Health Organization (WHO), using the WHO AnthroPlus[®] tool (version 1.0.4). The classifications were as follows: underweight (Z-score < -2), normal weight (Z-score between -2 and +1), overweight (Z-score > +1 and < +2), and obese (Z-score ≥ +2)¹⁵. The criteria established by Taylor et al. were used to classify waist circumference measurements as either normal or altered¹⁰.

For the assessment of laboratory parameters, blood samples were drawn from either the cubital or radial vein, collecting 15 ml after a minimum fasting period of 8 h. The CRP was ascertained using the Turbidimetry method, utilizing the AU680 device from Beckman Coulter[®], with compatible analysis kits from the same manufacturer. The hexokinase method was used for measuring glucose. Total cholesterol (TC), high-density lipoprotein (HDL), and triglycerides (Tg) were quantified using an automated enzymatic colorimetric method with the analysis kits from Biosystems[®] and their BS 200 model equipment. The determination of low-density lipoprotein (LDL) was carried out computationally, employing the Friedwald equation ($[\text{LDL}] = [\text{TC}] - ([\text{HDL}] + [\text{Tg}/5])$).

Adaptation of molecular degree of perturbation to examine plasma concentration biomarkers

The Metabolic Disturbance Degree (MDD) is adapted from the Molecular Degree of Perturbation (MDP). This metric offers a standard based on typical values from lipid profile, blood glucose measurements, and C-reactive protein levels, as detailed in Table 1. Its computation was achieved using the mdp package in R version 4.2.2¹⁶. For each test, the MDD score was determined by comparing the concentration variances from the average value for a given test in the reference population and then normalizing by the population's standard deviation.

Characteristics	General population (n=231)	Low perturbation (n=173)	High perturbation (n=58)	p-value
MDD score	1.12 [0.00; 2.76]	0.00 [0.00; 1.32]	4.26 [3.38; 6.24]	<0.001
Age, years	9.00 [7.00; 11.0]	9.00 [7.00; 11.0]	9.00 [7.00; 10.8]	0.734
Sex, male	114 (49.4%)	88 (50.9%)	26 (44.8%)	0.519
BMI Z-score	0.10 [- 0.77; 1.15]	- 0.14 [- 0.88; 0.58]	1.29 [- 0.16; 2.03]	<0.001
BMI categories				<0.001
Underweight	9 (3.90%)	8 (4.62%)	1 (1.72%)	
Normal weight	160 (69.3%)	134 (77.5%)	26 (44.8%)	
Overweight	38 (16.5%)	23 (13.3%)	15 (25.9%)	
Obese	24 (10.4%)	8 (4.62%)	16 (27.6%)	
Municipality				0.595
Serrinha	113 (48.9%)	81 (46.8%)	32 (55.2%)	
Teofilândia	42 (18.2%)	31 (17.9%)	11 (19.0%)	
Barrocas	48 (20.8%)	38 (22.0%)	10 (17.2%)	
Biritinga	28 (12.1%)	23 (13.3%)	5 (8.62%)	
Rural area	130 (56.3%)	96 (55.5%)	34 (58.6%)	0.793
Elevated waist circumference	35 (15.2%)	14 (8.09%)	21 (36.2%)	<0.001
Total cholesterol, mg/dL	164 [142; 186]	163 [139; 184]	166 [144; 188]	0.481
HDL, mg/dL	66.0 [56.0; 76.0]	70.0 [59.0; 78.0]	57.5 [49.5; 68.0]	<0.001
LDL, mg/dL	81.0 [64.0; 102]	78.0 [59.0; 101]	86.5 [70.0; 103]	0.092
Triglycerides, mg/dL	67.0 [52.0; 99.0]	64.0 [52.0; 86.0]	108 [59.2; 152]	<0.001
CRP, mg/dL	0.30 [0.20; 0.80]	0.30 [0.10; 0.50]	1.70 [0.60; 2.55]	<0.001
Blood glucose, mg/dL	84.0 [78.5; 89.0]	84.0 [79.0; 89.0]	83.0 [78.0; 88.8]	0.444

Table 1. Population characteristics. Table that represents the distribution of various characteristics across the general population and subdivided by the degree of metabolic perturbation. The p-value highlights significance of observed differences between the low and high perturbed groups. *MDD* Metabolic disturbance degree, *BMI* body mass index, *HDL* high-density lipoprotein, *LDL* low-density lipoprotein, *CRP* C-reactive protein.

