Original article

The role of waist-to-hip ratio for predicting nonalcoholic fatty liver disease among Korean pediatric patients

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Abstract. *Background:* The incidence of pediatric nonalcoholic fatty liver disease (NAFLD) has been increasing along with the explosive rise in childhood obesity since the COVID-19 pandemic. Auxiliary markers are needed to more easily screen for and detect NAFLD. This study investigated the potential of waist-to-hip ratio (WHR) as an early diagnostic tool in Korean pediatric patients with NAFLD. *Methods:* This study included 781 children aged 10–19 years who visited the Bundang CHA Pediatric Gastrointestinal Clinic with signs of obesity, weight gain, or elevated liver function test results between January 2022 and December 2023. Anthropometric measurements included height, weight, waist circumference, and hip circumference. Diagnosis of NAFLD was based on alanine aminotransferase levels and liver ultrasonography. *Results:* Among participants (460 boys and 321 girls; mean age, 11.40 years), 309 (39.6%) were diagnosed with NAFLD. Boys had a higher frequency of NAFLD (51.1% vs. 23.1% in girls). The WHR cutoff values were 0.825 for boys and 0.875 for girls using receiver operating characteristics curves, both of which were significantly associated with NAFLD. More patients with NAFLD had a WHR above the cutoff value than a BMI percentile >95, indicating the potential importance of WHR for assessing NAFLD risk in children and adolescents. *Conclusions:* Our data suggest that WHR cutoff values may represent more effective indicators than BMI percentile cutoff values for screening the risk of NAFLD in pediatric patients. Further research is warranted to fully understand the significance of these results for the screening and management of NAFLD in pediatric populations. (www.actabiomedica.it)

Key words: waist-to-hip ratio, nonalcoholic fatty liver disease, pediatric patients, obesity

Introduction

Nonalcoholic fatty liver disease (NAFLD) represents one of the most common complications of childhood obesity. The global prevalence of NAFLD is approximately one-third, with increasing rates over the past three decades (1, 2). With the increasing prevalence of childhood obesity worldwide, the frequency of NAFLD is also increasing in both developed and developing countries (2, 3). Particularly during the recent coronavirus disease 2019 (COVID-19) pandemic (2020–2022), risk factors such as reduced physical activity, imbalanced and increased calorie intake, psychological anxiety, and stress have led to a rapid increase in obesity-related complications such as NAFLD, metabolic syndrome, and diabetes mellitus (4, 5). The incidence of pediatric NAFLD is increasing more rapidly than ever before, requiring greater attention and effort from a public health perspective (2, 6). Therefore, it has become important not only to prevent obesity during childhood and adolescence, but also to actively intervene early in identified cases, to prevent the onset of NAFLD and quickly return patients to a healthy state. Appropriate screening and thorough evaluation, as well as related treatment programs and a team of specialized medical professionals to support them, are all highly beneficial for pediatric NAFLD. Currently, the most widely used indicator for evaluating obesity is body mass index (BMI), which generally considers 18.5–24.9 kg/m^2 to be a healthy range (7). However, during childhood and adolescence, as growth and puberty progress, patterns vary according to sex and age. Therefore, BMI percentiles for age and sex can be considered a more accurate indicator, with obesity defined as being at or above the 95th percentile (8). To conduct more detailed assessments, specific indicators reflecting muscle mass, such as muscle-to-body fat ratio (MFR) obtained through body composition analysis, are now being increasingly used over BMI—which only reflects height and weight (9). However, special measuring equipment is required for this, and high costs are involved, making it difficult to apply widely for screening the general pediatric population. Similarly to height and weight, waist and hip circumference also represent indicators that can be measured relatively easily without special equipment. They can also be used to evaluate the amount of abdominal fat that is actually associated with obesity and its complications (10). When evaluating patients with obesity, waist circumference is a key measurement that must be taken, particularly because it is included in the diagnostic criteria for metabolic syndrome (11). When measuring both waist circumference and hip circumference, it is important for the measurer to maintain precise positioning and a consistent measurement technique. As a result, these measurements have been somewhat underutilized compared to other anthropometric parameters. Several studies over in the years have reported on the association between the waist-to-height ratio (WHtR) and obesity, as well as NAFLD, in pediatric populations (12-14). Furthermore, the relationship between waist circumference and hip circumference, or WHR has also shown promising potential for clinical applications related to assessing obesity and its related complications (15). However, data on the association between WHR and NAFLD in children and adolescents, as well as its diagnostic utility, has not yet been reported. In this study, we evaluated the potential of WHR as an appropriate indicator for the early diagnosis of NAFLD in Korean pediatric patients, and intend to use it in future screenings and evaluations.

