

Ultrasound Diagnosis of Nonalcoholic Fatty Pancreas Disease in Children and Its Clinical Significance

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Research article

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Abstract

Background

The purpose of this study was to investigate the incidence of non-alcoholic fatty pancreatic disease (NAFPD) diagnosed by ultrasound in children and the related factors of NAFPD in children.

Methods

326 children (2–14 years old) were selected as the study subjects. All statistical analyses were performed using SPSS software 23.0 (SPSS Inc., Chicago, IL, USA).

Results

A total of 41 cases (12.6%) of the 326 children had NAFPD. The two experimental groups showed statistically significant differences in age, height, WHtR, TC, LDL, ALT, AST and GGT ($p < 0.05$), among which age and height were negatively correlated with NAFPD. Univariate analysis and multivariate analysis showed that WHtR > 0.472 ($p = 0.007$), TC > 5.3 mmol/L ($p < 0.001$), LDL > 2.49 mmol/L ($p = 0.002$) and ALT > 23.8 U/L ($p = 0.018$) were independent risk factors for occurrence of NAFPD.

Conclusions

(1) The high incidence of NAFPD in children was worthy of attention; (2) WHtR was an independent risk factor for NAFPD; (3) WHtR might be a sensitive index which could early screen children MetS and used in epidemiological investigation; (4) NAFPD was closely related to obesity and metabolic syndrome, and ultrasound could be used as the preferred imaging diagnosis method for NAFPD.

Background

In recent years, obesity has become a global public health problem, especially for children, whose growth rate is significantly higher than that of adults(1, 2). Without active and effective intervention on the current situation, the number of overweight and obese children will continue to rise. The growing burden of obesity worldwide has led to a dramatic rise in patients suffering from metabolic syndrome (MetS), which included central obesity (WC \geq 90th percentile) and 2 or more of the following 4 factors: TG level ≥ 1.7 mmol/L, HDL cholesterol < 1.03 mmol/L, systolic blood pressure ≥ 130 mmHg or diastolic blood pressure ≥ 85 mmHg, and fasting plasma glucose level ≥ 5.6 mmol/L(3). The excessive adipose tissue in obese individuals is endocrinologically active, leading to a proinflammatory state which generates several complications in target organs (liver, pancreas, heart and vessels) and even an increased risk for certain malignancies(4).

Similar to non-alcoholic fatty liver disease (NAFLD), which has become a common cause of chronic liver disease, non-alcoholic fatty pancreatic disease (NAFPD) also includes a variety of diseases, from pancreatic fat deposition (fatty pancreas and pancreatic steatopancreatitis) to possible pancreatic fibrosis(5). Despite the parallelism with NAFLD, which has been extensively investigated, our knowledge about NAFPD is still at the beginning, the interest in researching it is increasing(6). Currently, its clinical significance, outcome, relationship with chronic pancreatitis and pancreatic cancer are not well known yet(7). In addition, the diagnosis was not standardized and treatment protocols were not evidence-based.

NAFPD is associated with the severity of pancreatitis, pancreatic dysfunction in type 2 diabetes mellitus, pancreatic fistula and even the development of pancreatic cancer(8), Diagnostics is based on non-invasive imaging methods. The most accessible is abdominal ultrasound(9, 10), also endoscopic ultrasound, computed tomography or magnetic resonance imaging can be used(11).

In this study, we explored the detection rate of NAFPD through the abdominal ultrasound examination in different age children's pancreas. Moreover, we compared the differences in various metabolic indicators between NAFPD and non-NAFPD children, so that we could explore the application value and risk factors of transabdominal ultrasound in childhood NAFPD. Finally, our study provided reference for early diagnosis and treatment of clinical disease, then it could guide the clinical timely intervention, which can reduce and avoid the occurrence of related diseases.

Methods

Patients

From June to December 2017, we retrospectively analyzed the clinical data of 326 patients who underwent routine ultrasound examination at the Ultrasonic Department of Quanzhou First Hospital Affiliated to Fujian Medical University. There were 203 boys and 123 girls, and the ratio of boys to girls was 1.65 to 1, with an average age of 6.3 ± 3.5 years. The exclusion criteria were as follows: (1) BMI greater than or equal to 35 kg/m^2 ; (2) Drinking $> 20\text{g/d}$; (3) Patients with hepatitis A, B and autoimmune hepatitis; (4) Patients with pancreatitis and chronic nephropathy; (5) Children with metabolic disorders caused by drug treatment in the past year(12, 13). This retrospective study was approved by the Ethics Committee of Quanzhou First Hospital Affiliated to Fujian Medical University.

