Waist to height ratio: a simple screening tool for nonalcoholic fatty liver disease in obese children

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Simple predictors are needed for the screening of nonalcoholic fatty liver disease (NAFLD) in obese children. We aimed to assess the role of anthropometric parameters in the prediction of NAFLD. Three hundred and thirty two obese children (152 male, 180 female) aged 4.6-17.0 years were included in this study. Weight, height, waist (WC), and hip circumference were measured. Body mass index (BMI), waist-hip-ratio (WHR), and waist-height-ratio (WHtR) were calculated. Obesity was defined as BMI for age and sex ≥ 95th percentile. NAFLD was diagnosed using ultrasonography (US). NAFLD was present in 60.8% of obese children. Fatty liver prevalence differed significantly by gender and puberty (55.0% of girls vs 67.7% of boys, and 28.7% in prepubertal vs 71.3% in pubertal children; p<0.05). Significantly higher BMI, BMI standard deviation score (SDS), WC, and WHtR were found in obese children with NAFLD compared to obese children without NAFLD (p<0.05). Only WHtR was found to be an independent predictor for NAFLD in a logistic regression analysis (p<0.001, B:1.096, 95% CI 1.047–1.148). Fatty liver is common among obese children, particularly in obese boys. WHtR is a simple and easy index for predicting of NAFLD in obese children and can be used for mass screening in public health.

Key words: nonalcoholic fatty liver disease, obesity, anthropometry, mass screening tool.

Nonalcoholic fatty liver disease (NAFLD) is characterized by the accumulation of fat in the hepatocytes and is the one of the metabolic disorders associated with obesity[1]. NAFLD is the hepatic manifestation of metabolic syndrome[2]. Increased recognition of this form of liver disease parallels the dramatic increase in childhood and adolescent obesity over the past two decades[3]. Although simple steatosis has a benign prognosis, non-alcoholic steatohepatitis (NASH) with advanced histopathology may progress to cirrhosis[4,5]. Approximately 3–5% of patients with hepatic steatosis develop NASH, which may progress to end-stage liver disease or hepatocellular carcinoma[6]. Therefore, early recognition of NAFLD is important for earlier interventions, particularly in obese children.

Liver biopsy is the gold-standard method to diagnose NAFLD and hepatic fibrosis[7]. However, it must be considered a final step of differential diagnosis and is not applicable to every obese child due to its invasive nature. The European Society for Paediatric Gastroenterology, Hepatology and Nutrition recommends that abdominal ultrasounds and hepatic function tests be performed for all obese children older than 3 years to determine the presence of NAFLD[8]. A great number of noninvasive diagnostic tests have been proposed and serum alanine aminotranspherase (ALT) is the most used laboratory parameter in the evaluation of NAFLD for which elevated levels have been proposed as a marker of NAFLD in obese children[9,10].

The screening of all obese children for the presence of NAFLD with abdominal ultrasounds may not be a cost-effective approach, and alternative non-invasive markers for prediction

of NAFLD are needed. Anthropometric parameters, which are simply measured, may be predictors of metabolic syndrome in obese children[11]. The results of studies to date have emphasized that some anthropometric indices can be used to predict NAFLD. However, this issue is still controversial[12-14]. In this study, we aimed to assess the role of anthropometric parameters in the prediction of NAFLD and identify cutoff values for useful anthropometric indices in the prediction of NAFLD in obese children.

Material and Methods

Study design

Three hundred and thirty two obese children (152 male, 180 female) who visited pediatric endocrinology unit consecutively with a complaint of obesity were included in this study. The mean age of all patients was 11.94±2.65 years. Patients were excluded if the medical evaluation revealed additional diseases and/or if other diseases were already known. None of the patients were taking any medication, and none had a history of consumption of alcohol. The study was approved by the Scientific Ethics Committee of University. Informed written consent was obtained from the parents of all children who underwent radiological and biochemical investigation.

