CEP Clin Exp Pediatr Vol. 67, No. 7, 347–355, 2024
https://doi.org/10.3345/cep.2023.00892

Review article

Metabolic complications of obesity in children and adolescents

Hyunjin Park, MS[1,2], Jung Eun Choi, MD[3], Seunghee Jun, BS[1,2], Hyelim Lee, BS[1,2], Hae Soon Kim, MD, PhD[3], Hye Ah Lee, PhD[4], Hyesook Park, MD, PhD[1,2]

[1]Department of Preventive Medicine, College of Medicine, Ewha Womans University, Seoul, Korea; [2]Graduate Program in System Health Science and Engineering, Ewha Womans University, Seoul, Korea; [3]Department of Pediatrics, College of Medicine, Ewha Womans University, Seoul, Korea; [4]Clinical Trial Center, Ewha Womans University Mokdong Hospital, Seoul, Korea

The global prevalence of childhood and adolescent obesity, exacerbated by the coronavirus disease 2019 pandemic, affects school-aged children and preschoolers. Early-onset obesity, which carries a high risk of metabolic complications, may contribute to a lower age at the onset of cardiovascular disease. As metabolic diseases such as diabetes, dyslipidemia, and nonalcoholic fatty liver disease observed in adulthood are increasingly recognized in the pediatric population, there is an emphasis on moving disease susceptibility assessments from adulthood to childhood to enable early detection. However, consensus is lacking regarding the definition of metabolic diseases in children. In response, various indicators such as the pediatric simple metabolic syndrome score, continuous metabolic syndrome score, single-point insulin sensitivity estimator, and fatty liver index have been proposed in several studies. These indicators may aid the early detection of metabolic complications associated with pediatric obesity, although further validation studies are needed. Obesity assessments are shifting in perspective from visual obesity to metabolic health and body composition considerations to fill the gap in health impact assessments. Sarcopenic obesity, defined as the muscle-to-fat ratio, has been proposed in pediatric populations and is associated with metabolic health in children and adolescents. The National Health Screening Program for Children in Korea has expanded but still faces limitations in laboratory testing. These tests facilitate timely intervention by identifying groups at a high risk of metabolic complications. Early detection and intervention through comprehensive health screening are critical for mitigating long-term complications of childhood obesity.

Key words: Health services, Insulin resistance, Metabolic syndrome, Nonalcoholic fatty liver disease, Pediatric obesity

Key message

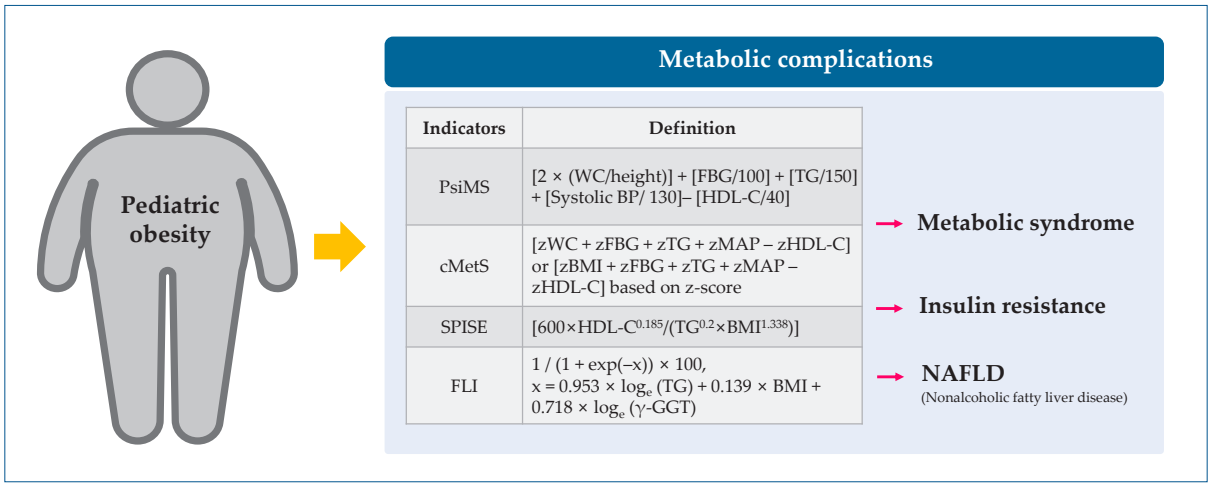
- Pediatric obesity increases the risk of metabolic complications (insulin resistance, dyslipidemia, nonalcoholic fatty liver disease) and long-term cardiovascular diseases.
- A new obesity definition and various indicators (continuous metabolic syndrome score, pediatric simple metabolic syndrome score, fatty liver index) have been proposed to evaluate children's susceptibility to metabolic disorders.
- Laboratory and body composition tests in pediatric screenings can identify groups at high risk of metabolic complications of obesity.

Introduction

The incidence of pediatric obesity has increased over the past few decades. From 1975 to 2016, the age-standardized mean body mass index (BMI) of children and adolescents reportedly increased globally per decade by 0.32 kg/m^2 for girls and 0.40 kg/m^2 for boys.[1)] The prevalence of pediatric obesity continues to rise, and this problem has been exacerbated during the coronavirus disease 2019 pandemic. Since the pandemic, the prevalence of overweight and obesity among school-aged children, derived from Korea's National School Health Examination, increased from 25.8% to 30.8%.[2)] This phenomenon has also been observed in the US[3,4)] and Europe.[5)] Furthermore, an emerging problem in pediatric obesity is the increase in severe obesity, which has become a major public health concern. A recent systematic meta-analysis of 9 million children and adolescents found a

Corresponding author: Hyesook Park, MD, PhD. Department of Preventive Medicine, College of Medicine, Ewha Womans University, 25 Magokdong-ro 2-gil, Gangseo-gu, Seoul 07804, Korea
✉ Email: hpark@ewha.ac.kr, http://orcid.org/0000-0001-6536-8787
Co-corresponding Author: Hye Ah Lee, PhD. Clinical Trial Center, Ewha Womans University Mokdong Hospital, 1071, Anyangcheon-ro, Yangcheon-gu, Seoul 07985, Korea
✉ Email: khyeah@ewha.ac.kr, http://orcid.org/0000-0002-4051-0350
Received: 5 July, 2023, Revised: 18 August 2023, Accepted: 18 August 2023

This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/4.0/) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.
Copyright © 2024 by The Korean Pediatric Society



Graphical abstract. PsiMS, pediatric simple metabolic syndrome score; WC, waist circumference; FBG, fasting blood glucose; TG, triglyceride; BP, blood pressure; HDL-C, high-density lipoprotein cholesterol; cMetS, continuous metabolic syndrome; MAP, mean arterial pressure; SPISE, single-point insulin sensitivity estimator; FLI, fatty liver index; BMI, body mass index; γ-GGT, gamma-glutamyl transferase.