Methods and Materials

Study population

This observational study was conducted between January 2022 and December 2023. The subjects were children and adolescents aged 10–19 years who visited the Bundang CHA Pediatric Gastrointestinal Clinic with signs of obesity, weight gain, or because of elevated liver function test results. Those with recent acute infectious episodes or chronic conditions that could have affected their liver enzyme levels, histories of medication use or alcohol consumption, positive serological markers for hepatitis B or C virus, or had known autoimmune hepatitis, immunocompromised statuses, or malignancies were excluded.

Anthropometric measurements

Anthropometric measurements were conducted with the children wearing light clothing and no shoes. One trained examiner measured height and weight to the nearest 0.5 cm and 0.5 kg, respectively, using an automated height–weight scale (DS-102; Dong Sahn Jenix, Seoul, Korea). BMI was calculated based on the measured weights and heights of the subjects, and the data were used to investigate the subjects' BMI percentiles according to age and sex, by comparing them to the 2017 Korean National Growth Charts for children and adolescent. Obesity was then diagnosed based on BMI levels above the 95th percentile for children of the same age and sex (16). Waist circumference was measured on the skin, midway between the lowest rib and the iliac crest at the end of expiration, and was recorded to the nearest 0.1 cm. Hip circumference measurements were taken around the widest portion of the buttocks, based on standard protocol, and WHR was calculated (14, 15).

NAFLD and evaluation: laboratory measurements and liver ultrasonography

The diagnostic criteria for pediatric NAFLD are defined as a serum alanine aminotransferase (ALT) level of >22 IU/L in girls and >25 IU/L in on blood tests, with normal levels of biomarkers related to other liver diseases and the presence of fatty liver on liver ultrasonography in the absence of any other structural abnormalities (17, 18). Blood samples were collected from the antecubital vein after 8 h of overnight fasting. Serum ALT, aspartate aminotransferase, gamma-glutamyltransferase, fasting glucose, total cholesterol, triglyceride, high-density lipoprotein cholesterol (HDL), and low-density lipoprotein cholesterol levels were measured in all of the subjects. Hepatitis B surface antigen and antibodies against the hepatitis C virus were also measured. Blood samples were collected in separator tubes containing silica and a gel clot (Becton, Dickinson and Company, Franklin Lakes, NJ, USA), centrifuged, and analyzed within two hours. All laboratory tests were performed using standard methods. Children with a final diagnosis of NAFLD on abdominal sonography were selected as the study subjects, all of whom had available laboratory tests and abdominal ultrasonography data.

Statistical analysis

Differences in continuous variables were investigated using the independent-samples Student's t-test, and differences in categorical ones were evaluated using Chi-squared and Fisher's exact tests. The predictability of WHR in boys and girls was determined using receiver-operating characteristic (ROC) curves. The Youden index was used to identify the optimal cutoff value for WHR, prioritizing high sensitivity (maximum sensitivity, +1; specificity, −1) (19). Multivariate and multiple logistic regression analyses were conducted to evaluate the correlations between WHR, biochemical markers, and ALT levels, adjusting for age; as well as to examine the relationships among WHR, biochemical markers, and NAFLD. All statistical analyses were performed using SPSS software versions 24 and 25 (IBM Corp., Armonk, NY, USA). Statistical significance was set at $P < 0.05$.

Ethical considerations

Written informed consent was obtained from the parents of all of the subjects prior to their enrolment in the study. This study was approved by the institutional review board of CHA University (approval no.: 2023-03-001-004).

Results

A total of 781 participants (460 boys and 321 girls; mean age, 11.40 years) participated in this study. A total of 533 (68.2%) were classified as obese (BMI percentile >95), 309 (39.6%) were diagnosed with NAFLD, and 64 (8.2%) had metabolic syndrome. The baseline characteristics of the participants, according to sex, are presented in Table 1. NAFLD showed a significantly higher frequency in the boys vs. the girls, and there was no significant difference in obesity prevalence between the sexes. However, metabolic syndrome was significantly more prevalent in the girls. According to these sex-based differences, the association between variables such as age, obesity, WHR, and NAFLD was analyzed separately between the boys and the girls.