Protocol

Children admitted to the clinic underwent initial clinical and anthropometric examination, followed by B-mode US liver evaluation. Thyroid function tests, diurnal cortisol levels, and basal ACTH levels were assessed to exclude hypothyroidism and hypercortisolism. Individuals with suspected FLD using B-mode had a complete evaluation of iron status (serum iron, transferrin, and ferritin concentrations) and serology to exclude hemochromatosis and viral hepatitis (hepatitis B surface antigen, hepatitis B-C total antibody, antibody against hepatitis A virus and hepatitis C virus antibody immunoglobulin G).

Anthropometric Measurements and Definitions

Weight was measured to the nearest 0.1 kg using a balance beam scale, with overcoat and shoes off, and height was measured to the nearest 0.1 cm with a manual height board. The body mass index (BMI; kg/m^2) was used as an index of relative weight. Comparison of weight, height and BMI among children requires the use of standard deviation scores (SDS). SDS for height, BMI, and weight were calculated based on national growth charts to compare weight, height and BMI status of children[15]. Obesity was defined as BMI for age and sex ≥ 95th percentile[16]. Waist circumference (WC) was measured by a trained person to the nearest 0.1 cm at the midpoint between the bottom of the rib cage and the top of the iliac crest with the subjects standing, their weight equally distributed on both feet, their arms at their sides, and their heads facing straight forward. Hip circumference was measured around the widest portion of the buttocks. WHtR (waist-height-ratio) and waist/hip ratio was calculated by WC (cm)/height (cm) and WC (cm)/hip (cm), respectively.

Ultrasonographic Evaluation

B-mode sonographic examination was performed by the same radiologist (Siemens Sonoline G 50 / Italy with 3.5 MHz convex transducers). The presence or absence and the severity of fatty infiltration was graded using a scale from 0 to 3, indicating absent, mild, moderate, and severe hepatosteatosis, respectively, corresponding to increasing degrees of hepatic echogenicity with poorer visualization of the intrahepatic vessels and diaphragm[17].

Statistical Analysis

Statistical Packard for Social Sciences (SPSS) for Windows statistical software version 18.0 was used for all calculations. Data distribution was analyzed using the Kolmogorov-Smirnov test. Anthropometric parameters were compared by Student's t-test between two groups. Logistic regression models were used to predict the presence of NAFLD with anthropometric parameters. The sensitivity and specificity of anthropometric indices for suspected NALFD were calculated by receiver operating characteristic (ROC) curve analysis. The optimal cut-off point was determined using the Youden index. Performance was expressed as sensitivity, specificity. In all analyses, a p-value ≤ 0.05 was considered significant.

Results

Two hundred and two (60.8%) obese children were identified as having NAFLD using B-mode USG. NAFLD was diagnosed in 67.8% of

Table I. Anthropometric Characteristics of Obese Children with and without NAFLD

Anthropometric characteristics	Obese patients without NAFLD (n= 130)	Obese patients with NAFLD (n=202)	P -value
Age (years)	11.56 ± 2.74	12.14±2.61	0.059
Gender(male/female)	49/81	103/99	<0.05
Prepubertal/Pubertal	53/77	58/144	<0.05
Height SDS	0.54 ± 1.17	0.61±1.25	0.599
Weight SDS	2.71 ± 1.14	3.02±1.11	<0.05
BMI (kg/m^2)SDS	2.50±0.60	2.75±0.60	<0.001
Waist circumference (cm)	88.75±11.97	96.62±13.21	<0.001
Waist/hip ratio	0.92±0.05	0.94±0.06	<0.05
WHtR	0.59±0.05	0.62±0.06	<0.001

NAFLD: nonalcoholic fatty liver disease, SDS: standard deviation score, BMI: body mass index, WHtR:waist to height ratio

boys (103/152) and 55.0% of girls (99/ 180). The difference between the two genders was significant (p<0.05). The frequency of NAFLD was significantly higher in pubertal obese children (65.2%) compared to prepubertal obese children (52.3%) (p<0.05).