Essentially, the MDD score quantifies the deviation, in standard deviations, from a healthy control group. The specific equation employed to compute the MDP in this research is presented below:

$$\text{Molecular degree of perturbation} = \frac{x_i - x_{\text{reference}}}{\sigma_{\text{reference}}}$$

where: $\sigma = \sqrt{\sum_{i=1}^n \frac{(x_i - \bar{x})^2}{n-1}}$, n = Number of data points, x_i = Each of the value of data, \bar{x} = Mean of the data points, σ = Standard deviation.

Within the scope of this study, we applied the MDD to six markers indicative of metabolic status. Those individuals presenting an MDD value exceeding the third quartile were classified as "Highly perturbed" (Fig. 1; Supplementary Table 1).

Statistical analysis

The sample size was calculated using WINPEPI (version 11.65; <http://www.brixtonhealth.com/pepi4windows.html>), considering a 5% alpha and 90% power for a two-sided 0.25 correlation coefficient between high sensitivity CRP and Z-score, estimating the need for 165 individuals¹⁷. Sociodemographic, clinical, and laboratory characteristics were compared across low and high degrees of MDD. For continuous variables, the Mann–Whitney U test was employed, while Fisher's exact test was used for categorical ones. To ascertain whether the BMI z-score and age-stratified waist circumference were independently linked to high scores on the Metabolic Disturbance Score, a backward logistic regression was conducted. During this analysis, sociodemographic factors were viewed as potential confounders. Hierarchical cluster analysis (Ward's method) of z-score scaled data was employed to depict the overall expression profile of indicated biomarkers in the study subgroups. To assess differences between patients' characteristics within each BMI strata, the Kruskal–Wallis test was employed along with Chi-squared test, with Bonferroni's adjustment for multiple comparisons.

We further conducted a post-hoc power analysis with the G*Power software (version 3.1.9.7; <https://www.psychologie.hhu.de/arbeitsgruppen/allgemeine-psychologie-und-arbeitspsychologie/gpower>), revealing a two-tailed alpha coefficient of 0.05 and a beta error of 0.17¹⁸. This was in relation to a 23% difference in the MDD score prevalence between the overweight and the normal weight groups. Our study does not have enough power to evaluate differences between the normal weight and underweight, due to a small sample of underweight patients.