NAFLD in boys and girls

We compared mean age, WHR, BMI, MFR, and biochemical markers according to the presence of NAFLD in both the boys and the girls, using independent-samples Student's t-tests. In the NAFLD group, compared to the non-NAFLD one, the mean age of the boys with NAFLD was 0.36 years higher (11.65±1.98 vs. 11.29±1.64, $P = 0.035$), and the WHR and mean BMI were significantly higher in the NAFLD group compared to the non-NAFLD one.

Table 1. Subject characteristics in the total participants according to sex

	Total (n=781)	Boys (n=460)	Girls (n=321)	*P*
Mean age (years)	11.43 ± 1.90	11.47 ± 1.83	11.36 ± 2.00	0.424
Mean WHR	0.866 ± 0.07	0.867 ± 0.07	0.865 ± 0.07	0.675
Mean BMI	25.63 ± 4.32	26.03 ± 4.42	25.06 ± 4.10	0.002
Mean ALT (IU/L)	35.65 ± 38.19	42.16 ± 41.79	26.39 ± 30.10	<0.001
NAFLD (n, %)	309 (39.6%)	235 (51.1%)	74 (23.1%)	<0.001
BMI >95percentile (n, %)	533 (68.2%)	308 (67%)	225 (70.3%)	0.211

Abbreviations: WHR, waist-hip ratio; BMI, body mass index; ALT, alanine aminotransferase; NAFLD, nonalcoholic fatty liver disease.

Although the number of participants with NAFLD was lower for the girls than the boys, the relationship was similar (P<0.001). For both the boys and girls, the children with NAFLD had a higher mean age compared to those without the condition. These children also had higher WHR and BMI values. In both the boys and girls, the mean ALT values for those with NAFLD were 56.38 and 65.60 IU/L, respectively. These values were significantly higher than those of the ones without NAFLD, who had values of 27.11 and 14.60 IU/L, respectively (P<0.001). In those with NAFLD, mean TG values were also higher—at 172.28 mg/dL for the boys and 153.79 mg/dL for the girls, compared to 169.75 and 111.58, respectively, for the boys and girls without NAFLD (P<0.001). Conversely, their HDL readings were significantly lower, as the boys and girls with NAFLD showed mean levels of 48.06 and 46.64 mg/dL, respectively, compared to the 52.05 and 50.73 mg/dL values, respectively, in the boys and girls without NAFLD (P<0.001). We then analyzed the association between ALT, WHR, and other biochemical markers via multivariate regression analysis adjusted for age. In the boys, WHR (t=5.009, P<0.001), and TG (t=3.171, P<0.001) were positively correlated; whereas WHR (t=6.129, P<0.001) and glucose levels (t=2.416, P = 0.016) showed a positive correlation in the girls.

WHR cutoff value for NAFLD

In both the boys and girls, the cutoff WHR values indicating NAFLD were determined using ROC curves (Figure 1). In the boys, the ROC cutoff value for WHR was 0.825 (area, 0.788; sensitivity, 0.885; specificity, 0.538); whereas in the girls, the WHR cutoff value was 0.875 (area, 0.826; sensitivity, 0.747; specificity, 0.769).

We compared the associations between these WHR cutoff values, as well as BMI percentiles, with NAFLD. The participants were divided into subgroups based on the WHR and BMI percentile cutoff values for each sex, and the distributions of the subjects were analyzed using the Chi-squared test (Figure 2). In both the boys and girls, the WHR and BMI percentile cutoff values showed statistically significant associations with NAFLD, for both the children and the adolescents. However, among the pediatric patients with NAFLD, a higher percents had WHR values above the cutoff than those with BMI percentiles above the cutoff. The percents of patients with NAFLD who had WHR values below the cutoff was significantly lower than the number with NAFLD whose BMI percentiles fell below the 95th. Additionally, the proportion of non-NAFLD boys below the WHR cutoff (53.8%) was higher compared to those below the BMI percentile cutoff (50.2%). Similarly, in girls, the proportion of non-NAFLD individuals below the WHR cutoff (36.6%) was slightly lower than those below the BMI percentile cutoff (35.4%).

Figure 3 presents the differences in the mean concentrations of biochemical markers according to WHR cutoff values in both the boys and girls. In both sexes, the mean ALT, glucose, and TG values were significantly higher in the children with WHR values above the cutoff. Conversely, their mean HDL levels were significantly lower.