1.7-fold increase in severe pediatric obesity compared to the early 2000s.[6]

Obesity can occur even in preschoolers. According to a World Health Organization report, an estimated 39 million children under 5 years of age were overweight and obese in 2020; half of the children were living in Asia.[7] Epidemiological studies revealed that obesity in early life is associated with obesity in adulthood.[8] Childhood obesity not only leads to lifelong obesity but also results in various metabolic complications throughout life. Indeed, early-onset chronic diseases, such as type 2 diabetes mellitus (T2DM) and nonalcoholic fatty liver disease (NAFLD), have been observed in obese children and adolescents.[9-11] Accordingly, the need for an appropriate evaluation of pediatric obesity and the importance of early intervention for its prevention and management have been emphasized.[12] In addition, obesity defined by BMI cannot fully explain health risks; therefore, other concepts were introduced to define obesity.

This review article discusses studies that have evaluated the complications associated with pediatric obesity and introduces the concept of sarcopenic obesity (SO). Finally, it reviews health screening programs for children in Korea.

Metabolic complications associated with pediatric obesity

1. Pediatric obesity associated with metabolic complications

Pediatric obesity is associated with a high risk for a wide range of metabolic, mental, respiratory, joint, and reproductive problems.[13] Metabolic complications related to pediatric obesity have been reported by several studies.

A few studies using cohort data have reported that obesity in children and adolescents is associated with metabolic complications, and early research focused primarily on the disease risk in adulthood. Metabolic complications are known risk factors for later cardiovascular disease (CVD), and several cohort studies have shown that childhood obesity is associated with CVD-related mortality.[14,15] Due to the long observation period required, few longitudinal studies have directly assessed the association between childhood obesity and CVD in adulthood.[16] However, evidence has accumulated that the progression of atherosclerosis, a major cause of CVD, begins early in life[17] and that childhood obesity and related metabolic complications can accelerate atherosclerosis.[18,19] The International Childhood Cardiovascular Cohort Consortium, which analyzed four cohorts (Bogalusa Heart Study, Muscatine Study, Childhood Determinants of Adult Health, and Young Finns Study), found that overweight or obese children who remained obese into adulthood were at an increased risk of type 2 diabetes mellitus (relative risk [RR], 5.4; 95% confidence interval [CI], 3.4–8.5), hypertension (RR, 2.7; 95% CI, 2.2–3.3), hypo-high-density lipoprotein (HDL) cholesterolemia (RR, 1.8; 95% CI, 1.4–2.3), high triglyceride (TG) levels (RR, 3.0; 95% CI, 2.4–3.8), and carotid atherosclerosis (RR, 1.7; 95% CI, 1.4–2.2).[20]

We reasonably expect that metabolic complications such as insulin resistance (IR), hypertension, and dyslipidemia will increase further with childhood obesity rates and that early and long-term exposure to these metabolic disorders will contribute to early CVD in an increasingly young adult population.[21] Recently, as metabolic diseases observed in adulthood have been increasingly recognized in adolescence, the focus of disease susceptibility assessments has shifted from adulthood to childhood and adolescence. Population-based cross-sectional studies of adolescents

found that overweight and obese status are more likely to involve high blood pressure, high fasting glucose levels, and abnormal lipid profiles, even at a young age.[22-24] Although international consensus is lacking on the screening and monitoring of pediatric NAFLD, it is a major chronic liver-related disease that occurs frequently in children and is considered a metabolic complication associated with obesity. Obesity plays a crucial role in NAFLD progression by increasing oxidative stress and mitochondrial dysfunction.[25] A systematic review reported that the prevalence of NAFLD in overweight and obese children was 34.2% (95% CI, 27.8%–41.2%), and the risk of NAFLD was 13.4 times (95% CI, 9.1–18.0) higher in overweight and obese than in normal-weight children.[26]

From a longitudinal perspective, a study of data from the Ewha Birth and Growth Study identified the trajectory of childhood BMI from 3 to 12 years and found those with a high BMI at an early age were more likely to have a high BMI throughout childhood.[27] Childhood obesity caused by genetic, lifestyle, and environmental factors can occur even in the early stages of life and seriously affect the occurrence and progression of metabolic diseases. Disease susceptibility can be observed during childhood and adolescence; therefore, early assessments and interventions are encouraged.

2. Metabolic complications assessment index

Unlike adults, for whom the diagnostic criteria for diseases are well defined, the consensus is inconsistent on the definition of metabolic diseases in children because of the relatively low prevalence in children. Nevertheless, many studies have suggested various indicators to evaluate an individual's susceptibility to metabolic diseases, and only a few are introduced here (Table 1).[28-32]

In 2017, Vukovic et al.[28] developed the pediatric simple metabolic syndrome score (PsiMS), a modified metabolic syndrome (MetS) scoring system based on the simple metabolic syndrome score originally developed for adults. This index can be easily calculated, and its usefulness was confirmed in a study of Korean adolescents (area under the curve [AUC], 0.958).[33] The continuous metabolic syndrome score (cMetS) is a reliable indicator for predicting the risk of MetS in children and adolescents. It is a more comprehensive and robust measure than dichotomous measures of MetS, thus allowing for better evaluations in pediatric epidemiological studies.[29,34] A systematic review noted that cMetS is useful for predicting the risk of MetS with high accuracy.[35]

The single-point insulin sensitivity estimator (SPISE) is an index that was developed to simplify the estimation of insulin sensitivity in adults and obese adolescents.[30] TG/HDL-cholesterol (HDL-C) was introduced approximately 20 years ago as an index for evaluating IR; however, it showed high variability among populations, suggesting the need for a cutoff point.[36] To improve its performance, Paulmichl et al.[30] developed the SPISE as a promising tool for estimating IR based on TG, HDL-C, and BMI. In adolescents aged 16–17 years, SPISE showed significantly better AUC values than the homeostatic model assessment for IR (HOMA-IR) and TG/HDL-C in discriminating MetS.[37] Finally, the fatty liver index (FLI) and hepatic steatosis index are primarily used as noninvasive/nonimaging indicators to define pediatric and adult NAFLD.[31,32] In the United States, an FLI for a multiethnic population was developed.[38] Although these indicators are used in epidemiological studies, evidence assessing the usefulness of the FLI and hepatic steatosis index in pediatric populations is lacking, and further evidence is required.