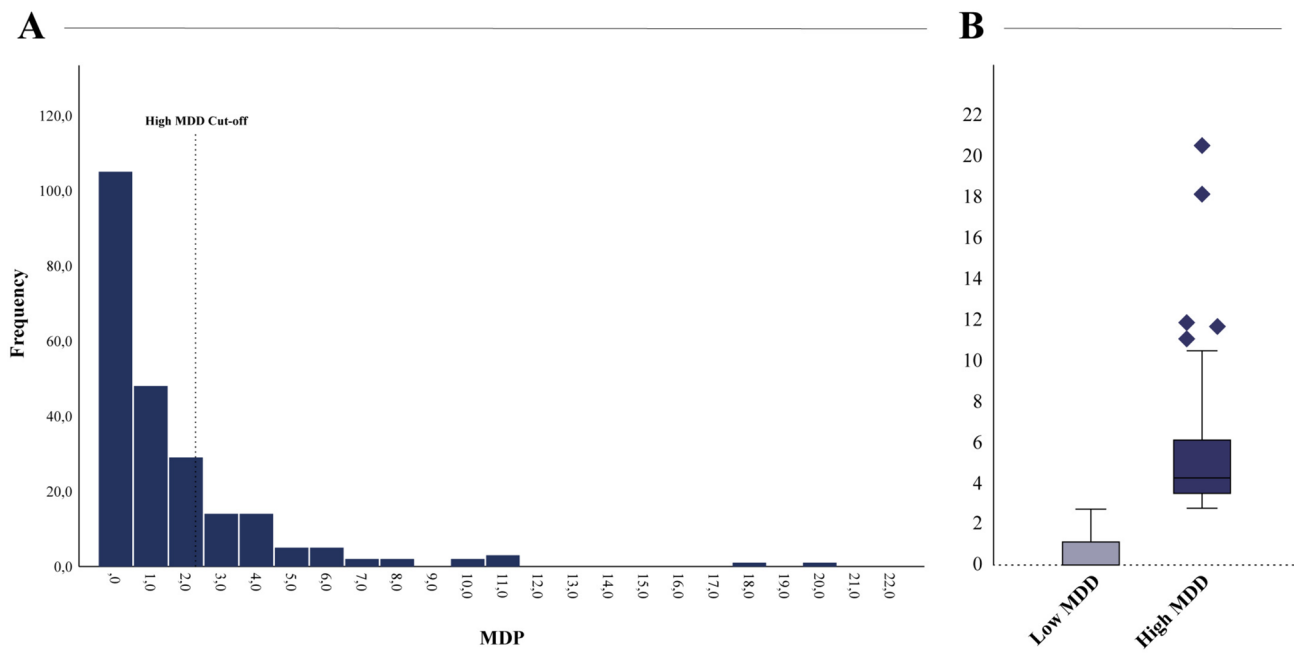


Figure 1. Frequency and distribution of MDD levels. Panel (A) displays the frequency distribution of Metabolic Disturbance Degree (MDD) scores among the studied population, with a dotted line indicating the threshold for high MDD cutoff. Panel (B) provides a visual comparison of MDD scores between the low and high MDD groups, using boxplots to highlight the range, median, and potential outliers in each group.

Results

Characteristics of participants

A total of 231 patients were evaluated. Of these, 114 (49.3%) were male, with a median age of 9 years (IQR 7–11), and most live in urban areas (130; 56.2%). Distribution by municipality shows that Serrinha, the most populous city and with a Human Development Index (HDI) of 0.634, contributed with almost half of the participants (113; 48.9%). This was followed by Barrocas (48; 20.8%) with an HDI of 0.610, Teofilândia (42; 18.2%) with an HDI of 0.566, and Biritinga (28; 12.1%) with an HDI of 0.538. Participants had a median BMI Z-Score of 0.10 (IQR 0.77–1.15), with 62 (26.8%) being classified as above normal levels, in addition to 35 (15.1%) having elevated waist circumference. The complete characterization of the population is reported in Table 1.

After adjusting for variables such as age, gender, and municipality, it was observed that only overweight and obesity have an independent direct association with elevated MDD, with an adjusted odds ratio of 2.75 (95% CI 1.16–6.50, p -value 0.021) and 6.33 (95% CI 1.72–23.20, p -value: 0.005), respectively (Fig. 2).

To evaluate the differences in metabolic patterns between each BMI category, a hierarchical cluster analysis of log-transformed and Z-score normalized median concentration values of each metabolic marker was conducted (Fig. 3). Regarding those in the obese group, it was demonstrated that the variable CRP and Triglycerides are higher, and also HDL is lower when compared to those in healthy weight. Other population characteristics according to BMI strata are available on Supplementary Table 2.

Discussion

This cross-sectional study provides a detailed association between risk factors for cardiovascular disease and anthropometric parameters of children aged 5–12 years in the semi-arid region of Bahia. In this population, when patients with obesity were compared to those of normal weight, pronounced elevations in Tg and CRP markers were seen, while there was a reduction in HDL titers. This difference is reinforced in the literature, in which childhood obesity plays a significant role in the prevalence of metabolic and cardiovascular diseases in children and adolescents¹⁹. Specifically, studies, such as that by Bloch et al., contributed significantly to understanding the profile of childhood adiposity and its implications in Brazilian children^{20,21}.