Anthropometric characteristics of obese children with and without NAFLD are presented in Table I. All of the anthropometric indices, including weight, weight SDS, BMI, BMI SDS, WC, WHR, WHtR except height SDS in obese children with NAFLD were significantly higher than those in obese children without NAFLD.

In the correlation analysis of antropometric indices, WHtR significantly correlated with weight, weight SDS, BMI, BMI SDS (r=0.405, r=0.428, r=0.634, r=0.648, p<0.001 respectively), but not correlated with age (r=0.10, p: 0.06).

A logistic regression model was done with the presence of NAFLD as a dependent variable and weight SDS, BMI SDS and waist-to-height ratio as independent variables. Other anthropometric indices were not included in this model. The model is shown in Table II. WHtR was found to be an independent predictor of the presence of NAFLD (p<0.001, B=1.096, 95% CI 1.047–1.148).

Receiver operating characteristic (ROC) curves were used to select possibly optimal measures and threesholds to detect NALFD. The diagnostic accuracy of NAFLD using the optimum cutoff values are shown in Table III. Highest sensitivity of WHtR with 92.0% was reached at a value of 0.50. At this value, PPV, NPV, and specificity were 60.52%, 52.38% and 12.79%, respectively. Despite it having the highest sensitivity, a value of 0.50 for WHtR has a very low specificity. The optimal cutoff value of WHtR and the sensitivity and specificity of estimation according to the Youden index for NAFLD was 0.62. At this value, PPV and NPV were 75.6% and 50.03%, respectively.

Discussion

In this study, we investigated whether anthropometric indices are markers for the

Table II. Independent Variables in Multiple Regression Analysis

Variable	B parameter estimation	Standard error	P- value	Exp (B) OR (95%Cl)
WHtR	0.092	0.23	0.000	1.096 (1.047-1.148)
BMI SDS	0.437	0.39	0.272	1.549(0.709-3.382)
Weight SDS	0.089	0.13	0.518	1.093(1.015-1.174)
Constant	-6.409	1.89	0.001	

WHtR:waist to height ratio, BMI: body mass index, SDS: standard deviation score

presence of fatty liver in obese children. It is found that obese children with NAFLD have significantly higher BMI SDS, weight SDS, WC, weight for height (W/H), and WHtR compared to obese children without NAFLD. In other words, obese children with NAFLD have significantly higher anthropometric indices with regard to obesity. WHtR was the only parameter that had a significant association with the presence of NAFLD in the logistic regression analysis.

The prevalence of NAFLD changes according to race and ethnicity and remains unknown due to the lack of population-based studies in children. Its prevalence among obese children has been found to be 12-80% in several studies around the world[18,19]. A high rate of fatty liver was found among our study group (60.8%) as reported previously in other populations[20]. In the present study, the prevalence of NAFLD increased with age. The prevalence was significantly higher in pubertal children, and in boys (67.8%) than in girls (55.0%). A similar result was obtained in a study that Akcam et al.[21] conducted. However, it was reported that the prevalence of NAFLD was unchanged among obese children in prepubertal, pubertal, or late pubertal stages in a longitudinal study[22].

Screening for the presence of NAFLD in obese children is important in primary prevention and for early intervention. Anthropometric indices such as WC, W/H, and WHtR have been proposed for metabolic syndrome prediction in obese children[22-24]. The results of previous studies showed waist circumference, waist-hip ratio, and WHtR in combination with other routinely available variables such as the homeostasis model assessment of insulin resistance (HOMA-IR), reduced physical activity, and alanine aminotransferase (ALT) might be used to identify obese children at the highest risk of NAFLD[12,13,23]. According to the results of Lin et al.[13], waist circumference is important in predicting NAFLD in obese children, but should be assessed together with glucose changes in an oral glucose-tolerance test. A higher waist circumference percentile was found in children who had been proven to have a fatty liver by biopsy. However, as in Lin's study, WC was a contributor together with other biochemical parameters for NAFLD prediction[23]. In the present study, WHtR was found to be the only independent predictor of the presence of NAFLD.