3. Studies using metabolic complication assessment indicators

These indicators have been used in several studies to evaluate the metabolic complications of pediatric obesity. In a study of adolescents (10–18 years) using the Korea

Table 1. Indicators used to evaluate obesity-related metabolic complications[28-32]

Indicator	Definition or formula	Interpretation
Pediatric siMS (PsiMS)[28]	[2× (WC/height (cm))]+[FBG (mg/dL)/100]+[TG (mg/dL)/150]+[systolic BP (mmHg)/130]– [HDL-C (mg/dL)/40]	A higher PsiMS score indicates a higher risk of having MetS in children and adolescents.
Continuous metabolic syndrome score (cMetS)[29]	[zWC+zFBG+zTG+zMAP–zHDL-C] or [zBMI+zFBG+zTG+zMAP–zHDL-C] *The cMetS is calculated by standardizing the z-scores based on age and sex.	A higher cMetS score indicates a higher risk of an unfavorable metabolic profile.
Single-point insulin sensitivity estimator (SPISE)[30]	$[600\times HDL\text{-}C^{0.185}/(TG^{0.2}\times BMI^{1.338})]$	The lower the SPISE, the higher the insulin resistance, indicating a higher risk of MetS and T2DM.
Fatty liver index (FLI)[31]	$1/(1+\exp(-x))\times 100$, $x=0.953\times \log_e(TG)+0.139\times BMI+0.718\times \log_e(\gamma\text{-GGT})$	FLI score below 30 rules out NAFLD, 30≤FLI<60 indicates an intermediate risk, and FLI ≥ 60 indicates a high risk of NAFLD
Hepatic steatosis index (HSI)[32]	8×ALT/AST ratio+BMI (+2, if diabetes; +2, if female)	HSI >36.0 indicates a high risk of NAFLD

siMS, simple metabolic syndrome score; WC, waist circumference; FBG, fasting blood glucose; TG, triglyceride; BP, blood pressure; HDL-C, high-density lipoprotein cholesterol; MetS, metabolic syndrome; MAP, mean arterial pressure; BMI, body mass index; T2DM, type 2 diabetes mellitus; γ-GGT, gamma-glutamyl transferase; NAFLD, nonalcoholic fatty liver disease; AST, aspartate aminotransferase; ALT, alanine aminotransferase.

National Health and Nutrition Examination Survey (KNHANES) data, mean PsiMS was significantly higher in MetS than in non-MetS participants (3.2 vs. 1.9 in boys, 3.1 vs. 1.8 in girls; all $P<0.001$).[33] In a cross-sectional cohort study of 2,107 overweight or obese children and adolescents (aged 5–18.4 years), participants in the lowest versus highest quartile of SPISE values were three times more likely to develop dysglycemia during follow-up.[39] Similar findings were observed in a study of 10–17-year-olds in which the SPISE index was significantly lower in MetS than in non-MetS participants (5.5 vs. 9.4 in boys and 4.4 vs. 8.6 in girls; all $P<0.001$).[40] Additionally, in the International Childhood Cardiovascular Cohort Consortium (average follow-up, 22.3 years), cMetS in childhood was associated with a 2.1-fold higher risk of MetS in adulthood.[41] The cMetS remained stable throughout childhood.[42] NAFLD is often asymptomatic and can lead to irreversible complications, highlighting the importance of early diagnosis to prevent progression. The global prevalence of NAFLD is 4.2%–9.6% and can reach 38% in pediatric obese populations.[43] In a study of overweight and obese children aged 5–15 years, those with an ultrasound-diagnosed fatty liver had significantly higher FLI values than those without a fatty liver (odds ratio, 3.5; 95% CI, 1.1–11.3).[39] These indicators provide valuable insight into the metabolic complications associated with childhood obesity and aid in the early identification and intervention to prevent long-term health consequences.

Changes in evaluation perspective for pediatric obesity

1. BMI as proxy for body composition

Obesity refers to the excessive accumulation of fat caused by an imbalance between energy intake and expenditure. Body weight comprises two components: body fat mass (FM) and fat-free body mass (FFM). BMI, a simplified measure commonly used to define obesity, was determined based on height and weight. However, although BMI can reflect high FM levels, it also includes individuals with naturally high FFM, limiting its ability to assess obesity accurately.[44] Furthermore, although obesity may be visually classified based on BMI, metabolic health levels can vary. Evaluating metabolic health using BMI alone may have limitations in distinguishing functional differences.[45] In children and adolescents, a BMI increase may not simply indicate an increase in FM, as body composition changes can occur depending on growth rate and pubertal development level.[45]

An example that effectively demonstrates the impact of body composition on health is the "obesity paradox," which reveals the incorrect results that can be derived when evaluating the relationship between high BMI and low mortality rates in the elderly population-based solely on BMI. Body composition offers a better explanation for this phenomenon.[46] In studies conducted on children and adolescents, the term "normal-weight obesity" define cases in which excessive body fat and low muscle mass coexist, resulting in a normal BMI. Despite having a normal BMI, these children may experience unfavorable metabolic health.[47] In fact, they exhibit lower cardiorespiratory and muscular fitness than children with normal body fat levels. They also display physical fitness deficits similar to those of overweight children, which can be partly attributed to low physical activity levels.[48] Muscle plays a vital role in glucose and lipid metabolism and can be assessed using FFM, lean body mass (LBM), and skeletal muscle mass (SMM).[49] However, considering muscle mass alone does not sufficiently reflect muscle quality and performance, grip strength has been used as a muscle strength indicator.[50,51] Grip strength correlates with muscle mass and body FM and has been found to be associated with metabolic risk[52] not only in adults but also in studies involving children and adolescents.[53] With the accumulation of research findings suggesting differences in health impacts based on metabolic health or body composition rather than just visual obesity, new paradigms are being proposed for evaluating obesity.