Collection the gender, age, height (m), weight (Kg), waist circumference (WC) (cm), Systolic blood pressure (SBP, mmHg), Diastolic blood pressure (DBP, mmHg) and medical history of the subjects were recorded. BMI and WHtR ($\text{BMI} = \text{weight}/\text{height}^2$, $\text{WHtR} = \text{waist circumference}/\text{height}$) were calculated. The basic information, life habits, current medical history and previous history were uniformly inquired, collected and sorted out by pediatricians. All enrolled children were isolated from peripheral venous blood after 8 hours of fasting, and triglyceride (TG), total cholesterol (TC), high-density lipoprotein (HDL), low-density lipoprotein (LDL), fasting glucose (FBG), uric acid (UA), alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP) and glutamyl transpeptidase (GGT) were measured by automatic biochemical analyzer (DXC800).

All patients were examined by a single ultrasound physician with 10 years' experience. In order to obtain the pancreas ultrasonography in the evaluation of NAFLD, all patients were at least 12 hours on an empty stomach and in supine position, with 5 MHz probes (Philips iU Elite; Bothell, Washington) on abdominal transverse and longitudinal scan line, which under the condition without the use of harmonic imaging. Moreover, two sonographers worked together to assess the quality of ultrasonic ultrasonographic. Results was reviewed by senior physician when there is disagreement.

Definitions

Diagnostic criteria for NAFLD were as follows(8): echo enhancement of the pancreas was higher than that of the kidney, but since the pancreas and kidney could not be displayed on the same screen at the same time, the sonographers compared the liver with the pancreas, and then compared the right kidney with the liver (figure 1).

Statistical analysis

SPSS software 23.0 (SPSS Inc., Chicago, IL, USA) was used for data analysis. The data were presented as the mean±standard deviation (±SD) for continuous variables and as a number for categorical variables. Chi-squared tests was used to evaluate differences in proportions, and Student's t-tests were used to evaluate continuous variables. P values less than 0.05 ($p<0.05$) were considered statistically significant.

Results

Patient clinical characteristics

The clinical characteristics of the 326 patients (285 non-NAFLD vs. 41 NAFLD) are listed in Table 1. The non-NAFLD cohort comprised more elderly patients and more higher patients than the NAFLD cohort (all $p<0.05$). The WHtR of NAFLD group was significantly higher than non-NAFLD group ($p<0.001$). The peripheral venous blood biochemical indexes including TC, LDL, AST, ALT and GGT were significantly higher in the NAFLD group than in the non-NAFLD group (all $p<0.05$). However, there was no significant differences in BMI, WC, SBP (systolic blood pressure), DBP (diastolic blood pressure), TG, HDL, FBG, UA, ALP between the two cohorts ($p>0.05$).

Predictable risk factors for NAFLD

Univariate analysis and multivariate analysis were used to evaluate the factors that that associated with NAFLD. On univariate analysis, age, height , WHtR vlue, TC∓LDL, AST, ALT and GGT were associated with NAFLD (Table 2).

Multivariate analysis found that WHtR, TC, LDL and ALT were independent risk factors for NAFLD. (Table 3) To evaluate the potential diagnostic value, a ROC curve was generated for WHtR value. $WHtR\geq 0.454$ was used as the standard for NAFLD prediction. We found that the area under the ROC curve (AUC) was

0.722. In the cut off value of 0.454, the sensitivity and specificity were 75.6%, and 66.7% respectively. (Figure 2).

Discussion

Risk factors for NAFLD include obesity, age increase, male, hypertension and dyslipidemia(14). However, most of the subjects studied are adults. Only a few studies(15) have been conducted on school-age children and adolescents with obesity and metabolic syndrome, and no studies have been found in the general children group.

Currently, the internationally recognized indicators to measure the degree of childhood obesity include BMI, WC, WHtR, etc. Research has shown that WHtR was superior to BMI, WC and waist-hip ratio in predicting Metabolic Syndrome(MetS)(16, 17). In our study also found that WHtR in the prediction of dangerous NAFLD most relevant. Meanwhile, children who are overweight and obese need to consult BMI and WC boundary table(18). Similarly, blood pressure level of children increases with age(19), which requires us to refer to percentile boundary table of blood pressure of children of different ages and heights to assess the risk of NAFLD(20), which increases the workload of screening and is not conducive to epidemiological investigation. Therefore, WHtR as a routine physical examination indicator for children can better assess and screen the risk factors of cardiovascular disease and MetS risk in children.