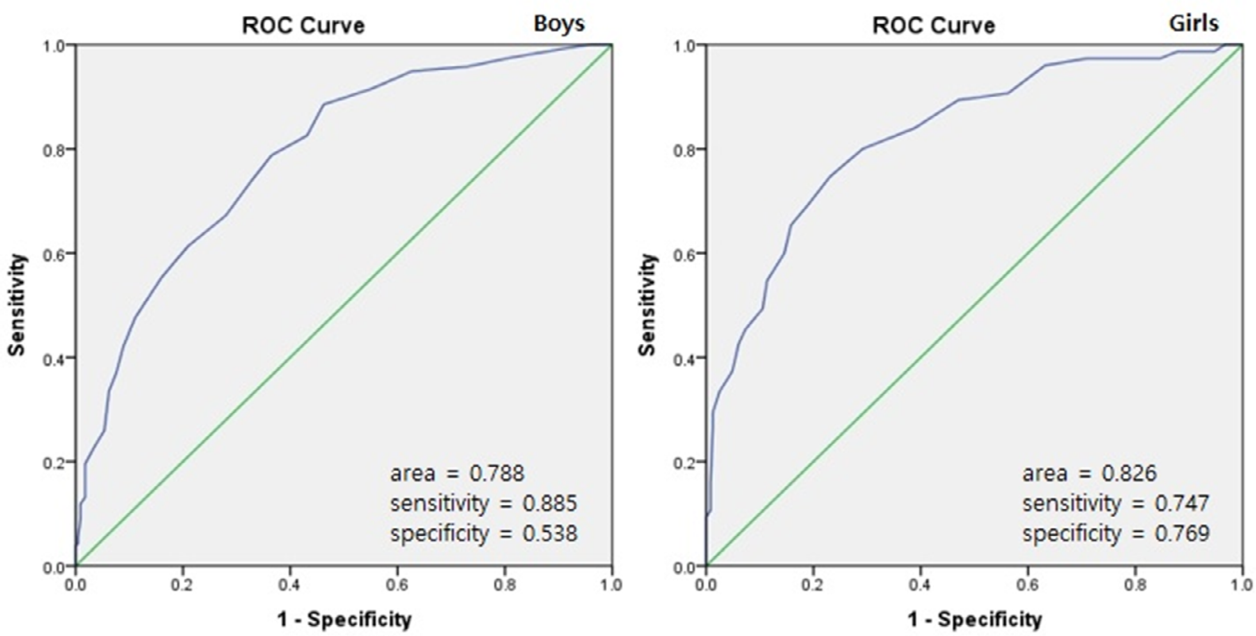

Figure 1. Receiving operating characteristics (ROC) curves for WHR in boys and girls.
Abbreviations: Receiving operating characteristics, ROC; WHR, waist-hip ratio.