Furthermore, in the present study, it was demonstrated that there is a progressive association between weight gain and rates of metabolic disturbance, reinforcing the dose–response relationship inherent in epistemological concepts²². This finding indicates that individuals with obesity exhibit more pronounced metabolic disturbances, whereas those overweight face a comparatively lower risk. This is consistent with previous research, such as that by Weiss et al., which also found a dose–response relationship between the severity of obesity and the prevalence of metabolic syndrome components²³.

A noteworthy observation from the study is the lack of an independent association between waist circumference and the metabolic profile. Previous studies have highlighted waist circumference as a significant predictor of metabolic risk factors in children^{24–26}. This discrepancy suggests that there may be context-specific factors influencing this association. One possible explanation is the difference in body fat distribution patterns among children in different regions, influenced by genetic, environmental, and lifestyle factors. Also, it is possible that

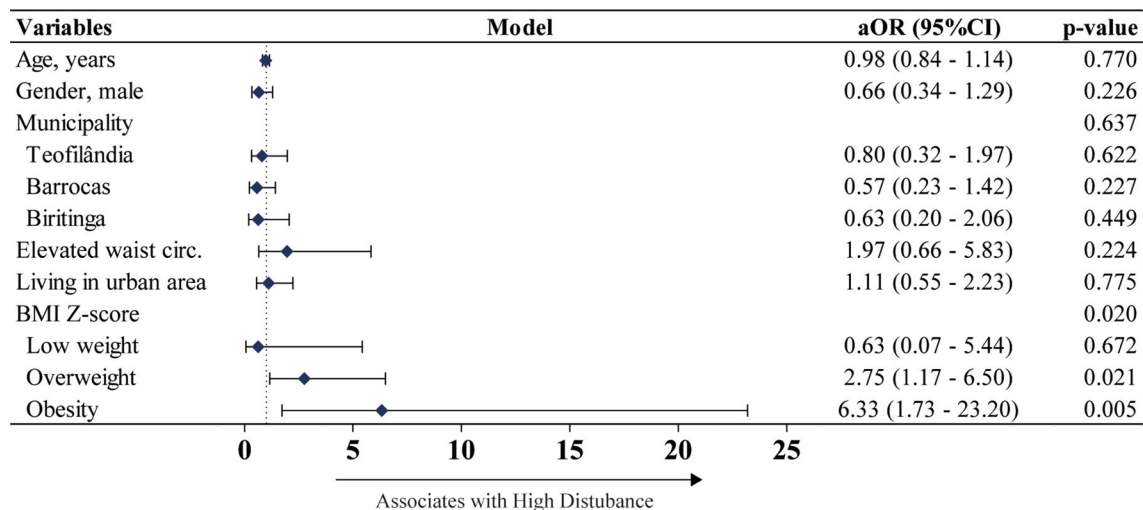


Figure 2. Determinants of high metabolic disturbance degree. The forestplot displays the adjusted odds ratios (OR) and their 95% confidence intervals (95% CI) derived from a binary regression analysis. aOR values greater than 1 suggest an increased risk of association with high metabolic perturbation. The vertical dotted line at aOR = 1 references no association.