When using body composition indicators, it is imperative to consider their correlation with body size. Because a decrease in FFM can increase the proportion of fat, interpreting the meaning of body composition indicators alone can be challenging when making comparisons. Indeed, some studies have reported differences in the results depending on the evaluation criteria.[44] Some studies have presented muscle mass as a ratio of weight to height squared or calculated the ratio of muscle mass to FM to supplement the interpretation of research findings, thereby addressing these challenges.

2. Studies evaluating relationship between body composition indices and metabolic complications

Studies have reported associations between obesity and major metabolic complications such as impaired glucose metabolism, MetS, and NAFLD. Various body composition indicators are associated with these complications. Muscle is considered an essential tissue in human endocrine function and metabolism, and its involvement in glucose and lipid metabolism has been explained by various biological mechanisms.[49] In a recent systematic literature review of 15 research papers, differences in FFM or LBM were evaluated between children and adolescents with IR/glucose tolerance (GT)/MetS and those without these conditions. Children and adolescents with IR/GT/MetS

exhibited lower FFM or LBM in terms of percentages. This suggests a higher proportion of adiposity in relation to body weight, indicating the influence of adiposity on IR.[44] Another systematic literature review evaluated the correlation between FM percentage and glucose metabolism in children and adolescents.[54] FM percentage showed a correlation of 0.48 with fasting plasma insulin and a correlation of 0.44 with HOMA-IR based on data from 11 studies.

NAFLD is recognized as a major chronic disease in the pediatric population and is understood as a condition that is not simply limited to liver abnormalities but also involves various metabolic risks.[55] In a study evaluating the association between muscle mass and NAFLD risk in overweight children and adolescents, a lower muscle mass was associated with a higher risk of NAFLD, while an inverse relationship was noted between muscle mass and nonalcoholic steatohepatitis as evaluated through biopsy.[56] Furthermore, in a study that assessed the grip strength to body weight ratio and considered muscle strength, differences were observed based on the presence of MetS, with a lower grip strength/body weight ratio observed in adolescents with MetS.[50] Studies focusing on obese children have also used muscle-to-fat ratio (MFR) to predict the risk of metabolic disorders.[57]

Abdominal fat accumulation during childhood and adolescence may be directly associated with unfavorable cardiovascular and metabolic health profiles irrespective of overall body fat levels.[58] The prospective study conducted by Park et al.[59] evaluated the association between SO at ages 7–9 years and cMetS at ages 13–15 years. Children with SO had higher cMetS during adolescence than those without SO; this trend was consistent in the evaluation of other MetS indicators. Furthermore, being overweight during childhood and adolescence had a positive interaction effect on adolescent metabolic health. As evidence suggests the limitations of BMI in explaining health effects, there is growing recognition of the need to evaluate body composition and alternative indicators to assess health outcomes.

3. Definition and prevalence of SO

A high BMI is associated with various metabolic health outcomes. However, individuals with the same body weight do not always experience the same health effects. Additionally, the impact of muscle mass on IR and lipid metabolism may vary depending on the FM index.[49] SO, which refers to the coexistence of muscle loss and obesity, has been linked to various metabolic disorders.[60] MFR calculations are commonly used to define SO using appendicular skeletal muscle mass or SMM.[51,61] The handgrip strength-to-BMI ratio is another indicator used to evaluate SO.[51] However, a consistent definition of SO in children and adolescents is lacking, leading to the use

Table 2. Summary of studies on sarcopenic obesity prevalence[51,56,59,61-67]

Study	Region, No. of study subjects, and range of age	Definition for sarcopenic obesity	Measures of sarcopenic obesity	Prevalence
McCarthy et al.[62] (2014)	UK, n=1,985, children aged 5–18.8 yr	2SD lower than the mean MFR for the 3rd BMI quintile.	MFR	8.3% and 15.5% in boys and girls of 5–10 yr, 9.7% and 5.7% in boys and girls of 10–18 yr
Kim K et al.[61] (2016)	Republic of Korea, n=1,919, children aged 10–18 yr	1SD lower than the mean MFR for the 3rd BMI quintile.	Skeletal muscle-to-body fat ratio	32.1% and 24.3% in boys and girls
Steffl et al.[63] (2017)	Czech Republic, n=730, children aged 4–14 yrs	2SD lower than the mean MFR for the 3rd BMI quintile.	MFR	7.2% and 9.3% in boys and girls
Moon et al.[64] (2018)	Republic of Korea, n=1,233, children aged 12–18 yr	Lower 10% of gender-specific ASM/ WT (%) (cutoff value of ASM/WT was 28.43 % and 21.94% in boys and girls) and WHtR>0.47	ASM/WT (%)	Total: 5.6% (32/571)
Gontarev et al.[51] (2020)	Macedonia, n=402, children aged 6–10 yr	2SD lower than the mean MFR for the 3rd BMI quintile.	MFR	9.2% and 5.9% in boys and girls
Park et al.[59] (2023)	Republic of Korea, n=227, children aged 7–9 yr	Criteria derived from the study by McCarthy et al.[61]	MFR	Total: 19.5%, Overweight: 84.4%
Gätjens et al.[65] (2021)	Germany, n=15,392, children aged 5–17 yr	FM/FFM-ratio (kg/kg) as defined by values exceeding the 90th percentile	FM/FFM-ratio (kg/kg)	62.7% and 69.7% in overweight boys and girls
Sack et al.[66] (2022)	Germany, n=119, children aged 8–16 yr	Criteria derived from the study by McCarthy et al.[61]	MFR	69.9% and 30.1% in boys and girls with obesity
Videira-Silva et al.[67] (2017)	Portugal, n=240, children aged 10–17 yr	≤p25 for %SMM, based on reference charts for youth	SMM (kg)/ body WT*100	33.3% and 20.2% in overweight boys and girls
Pacifico et al.[56] (2020)	Italy, n=234, children aged 6–18 yr	The lowest tertile of RMM	RMM=100xmuscle mass (kg)/muscle mass (kg)+ FM (kg)	28.8% and 39.2% in overweight boys and girls