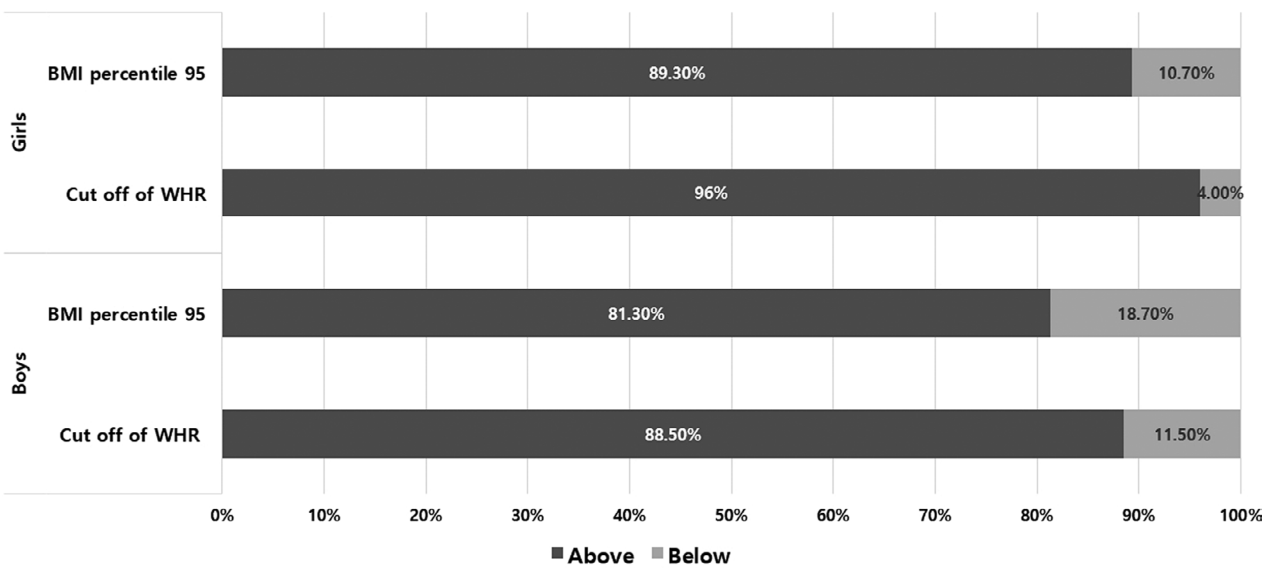

Figure 2. Comparison of ratio according to being above or below the WHR cutoff value and the 95th BMI percentile in children with NAFLD.
Abbreviations: WHR, waist-hip ratio; NAFLD, nonalcoholic fatty liver disease; BMI, body mass index; WHR cutoff values: 0.825 (boys); 0.875 (girls).

Discussion

This study aimed to investigate indicators that might prove useful for identifying and diagnosing NAFLD in Korean children and adolescents, with a particular focus on the clinical utility of WHR. Owing to differences in the clinical characteristics related to obesity between boys and girls, separate analyses