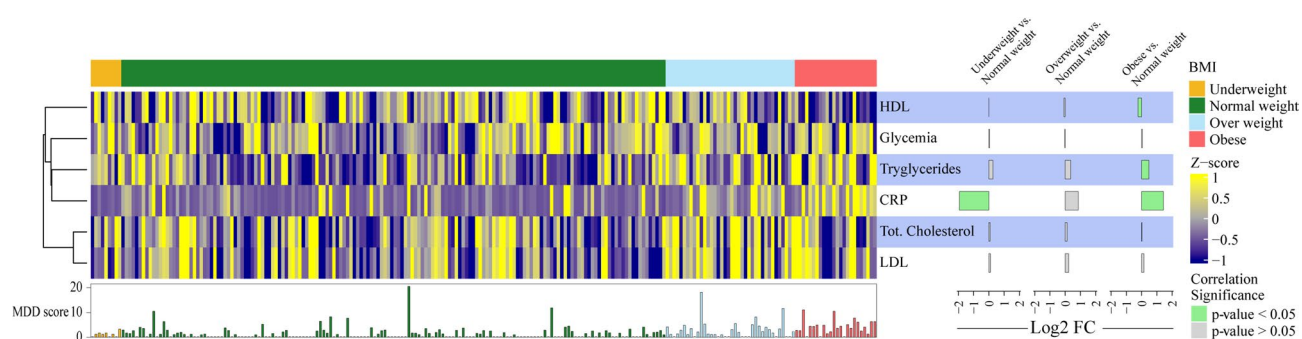


Figure 3. Association of obesity with metabolic disturbances. Hierarchical cluster analysis (Ward's method) was used to show the samples' metabolic profile with the z-score scaled data of each individual marker. The bars at the right side depict each marker's log₂ fold change values across different BMI categories. Green bars represent statistically significant differences estimated by the t-test. *HDL* High-density lipoprotein, *LDL* low-density lipoprotein, *CRP* C-reactive protein.

the number of participants with heightened waist circumference (38; 12.2%) was relatively small to assess this association.

Additionally, factors such as age, gender and residential area—urban or rural—did not play a significant role in the process of metabolic changes occurring in the population analyzed. Particularly regarding the environment, this result challenges the previous understanding that the rural environment is protective for obesity in children, highlighting the complexity of these interactions and the need for large-scale approaches to this problem in the country²⁷.

This study underscores the need for innovative public health strategies to address childhood obesity. Intervention programs that have been effective in other regions, such as the multi-disciplinary community initiatives, could be adapted for the semi-arid region of Bahia²⁸. Such programs should consider local socioeconomic and cultural factors, as our results suggest that urban and rural settings in this region do not significantly differ in obesity's impact on metabolic changes.

The MDD score proposed here is an adaptation of the molecular degree of perturbation concept, which reflects the distance between the levels of a biomarker, from its expression in healthy state. This evaluation offers a composite measure of metabolic health in contrast to the concept of metabolic syndrome, in which the measure of inflammatory markers, such as CRP, is absent. In terms of clinical relevance, the MDD could be considered for integration into pediatric screening protocols to identify children at high grade metabolic complications earlier.

This study employs internationally recognized anthropometric and biochemical reference values, ensuring comparability across populations and facilitating replication in diverse socioeconomic contexts due to the variables' wide availability and low cost. However, the study's cross-sectional nature limits our ability to infer causality. Longitudinal studies are needed to track the progression of metabolic disturbances over time and to

evaluate intervention outcomes. Furthermore, future research should include dietary quality and physical activity variables to provide a more comprehensive risk assessment.

Addressing obesity and its associated metabolic disturbances in children presents a significant opportunity for long-term health benefits²⁹. This proactive approach in children is crucial, considering the increasing prevalence of obesity in younger age groups and its implications for future health. By targeting the pediatric population, the study not only addresses an immediate health concern but also contributes to the broader goal of preventing chronic diseases in adulthood, thus offering a greater prospect of health gains in the long term. Finally, considering the complexity of the approach that childhood obesity requires, the present study aimed to enhance understanding of this condition within a vulnerable population. Its results may guide healthcare professionals, educators, policymakers, and community leaders in developing effective prevention and treatment strategies that are sensitive to the socio-cultural determinants of health.

Conclusion

The study's findings underscore the heightened metabolic disturbances in obese individuals, whereas those overweight face a lower risk compared to their healthy-weight counterparts. It advocates for the inclusion of comprehensive metabolic assessments in routine pediatric care, especially in low- and middle-income countries, to better manage and prevent obesity-related metabolic complications. This approach could significantly improve health outcomes for children in these regions.

Data availability

The data that support the findings of this study are not openly available due to reasons of sensitivity and are available from the corresponding author upon reasonable request.

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Competing interests

The authors declare no competing interests.

Additional information

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