SD, standard deviation; MFR, muscle-to-fat ratio; ASM, appendicular skeletal muscle mass; WT, weight; WHtR, waist circumference-to-height ratio; BMI, body mass index; FM, body fat mass; FFM, fat-free mass; SMM, skeletal muscle mass; RMM, relative muscle mass.

of various criteria in different studies to estimate its prevalence. The reported prevalence is 5.7%–32.1% in the general population and 20.2%–84.4% in overweight and obese populations (Table 2).[51,56,59,61-67]

4. Need for new definition of obesity, including body composition

Computed tomography and magnetic resonance imaging are accurate methods for measuring body composition. However, owing to their high cost and limited accessibility, bioelectrical impedance analysis and dual-energy x-ray absorptiometry are becoming more commonly used to assess body composition. In addition, grip strength has been suggested as a low-cost and easily measurable indicator of body composition. McCarthy et al.[62] proposed using MFR as an indicator of metabolic health in children and suggested cutoff points to define SO. Subsequently, regarding the diagnostic criteria for pediatric/adolescent SO, Kim et al.[61] applied the method proposed by McCarthy et al.[62] to domestic research and utilized KNHANES data to make suggestions. However, specific criteria based on sex and age are necessary during the growth period, and consideration should be given to the onset of puberty owing to differences in adipocyte composition.[68] Therefore, standardized measurement methods are required to define SO, and the development of national-level criteria is required.

National Health Screening Program for children in Korea

Health screening programs are important for the early detection of diseases or conditions and the prevention of chronic diseases. In Korea, the National Health Screening Program (NHSP) for adults was initiated in 1980, and the target population and diseases are expanding as health demands change in society.[69] The NHSP for children was started in 2007 to monitor the growth and development of infants and children under 6 years of age and is conducted eight times from 14 days after birth. This program consists of physicians administering physical examinations, anthropometric measurements, health education, oral examinations, and developmental evaluation.[70] However, there are limitations in assessing physical and cognitive development, excluding laboratory tests that can assess metabolic health.

Through the National School Health Examination, students in certain grades (1st and 4th grades of elementary school, 1st grade of middle and high school) receive health examinations at schools or hospitals under Ministry of Education supervision. However, screening blood tests for obesity complications are only performed on overweight students except for 1st graders in elementary schools. Despite the high risk of obesity-related complications, opportunities for intervention and treatment may be lost. Moreover, out-of-school youths were excluded.[71] Therefore, establishing a system that connects doctors and schools and provides timely feedback is an urgent health issue for early intervention in obesity.

The NHSP includes BMI measurements for all children and adolescents who undergo routine checkups. BMI is generally used as a screening and diagnostic tool for detecting obesity because it is easy to use and inexpensive. Meanwhile, body fat percentage may be very different even if the BMI is the same, and the amount of FM can increase the risk of MetS independent of BMI. Therefore, to detect obesity complications early, national examinations of children and adolescents should include body composition and laboratory tests to evaluate metabolic health rather than measuring body height and weight.

The critical periods in pediatric obesity are reportedly gestation, early infancy, the adiposity rebound period, and adolescence. Adiposity rebound refers to an increase in BMI following the minimum BMI in early childhood in the preschool period.[72] The earlier the timing of adiposity rebound, the higher the probability of obesity and metabolic complications.[73] Disease susceptibility can be observed at an early age, and lipid abnormalities such as high TG and low HDL-C levels have been reported in obese children under 10 years of age.[74,75] Furthermore, the American Academy of Pediatrics guidelines recommend that pediatricians evaluate hypertension by measuring the blood pressure of overweight children during adolescence at every visit starting at 3 years of age.[76] Recent studies demonstrated that lifestyle changes are effective even in preschoolers aged 2–5 years.[77,78]

Healthcare providers and physicians who conduct the NHSP should encourage children to engage in healthy behaviors and lifestyle treatments. Moreover, based on BMI classification, laboratory evaluations can be performed in clinically indicated children. Laboratory tests for metabolic complications should begin before 10 years of age.[76] For obese children 2–9 years of age, screening for dyslipidemia may be included. Children 10 years and older with overweight status should be evaluated for glucose metabolism and liver function for the detection of IR or NAFLD. Early detection and treatment in these populations can reduce future complications of obesity and motivate treatment engagement.

Conclusion

Pediatric obesity is a major public health issue because

early-onset obesity and its complications can increase one's risk of metabolic disorders and CVD in later life. Various indicators have been proposed to screen for obesity-related metabolic complications, and evaluating these indicators is possible even at a young age. This finding suggests a new paradigm for assessing obesity rather than BMI to evaluate health appropriately. Expanding health screening and laboratory tests can promote the early detection and intervention of obesity-related metabolic complications, ultimately reducing long-term complications.

Footnotes

Conflicts of interest: No potential conflict of interest relevant to this article was reported.

Funding: This research was supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (MSIT) (No. RS-2023- 00253552) and by the BK21 FOUR (Fostering Outstanding Universities for Research) funded by the Ministry of Education and National Research Foundation of Korea (NRF-5199990614253).