Our study found that the incidence of NAFLD in children was negatively correlated with age and height, but not gender. What's more, the amount of exercise of preschool children is less than that of school-age children, and they are more prone to fat deposition, this may also be in line with the findings of Afshin A et al, that childhood obesity rates first decline with age before age 14 and then increase(1). Also there was no gender difference in obesity rates before age 20, and childhood obesity rates were the same for boys and girls at all ages.

NAFLD includes features of MetS, which translates into strong association with type 2 DM, NAFLD and cardiovascular risk(21). TG, TC and LDL levels of NAFLD patients were generally higher than those of normal healthy people, while HDL levels were lower(22). Our study found that the TC, LDL, AST, ALT and GGT in patients with NAFLD, TC, LDL, AST, ALT and GGT were higher than the non-NAFLD negative group, however, HDL was lower than the non-NAFLD negative group. This result showed that NAFLD patients in a variety of abnormal biochemical indexes, especially blood lipid metabolic disorder (TC, LDL concentration increase HDL levels), with the risk of MetS. At the same time, this study demonstrated that low levels of blood lipid metabolism disorders were more likely to happen NAFLD, which was similar to our previous study found that the detection of the metabolic syndrome caused by ectopic fat deposition in the examination, abdominal ultrasound examination of the pancreas was superior to the liver(9).

The AST and ALT of NAFLD patients in this study were also higher than those in the negative group, which is the same as the research results of Kim DR et al(23) that in elder obese children and adolescents. GGT has long been used as a marker of alcoholism and liver disease, also GGT can be used as a predictor of MetS(24). In this study, it was found that the GGT level of NAFLD patients was higher

than that of the negative group. However, previous studies have shown that the risk of MetS in obese children and adolescents with increased GGT was significantly increased compared to normal(25).

To our knowledge, this is the first and largest study assessing the clinical value of WHtR in children NAFLD. At the same time, WHtR can be used as a sensitive indicator for early screening of children's MetS and used for epidemiological investigation. When WHtR is found to exceed the optimal threshold during the physical examination of children and adolescents, clinicians may be prompted to take necessary measures, such as noninvasive ultrasonography to assess the occurrence of NAFLD and to assess the need to reduce their chance of MetS by increasing exercise, diet control, etc.

This study has several limitations. First, this study is limited by its retrospective nature and its inherent selection bias. Second, this is a single-center study. It would be necessary to conduct larger, multi-center studies of the general population in the future. Third, we just ultrasound examination but no MRI, CT or histological examination (biopsy) to assess NAFLD. Therefore, the results of MRI, CT and biopsy specimens cannot be compared with the results of ultrasound examination, and further studies are necessary to compare the results in the future.

In conclusion, we explored the detection rate of NAFLD through the abdominal ultrasound examination in different age children's pancreas. The results showed that WHtR, TC, LDL and ALT were independent risk factors for NAFLD. A ROC curve was generated for WHtR value to evaluate the potential diagnostic value of WHtR. We found that the area under the ROC curve (AUC) was 0.722. The sensitivity and specificity were 75.6%, and 66.7% respectively. Thus, our study provided reference for early diagnosis and treatment of clinical disease, then it could guide the clinical timely intervention, which can reduce and avoid the occurrence of related diseases.

Conclusions

Our study shows that : (1) the incidence of NAFLD in children is more than 10%, which is worthy of attention; (2) WHtR was an independent risk factor for NAFLD; (3) WHtR can be used as an early screening indicator for children MetS, especially for epidemiological investigation.

Abbreviations

NAFLD: non-alcoholic fatty pancreatic disease; NAFLD: non-alcoholic fatty liver disease;

MetS: metabolic syndrome; SBP: Systolic blood pressure; DBP: Diastolic blood pressure;

BMI: weight/height²; WHtR: waist circumference/height; TG: triglyceride; TC: total cholesterol; HDL: high-density lipoprotein; LDL: low-density lipoprotein; FBG: fasting glucose; UA: uric acid; ALT: alanine aminotransferase; AST: aspartate aminotransferase; ALP: alkaline phosphatase; GGT: glutamyl transpeptidase

Declarations

Ethics approval and consent to participate

This retrospective study was approved by the Ethics Committee of Quanzhou First Hospital Affiliated to Fujian Medical University.