Consistent with our study, Maffeis and colleagues suggest that WHtR is significant in predicting NAFLD[23]. Maffeis et al.[24] proposed a prediction equation model for NALFD that included WHtR, ALT, adiponectin, and

Table III. The Diagnostic Value of WHtR with Suggested Cut-Offs in the Evaluation of Nonalcoholic Fatty Liver Disease in Obese Children

Waist /Height Ratio	Sensitivity (95%Cl)	Specificity (95%CI)
0.50	95.0 (90.8-97.4)	4.0 (1.4-9.1)
0.51	94.5 (90.2-97.1)	6.9 (3.4-13.1)
0.52	94.5 (90.2-97.19	6.9 (3.4-13.1)
0.53	91.5 (86.6-94.8)	9.2 (5.0-15.9)
0.54	90.0 (84.9-93.6)	13.0 (8.0-15.1)
0.55	87.1 (81.5-.91.2)	20.0 (13.7-28.1)
0.56	82.1 (76.0-87.0)	25.3 (18.3-33.9)
0.57	78.7 (72.2-84.0)	31.5 (23.8-40.3)
0.58	73.3 (66.5-79.1)	40.0 (31.6-48.9)
0.59	67.8 (60.8-74.10)	47.6 (38.92-56.5)
0.60	60.3 (53.2-57.1)	52.3 (43.4-61.07)
0.61	54.9 (47.8-.61.8)	60.7 (51.7-69.0)
0.62*	48.4 (41.4-55.6)	73.8 (65.2-80.9)

*The optimal cutoff value corresponding to the highest Youden's index
Youden's index = sensitivity + specificity – 1, CI: confidence interval

HOMA-IR. Maffeis et al.[24] reported that the optimal cut-off point of WHtR to be used in the NAFLD prediction in obese children who are 10 years old was 0.59 according to the Youden index. This value showed 85% sensitivity and 89.5% specificity. The removal of adinopectin decreased sensitivity by 19% at all possible cutoffs[24]. In a study conducted with 7229 students in China, WHtR was also shown to be a major independent risk factor for NAFLD. In that study, the optimal cut-off value of WHtR for the presence of NAFLD was 0.47[14]. In the present study, WHtR showed a high correlation with the adiposity indices, but did not significantly correlate with age. This age independence makes WHtR useful and more important than other anthropometric indices that are age dependent in children and adolescents. The optimal cut-off level of WHtR for predicting NAFLD was 0.62 according to the Youden index in the present study. This value has low sensitivity (48.4 %), but high specificity (73.8%). As stated above, proposed anthropometric indices alone were not highly sensitive indicators for predicting NAFLD in obese children even in previous studies[14,23-24]. However, it can be suggested that any cutoff points with higher sensitivity can be chosen for population screening at all ages.

This study has a large study sample. However, potential limitations must be considered. First, this is a cross-sectional rather than a population-based study, which may lead to overestimation of the prevalence of NAFLD in obese children. Second, a diagnosis of NAFLD was not confirmed by liver biopsy. Third, it was a cross sectional study and may lack evidence of the predictive values of WHtR. However, this value is not diagnostic; it is a predictor for the screening of NAFLD among obese children.

In conclusion, fatty liver is common among obese children aged 4 to 17 years, particularly in obese boys. Puberty is a risk for the development of NAFLD. Obese children with NAFLD have significantly higher anthropometric indices such as waist circumference, BMI SDS, and WHtR. WHtR is a simple and easy index for predicting NAFLD in obese children. Anthropometric indices should be evaluated among obese children and WHtR may be recommended as a practical tool for mass screening but should be confirmed by prospective study design.

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