ORCID:
Hyunjin Park https://orcid.org/0000-0001-6536-8787
Jung Eun Choi https://orcid.org/0000-0001-8956-4192
Seunghee Jun https://orcid.org/0000-0002-0530-8720
Hyelim Lee https://orcid.org/0009-0002-4230-0952
Hae Soon Kim https://orcid.org/0000-0002-6976-6878
Hye Ah Lee https://orcid.org/0000-0002-4051-0350
Hyesook Park https://orcid.org/0000-0002-9359-6522

References

1. NCD Risk Factor Collaboration (NCD-RisC). Worldwide trends in body-mass index, underweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2416 population-based measurement studies in 128·9 million children, adolescents, and adults. Lancet 2017;390:2627-42.
2. Ministry of Education. Result of the 2021 National School Health Examination Sample Surveys [Internet]. Sejong (Korea): Ministry of Education; c2021 [cited 2023 May 8]. Available from:https://www.moe.go.kr/board Cnts/viewRenew.do?boardID=294&boardSeq=93071&lev=0&searchType=null&statusYN=W&page=1&s=moe&m=020402&opType=N.
3. Lange SJ, Kompaniyets L, Freedman DS, Kraus EM, Porter R; DNP3, et al. Longitudinal trends in body mass index before and during the COVID- 19 pandemic among persons aged 2-19 years - United States, 2018-2020. MMWR Morb Mortal Wkly Rep 2021;70:1278-83.
4. Woolford SJ, Sidell M, Li X, Else V, Young DR, Resnicow K, et al. Changes in body mass index among children and adolescents during the COVID-19 pandemic. JAMA 2021;326:1434-6.
5. Gov.UK, National child measurement programme (NCMP): changes in child BMI between 2019 to 2020 and 2020 to 2021 [Internet]. United Kingdom: Gov.UK, c2022 [cited 2023 May 8]. Available from: https://www.gov.uk/government/statistics/national-child-measurement-program me-ncmp-changes-in-child-bmi-between-2019-to-2020-and-2020-to-20 21.
6. Pinhas-Hamiel O, Hamiel U, Bendor CD, Bardugo A, Twig G, Cukierman- Yaffe T. The global spread of severe obesity in toddlers, children, and adolescents: a systematic review and meta-analysis. Obes Facts 2022;15:118-34.
7. World Health Organization. Obesity and overweight [Internet]. Geneva (Switzerland): World Health Organization, c2021 [cited 2023 May 1]. Available from: https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight.
8. Freedman DS, Khan LK, Serdula MK, Dietz WH, Srinivasan SR, Berenson GS. The relation of childhood BMI to adult adiposity: the Bogalusa Heart Study. Pediatrics 2005;115:22-7.
9. Abbasi A, Juszczyk D, van Jaarsveld CHM, Gulliford MC. Body mass index and incident type 1 and type 2 diabetes in children and young adults: a retrospective cohort study. J Endocr Soc 2017;1:524-37.
10. Twig G, Zucker I, Afek A, Cukierman-Yaffe T, Bendor CD, Derazne E, et al. Adolescent obesity and early-onset type 2 diabetes. Diabetes Care 2020;43:1487-95.
11. Shaunak M, Byrne CD, Davis N, Afolabi P, Faust SN, Davies JH. Non-alcoholic fatty liver disease and childhood obesity. Arch Dis Child 2021;106:3-8.
12. World Health Organization. Guidelines on physical activity, sedentary behaviour and sleep for children under 5 years of age. Geneva (Switzerland): World Health Organization, 2019.
13. Halfon N, Kandyce L, Slusser W. Associations between obesity and comorbid mental health, developmental, and physical health conditions in a nationally representative sample of US children aged 10 to 17. Acad Pediatr 2013;13:6-13.
14. Must A, Jacques PF, Dallal GE, Bajema CJ, Dietz WH. Long-term morbidity and mortality of overweight adolescents: a follow-up of the Harvard Growth Study of 1922 to 1935. N Engl J Med 1992;327:1350-5.
15. Gunnell DJ, Frankel SJ, Nanchahal K, Peters TJ, Davey Smith G. Childhood obesity and adult cardiovascular mortality: a 57-y follow-up study based on the Boyd Orr cohort. Am J Clin Nutr 1998;67:1111-8.
16. Nadeau KJ, Maahs DM, Daniels SR, Eckel RH. Childhood obesity and cardiovascular disease: links and prevention strategies. Nat Rev Cardiol 2011;8:513-25.
17. McGill HC Jr, McMahan CA, Herderick EE, Malcom GT, Tracy RE, Strong JP. Origin of atherosclerosis in childhood and adolescence. Am J Clin Nutr 2000;72(5 Suppl):1307S-1315S.
18. Lai CC, Sun D, Cen R, Wang J, Li S, Fernandez-Alonso C, et al. Impact of long-term burden of excessive adiposity and elevated blood pressure from childhood on adulthood left ventricular remodeling patterns: the Bogalusa Heart Study. J Am Coll Cardiol 2014;64:1580-7.
19. Magnussen CG, Venn A, Thomson R, Juonala M, Srinivasan SR, Viikari JS, et al. The association of pediatric low- and high-density lipoprotein cholesterol dyslipidemia classifications and change in dyslipidemia status with carotid intima-media thickness in adulthood evidence from the cardiovascular risk in Young Finns study, the Bogalusa Heart study, and the CDAH (Childhood Determinants of Adult Health) study. J Am Coll Cardiol 2009;53:860-9.
20. Juonala M, Magnussen CG, Berenson GS, Venn A, Burns TL, Sabin MA, et al. Childhood adiposity, adult adiposity, and