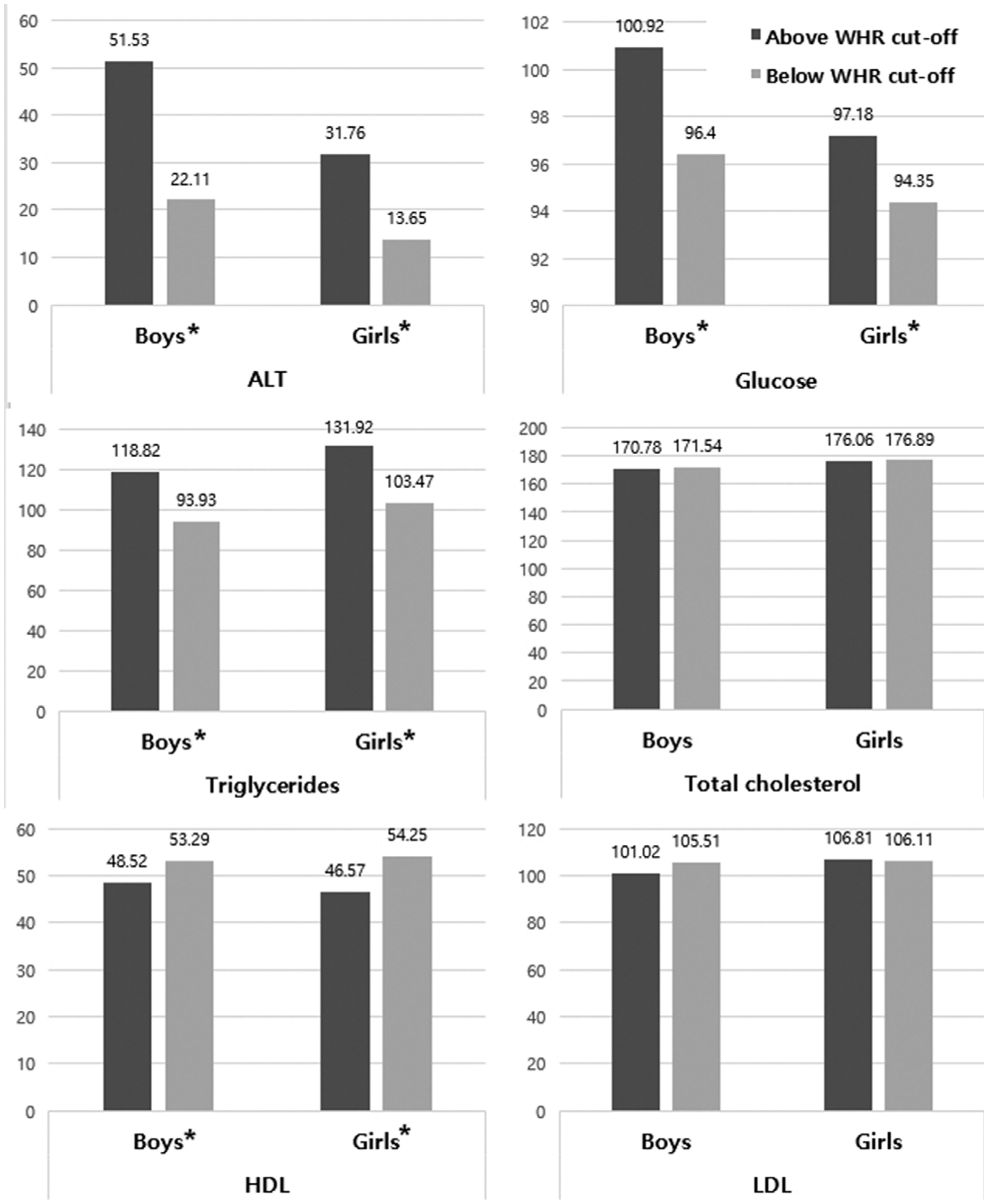

Figure 3. Differences in mean concentrations of biochemical markers according to whether the subjects were above or below the WHR cutoff value for their sex. (**p*<0.05)

Abbreviations: WHR, waist-hip ratio; ALT, alanine aminotransferase; HDL, high-density lipoprotein; LDL, low-density lipoprotein

were conducted based on sex. Our findings suggest that WHR, along with other factors such as age and metabolic markers, may play a significant role in the development and assessment of NAFLD in children and adolescents, with potential sex-specific differences present in terms of risk factors and associations. NAFLD is characterized by the accumulation of fat in the livers of individuals who do not consume excessive alcohol. This can lead to liver inflammation, fibrosis, cirrhosis, and liver failure. NAFLD is also closely associated with obesity, insulin resistance, diabetes, and metabolic syndrome (18, 20, 21). The prevalence of obesity among the pediatric population is increasing globally—and particularly in South Korea—owing to the adoption of Western-style diets and lack of exercise. This increase has, in turn, contributed to a rising incidence of NAFLD (21, 22). Over the past two years, during the recent COVID-19 pandemic, there has been a sharp increase in the prevalence of NAFLD, insulin resistance, and type 2 diabetes among Korean children and adolescents, with a more significant trend being observed in boys (4, 5). Although WHR, along with BMI, is considered a key indicator in metabolic-related diseases such as obesity, diabetes, or NAFLD, it has not been widely used compared to BMI—which can be calculated using only height and weight. This is because WHR requires precise measurements that limit its widespread use, despite its clinical utility. The pathophysiology of metabolic diseases such as NAFLD is more closely associated with central obesity than with overall body weight. Consequently, there is a growing need for anthropometric predictors that accurately reflect visceral adiposity rather than total body weight. In this clinical context, previous studies have identified WHR, WHtR, muscle mass, and MFR as important indicators (9, 12-15, 21, 23, 24). However, limited research has been conducted in pediatric populations, owing to the challenges and costs associated with measuring indicators of muscle mass. This is because WHR requires precise measurements that limit its widespread use, despite its clinical utility. The pathophysiology of metabolic diseases such as NAFLD is more closely associated with central obesity than with overall body weight. Consequently, there is a growing need for anthropometric predictors that accurately reflect visceral adiposity rather than total body weight. In this clinical context, previous studies have identified WHR, WHtR, muscle mass, and MFR as important indicators (27, 28) Although obesity-associated metabolic diseases show significant differences in prevalence and risk according to race or ethnicity, previous studies on WHR in children and adolescents in Asia, including South Korea, have been limited in both number and scale.