Consent to publish

We agreed to publish the article in BMC Endocrine Disorders.

Availability of data and materials

Data and materials are truly available.

Competing interest

There is no conflict of interest here.

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Authors' Contributions

CH and YY were involved in diagnosis of NAFLD and NAFLD; CH and CC were involved in the collection and assembly of patients' data; CH and SL were involved in design and writing of this study. All authors read and approved the final manuscript.

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Tables

Table 1. Comparison of NAFPD positive group and NAFPD negative group $\bar{x}\pm SD$			
indicators	NAFPD(-) (n=285)	NAFPD(+)(n=41)	<i>P</i>
Sex(M/F)			0.598
Male	179	24	
Female	106	17	
Age(y)	6.5 \pm 3.4	4.3 \pm 3.0	<0.001
Height(m)	116.9 \pm 20.6	103.3 \pm 21.7	<0.001
BMI(kg/m ²)	17.3 \pm 3.3	17.8 \pm 5.5	0.406
WC(m)	51.8 \pm 8.9	49.6 \pm 14.9	0.186
WHtR	0.448 \pm 0.036	0.472 \pm 0.054	<0.001
SBP(mmHg)	102.0 \pm 11.2	101.4 \pm 16.2	0.754
DBP(mmHg)	65.1 \pm 7.5	65.6 \pm 10.6	0.685
TG(mmol/L)	0.83 \pm 0.53	0.87 \pm 0.48	0.692
TC(mmol/L)	3.69 \pm 0.69	5.30 \pm 1.86	<0.001
HDL(mmol/L)	1.16 \pm 0.34	1.12 \pm 0.35	0.510
LDL(mmol/L)	2.25 \pm 0.66	2.49 \pm 10.75	0.030
FBG(mmol/L)	4.82 \pm 1.23	4.73 \pm 1.38	0.673
UA(umol/L)	310.4 \pm 115.4	309.0 \pm 123.8	0.944
AST(U/L)	29.9 \pm 14.3	39.0 \pm 16.5	0.001
ALT(U/L)	16.1 \pm 12.2	23.7 \pm 23.2	0.006
ALP(U/L)	198.4 \pm 136.0	229.0 \pm 211.2	0.250
GGT(U/L)	12.8 \pm 9.8	20.8 \pm 31.0	0.012

Table 2. Univariate analysis of morbidity risk factors for NAFPD				
variable	B	SE	P	OR(95%CI)
Age	-0.2	0.003	<0.001	0.981(0.974,0.987)
Sex	-0.179	0.34	0.598	0.836(0.429,1.627)
Weight	-0.118	0.112	0.276	0.977(0.947,1.007)
Height	-0.42	0.012	<0.001	0.959(0.937,0.983)
BMI	0.035	0.042	0.406	1.036(0.954,1.125)
WC	-0.026	0.020	0.186	0.974(0.938,1.013)
WHtR	1.080	0.351	0.002	2.833(1.427,5.625)
SBP	-0.004	0.014	0.754	0.996(0.968,1.024)
DBP	0.008	0.020	0.685	1.008(0.969,1.050)
TG	0.121	0.305	0.692	1.126(0.621,2.051)
TC	2.195	0.328	<0.001	8.981(4.723,17.078)
HDL	-0.327	0.495	0.510	0.721(0.273,1.904)
LDL	0.525	0.242	0.030	1.691(1.052,2.719)
FBG	-0.057	0.135	0.673	0.945(0.726,1.230)
UA	0.000	0.001	0.944	1.000(0.997,1.003)
AST	0.030	0.009	0.001	1.030(1.012,1.049)
ALT	0.025	0.009	0.006	1.025(1.007,1.043)
ALP	0.001	0.001	0.250	1.001(0.999,1.003)
GGT	0.025	0.010	0.012	1.025(1.005,1.045)

Table 3. Multivariate analysis of morbidity risk factors for NAFPD

variable	<i>P</i>	OR(95%CI)
Age	0.454	0.772(0.651,0.915)
Height	0.090	1.388(0.951,2.028)
WC	0.258	1.075(0.948,1.220)
WHtR	0.007	2.669(1.314,5.419)
TC	<0.001	18.353(7.026,47.938)
LDL	0.002	1.293(1.133,1.648)
ALT	0.018	1.037(1.006,1.069)
GGT	0.12	1.018(0.995,1.041)