cardiovascular risk factors. N Engl J Med 2011;365:1876-85.
21. Litwin SE. Childhood obesity and adulthood cardiovascular disease: quantifying the lifetime cumulative burden of cardiovascular risk factors. J Am Coll Cardiol 2014;64:1588-90.
22. Lambert M, Delvin EE, Levy E, O'Loughlin J, Paradis G, Barnett T, et al. Prevalence of cardiometabolic risk factors by weight status in a population- based sample of Quebec children and adolescents. Can J Cardiol 2008;24:575-83.
23. Lee J, Cha SG, Lee JS, Kim ST, Song YH. Association between obesity and cardiovascular disease risk factors in different age groups of adolescents: an analysis of data from the Korean National Health and Nutritional Examination Survey. Children (Basel) 2023;10:827.
24. Sinha R, Fisch G, Teague B, Tamborlane WV, Banyas B, Allen K, et al. Prevalence of impaired glucose tolerance among children and adolescents with marked obesity. N Engl J Med 2002;346:802-10.
25. Furthner D, Weghuber D, Dalus C, Lukas A, Stundner-Ladenhauf HN, Mangge H, et al. Nonalcoholic fatty liver disease in children with obesity: narrative review and research gaps. Horm Res Paediatr 2022;95:167-76.
26. Anderson EL, Howe LD, Jones HE, Higgins JP, Lawlor DA, Fraser A. The prevalence of non-alcoholic fatty liver disease in children and adolescents: a systematic review and meta-analysis. PLoS One 2015;10:e0140908.
27. Kim UJ, Choi EJ, Park H, Lee HA, Park B, Min J, et al. BMI trajectory and inflammatory effects on metabolic syndrome in adolescents. Pediatr Res 2023;94:153-60.
28. Vukovic R, Milenkovic T, Stojan G, Vukovic A, Mitrovic K, Todorovic S, et al. Pediatric siMS score: a new, simple and accurate continuous metabolic syndrome score for everyday use in pediatrics. PLoS One 2017;12:e0189232.
29. Wijndaele K, Beunen G, Duvigneaud N, Matton L, Duquet W, Thomis M, et al. A continuous metabolic syndrome risk score: utility for epidemiological analyses. Diabetes Care 2006;29:2329.
30. Paulmichl K, Hatunic M, Højlund K, Jotic A, Krebs M, Mitrakou A, et al. Modification and validation of the Triglyceride-to–HDL cholesterol ratio as a surrogate of insulin sensitivity in White juveniles and adults without diabetes mellitus: the single point insulin sensitivity estimator (SPISE). Clin Chem 2016;62:1211-9.
31. Bedogni G, Bellentani S, Miglioli L, Masutti F, Passalacqua M, Castiglione A, et al. The Fatty Liver Index: a simple and accurate predictor of hepatic steatosis in the general population. BMC Gastroenterol 2006;6:33.
32. Lee JH, Kim D, Kim HJ, Lee CH, Yang JI, Kim W, et al. Hepatic steatosis index: a simple screening tool reflecting nonalcoholic fatty liver disease. Dig Liver Dis 2010;42:503-8.
33. Lee YJ, Seo MY, Kim SH, Park MJ. Validity of the pediatric simple metabolic syndrome score. Obes Res Clin Pract 2020; 14:508-13.
34. Okosun IS, Lyn R, Davis-Smith M, Eriksen M, Seale P. Validity of a continuous metabolic risk score as an index for modeling metabolic syndrome in adolescents. Ann Epidemiol 2010;20:843-51.
35. Khazdouz M, Hasani M, Mehranfar S, Ejtahed HS, Djalalinia S, Mahdavi Gorabi A, et al. Validity of continuous metabolic syndrome score for predicting metabolic syndrome; a systematic review and meta-analysis. J Diabetes Metab Disord 2021;20:497-510.
36. Sumner AE, Finley KB, Genovese DJ, Criqui MH, Boston RC. Fasting triglyceride and the triglyceride-HDL cholesterol ratio are not markers of insulin resistance in African Americans. Arch Intern Med 2005;165:1395-400.
37. Correa-Burrows P, Blanco E, Gahagan S, Burrows R. Validity assessment of the singlepoint insulin sensitivity estimator (SPISE) for diagnosis of cardiometabolic risk in post pubertal Hispanic adolescents. Sci Rep Sci Rep 2020;10:14399.
38. Arshad T, Paik JM, Biswas R, Alqahtani SA, Henry L, Younossi ZM. Nonalcoholic fatty liver disease prevalence trends among adolescents and young adults in the United States, 2007-2016. Hepatol Commun 2021;5:1676-88.
39. Stein R, Koutny F, Riedel J, Dörr N, Meyer K, Colombo M, et al. Single point insulin sensitivity estimator (SPISE) as a prognostic marker for emerging dysglycemia in children with overweight or obesity. Metabolites 2023;13:100.
40. Dudi P, Goyal B, Saxena V, Rabari K, Mirza AA, Naithani M, et al. Single point insulin sensitivity estimator as an index for insulin sensitivity for metabolic syndrome: a study in North Indian population. J Lab Physicians 2019;11:244-8.
41. Koskinen J, Magnussen CG, Sinaiko A, Woo J, Urbina E, Jacobs DR Jr, et al. Childhood age and associations between childhood metabolic syndrome and adult risk for metabolic syndrome, type 2 diabetes mellitus and carotid intima media thickness: the International Childhood Cardiovascular Cohort Consortium. J Am Heart Assoc 2017;6:e005632.
42. Choi EJ, Lee HA, Park B, Park B, Kim HS, Hong YS, et al. Trajectory patterns for continuous metabolic syndrome score in childhood and the cardiovascular risk in adolescence. Sci Rep 2021;11:22564.
43. Fernandes DM, Pantangi V, Azam M, Salomao M, Luga AC, Lefkowitch JH, et al. Pediatric nonalcoholic fatty liver disease in New York City: an autopsy study. J Pediatr 2018;200:174-80.
44. Córdoba-Rodríguez DP, Iglesia I, Gomez-Bruton A, Rodríguez G, Casajús JA, Morales-Devia H, et al. Fat-free/lean body mass in children with insulin resistance or metabolic syndrome: a systematic review and meta-analysis. BMC Pediatr 2022;22:58.
45. Bosy-Westphal A, Müller MJ. Diagnosis of obesity based on body composition-associated health risks-Time for a change in paradigm. Obes Rev 2021;22 Suppl 2:e13190.
46. Han SS, Kim KW, Kim KI, Na KY, Chae DW, Kim S, et al. Lean mass index: a better predictor of mortality than body mass index in elderly Asians. J Am Geriatr Soc 2010;58:312-7.
47. Wiklund P, Törmäkangas T, Shi Y, Wu N, Vainionpää A, Alen M, et al. Normal-weight obesity and cardiometabolic risk: A 7-year longitudinal study in girls from prepuberty to early adulthood. Obesity (Silver Spring) 2017;25:1077-82.
48. Musálek M, Pařízková J, Godina E, Bondareva E, Kokštejn J, Jírovec J, et al. Poor skeletal robustness on lower extremities and weak lean mass development on upper arm and calf: normal weight obesity in middle-school-aged children (9 to 12). Front Pediatr 2018;6:371.
49. Gao L, Cheng H, Yan Y, Liu J, Shan X, Wang X, et al. The associations of muscle mass with glucose and lipid metabolism are influenced by body fat accumulation in children and adolescents. Front Endocrinol (Lausanne) 2022;13:976998.
50. Kang Y, Park S, Kim S, Koh H. Handgrip strength among Korean adolescents with metabolic syndrome in 2014–2015. J Clin Densitom 2020;23:271-7.
51. Gontarev S, Jakimovski M, Georgiev G. Using relative handgrip strength to identify children at risk of sarcopenic obesity. Nutr Hosp 2020;34:490-6.
52. Rush EC, Coppinger T, Jalili-Moghaddam S, Tautolo ES, Plank LD. Relationships between physical function, body composition and metabolic health in Pacific Island youth. PLoS One 2022;17:e0260203.
53. Jung HW, Lee J, Kim J. Handgrip strength is associated with