In this study, we reassessed the relationship between WHR and NAFLD by measuring WHR in 781 Korean pediatric patients at risk for obesity, and compared its association with biochemical parameters. The boys with NAFLD had higher mean age, WHR, and BMI values, as well as lower mean fasting glucose levels, compared to those without NAFLD. Both sexes showed a significant association between WHR, ALT, and NAFLD in our multivariate regression analysis. In terms of NAFLD screening, we calculated the WHR cutoff value using ROC curve analysis, and evaluated its clinical utility. The WHR cutoff values for boys and girls were 0.825 (area, 0.788; sensitivity, 0.885; specificity, 0.538) and 0.825 (area, 0.826; sensitivity, 0.747; specificity, 0.769), respectively. These values were significantly associated with NAFLD in both sexes. Compared to previous studies, the cutoff values for WHR in this study were higher (23). This may have been due to the small number of non-obese participants in our study population. Notably, although the prevalence of NAFLD was higher in the boys than the girls, the WHR cutoff value for the girls was higher than that for the boys. This pattern has also been observed in previous related studies. To evaluate whether WHR cutoff values can be used to screen for NAFLD, we examined the association between the WHR and BMI percentile cutoff values according to age and sex with NAFLD in both sexes. Both boys and girls showed statistically significant associations between the WHR and BMI percentile cutoff values and NAFLD, among both the children and the adolescents. Among our cohort of pediatric patients with NAFLD, we found a higher proportion with WHR values above the WHR cutoff value than those with BMI percentiles above that respective cutoff value. Additionally, the number of patients with NAFLD who had WHR values below the WHR cutoff was significantly lower than that of the patients with NAFLD whose BMI percentiles were below the 95th percentile (boys, 27 vs. 44; girls, 3 vs. 8). Screening for NAFLD appeared to be more efficient when the WHR cutoff value was used, over the BMI percentile one, to define obesity. Furthermore, the WHR cutoff value was used alongside both indicators, only 19 patients with NAFLD (16 boys and 3 girls) were missed by the screening process. Although WHR may not completely replace BMI percentile in the screening of pediatric NAFLD, it can be useful in identifying at-risk individuals and reducing missed cases that occur when using BMI percentile alone as a reference and in conducting more thorough screenings. For instance, children classified as overweight but with a high WHR may warrant further evaluation for NAFLD and associated metabolic diseases. Measuring and utilizing WHR in pediatric populations can help detect NAFLD earlier or reduce the incidence of NAFLD through early intervention. Additionally, monitoring WHR in routine screening may help determine whether to proceed with invasive or costly examinations. As a result, this approach could reduce the risk of complications associated with NAFLD, such as hepatic fibrosis or cirrhosis, as well as the risk of other accompanying metabolic diseases, thereby decreasing the social costs associated with these conditions. This study has several limitations. First, it does not adequately consider the fact that WHR can be influenced by growth patterns and pubertal development. In the case of Korean children and adolescents, the incidence of obesity increases around puberty, which means that WHR is likely to increase with age for both sexes (29). In the future, it will be necessary to include relevant data and reference values in the process of developing and updating the Korean growth chart. Next, although the sample size of our study was not small, larger-scale studies that include healthy pediatric controls, conducted in South Korea as well as in other regions of Asia, are warranted to determine a more accurate WHR cutoff value for diagnosing NAFLD. The difference in WHR cutoff values between this study and previous related ones is considered to be due to the ethnic characteristics of Asians, as well as the particular limitations of this study. However, Asian ethnic groups show a higher prevalence of fatty liver compared to other regions, and particularly in Korea, there has been an explosive increase in the prevalence of obesity and NAFLD in recent years (1, 30). Therefore, instead of generalizing WHR cutoff values across diverse ethnic groups, it is essential to conduct targeted studies focused on children and adolescents within each specific ethnic group. Further research is warranted to fully understand the significance of these results in terms of screening and managing NAFLD in pediatric and adolescent patient populations.

Conclusion

WHR represents a valuable indicator that complements BMI percentile for age and sex when screening for pediatric NAFLD. Our findings suggest that WHR, along with other factors such as age and metabolic markers, may play a significant role in the development and assessment of NAFLD in children and adolescents, with potential sex-specific differences in risk factors and associations. It is therefore recommended that clinicians measure both waist and hip circumferences, in addition to height and weight, during physical examinations of children and adolescents. Additionally, there is a need for longitudinal studies to validate the WHR cutoff value in diverse pediatric populations, ensuring its effectiveness and applicability across different demographic groups.

Ethic Approval: This study was approved by the institutional review board of CHA University (approval no.: 2023-03-001-004).

Conflict of Interest: Each author declares that he or she has no commercial associations (e.g., consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

Authors Contribution: YJC conducted the main research, organized and statistically analyzed the data and drafte the manuscript. YWK, SYC, YML, IHY, and THK assisted with data collection and provided significant insights into the statistical analysis. SJ collected the data, supervised the main research and approved the manuscript for publication. All authors discussed the results and contributed to the final manuscript.

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