metabolic syndrome and insulin resistance in children and adolescents: analysis of Korea National Health and Nutrition Examination Survey 2014-2018. J Obes Metab Syndr 2022; 31:334-44.
54. Chen F, Liu J, Hou D, Li T, Chen Y, Liao Z, et al. The relationship between fat mass percentage and glucose metabolism in children and adolescents: a systematic review and meta-analysis. Nutrients 2022;14:2272.
55. Bush H, Golabi P, Younossi ZM. Pediatric non-alcoholic fatty liver disease. Children (Basel) 2017;4:48.
56. Pacifico L, Perla FM, Andreoli G, Grieco R, Pierimarchi P, Chiesa C. Nonalcoholic fatty liver disease is associated with low skeletal muscle mass in overweight/obese youths. Front Pediatr 2020;8:158.
57. Salton N, Kern S, Interator H, Lopez A, Moran-Lev H, Lebenthal Y, et al. Muscle-to-fat ratio for predicting metabolic syndrome components in children with overweight and obesity. Child Obes 2022;18:132-42.
58. Wu AJ, Aris IM, Rifas-Shiman SL, Oken E, Taveras EM, Chavarro JE, et al. Associations of midchildhood to early adolescence central adiposity gain with cardiometabolic health in early adolescence. Obesity (Silver Spring) 2021;29:1882-91.
59. Park H, Jun S, Lee HA, Kim HS, Hong YS, Park H. The effect of childhood obesity or sarcopenic obesity on metabolic syndrome risk in adolescence: the Ewha Birth and Growth Study. Metabolites 2023;13:133.
60. Zembura M, Matusik P. Sarcopenic obesity in children and adolescents: a systematic review. Front Endocrinol (Lausanne) 2022;13:914740.
61. Kim K, Hong S, Kim EY. Reference values of skeletal muscle mass for Korean children and adolescents using data from the Korean National Health and Nutrition Examination Survey 2009-2011. PLoS One 2016;11:e0153383.
62. McCarthy HD, Samani-Radia D, Jebb SA, Prentice AM. Skeletal muscle mass reference curves for children and adolescents. Pediatr Obes 2014;9:249-59.
63. Steffl M, Chrudimsky J, Tufano JJ. Using relative handgrip strength to identify children at risk of sarcopenic obesity. PLoS One 2017;12:e0177006.
64. Moon JH, Kong MH, Kim HJ. Low muscle mass and depressed mood in Korean adolescents: a cross-sectional analysis of the fourth and fifth Korea National Health and Nutrition Examination Surveys. J Korean Med Sci 2018;33:e320.
65. Gätjens I, Schmidt SCE, Plachta-Danielzik S, Bosy-Westphal A, Müller MJ. Body composition characteristics of a load-capacity model: age-dependent and sex-specific percentiles in 5- to 17-year-old children. Obes Facts 2021;14:593-603.
66. Sack C, Ferrari N, Friesen D, Haas F, Klaudius M, Schmidt L, et al. Health risks of sarcopenic obesity in overweight children and adolescents: data from the CHILT III Programme (Cologne). J Clin Med 2022;11:277.
67. Videira-Silva A, Fonseca H. Skeletal muscle and metabolic risk in overweight adolescents. an indicator of premature sarcopenic obesity. Int J Health Sci 2017;7:34-43.
68. Holtrup B, Church CD, Berry R, Colman L, Jeffery E, Bober J, et al. Puberty is an important developmental period for the establishment of adipose tissue mass and metabolic homeostasis. Adipocyte 2017;6:224-33.
69. Shin DW, Cho JH, Park JH, Cho BL. National General Health Screening Program in Korea: history, current status, and future direction: a scoping review. Precis Future Med 2022;6:9-31.
70. Eun BL, Chung HJ. Overview of the National Health Screening Program for infant and children. Korean Med Assoc 2008;51:74-83.
71. Kang SY, Seo MY, Kim SH, Park MJ. Changes in lifestyle and obesity during the COVID-19 pandemic in Korean adolescents: based on the Korea Youth Risk Behavior Survey 2019 and 2020. Ann Pediatr Endocrinol Metab 2022;27:281-8.
72. Ip EH, Marshall SA, Saldana S, Skelton JA, Suerken CK, Arcury TA, et al. Determinants of adiposity rebound timing in children. J Pediatr 2017;184:151-6.
73. Kang MJ. The adiposity rebound in the 21st century children: meaning for what? Korean J Pediatr 2018;61:375-80.
74. Skinner AC, Staiano AE, Armstrong SC, Barkin SL, Hassink SG, Moore JE, et al. Appraisal of clinical care practices for child obesity treatment. Part I: interventions. Pediatrics 2023;151: e2022060642.
75. Skinner AC, Perrin EM, Moss LA, Skelton JA. Cardiometabolic risks and severity of obesity in children and young adults. N Engl J Med 2015;373:1307-17.
76. Hampl SE, Hassink SG, Skinner AC, Armstrong SC, Barlow SE, Bolling CF, et al. Clinical practice guideline for the evaluation and treatment of children and adolescents with obesity. Pediatrics 2023;151:e2022060640.
77. Quattrin T, Roemmich JN, Paluch R, Yu J, Epstein LH, Ecker MA. Efficacy of family-based weight control program for preschool children in primary care. Pediatrics 2012;130:660-6.
78. Stark LJ, Spear Filigno S, Bolling C, Ratcliff MB, Kichler JC, Robson SM, et al. Clinic and home-based behavioral intervention for obesity in preschoolers: a randomized trial. J Pediatr 2018;192:115-21.e1.

How to cite this article: Park H, Choi JE, Jun S, Lee H, Kim HS, et al. Metabolic complications of obesity in children and adolescents. Clin Exp Pediatr 2024;67:347-55.