Figures

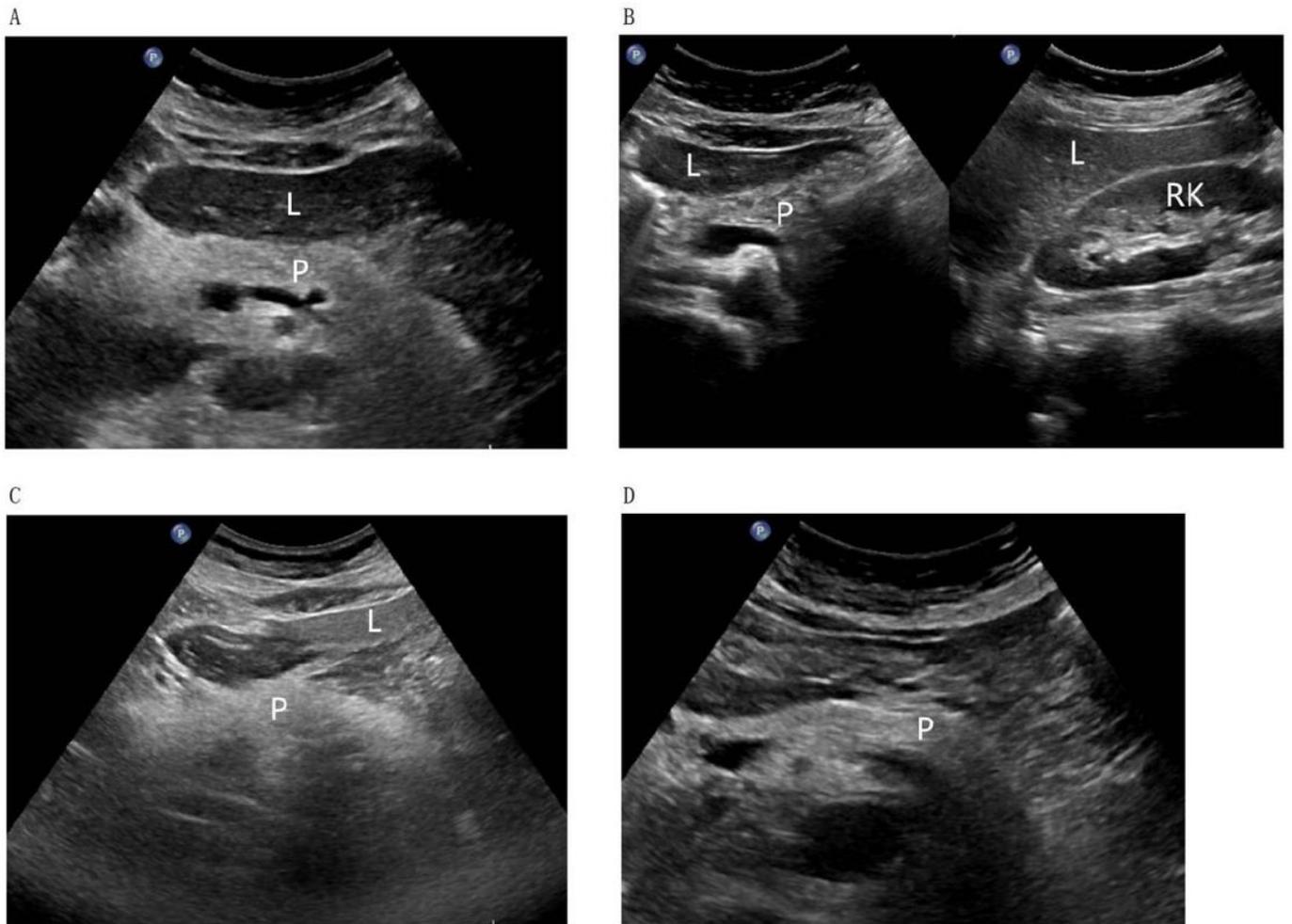


Figure 1

A. Enhanced pancreatic echo with normal liver echo; B. Enhanced pancreatic echo with normal hepatic and renal echo; C. Enhanced pancreatic echo with enhanced hepatic echo; D. Enhanced pancreatic echo.

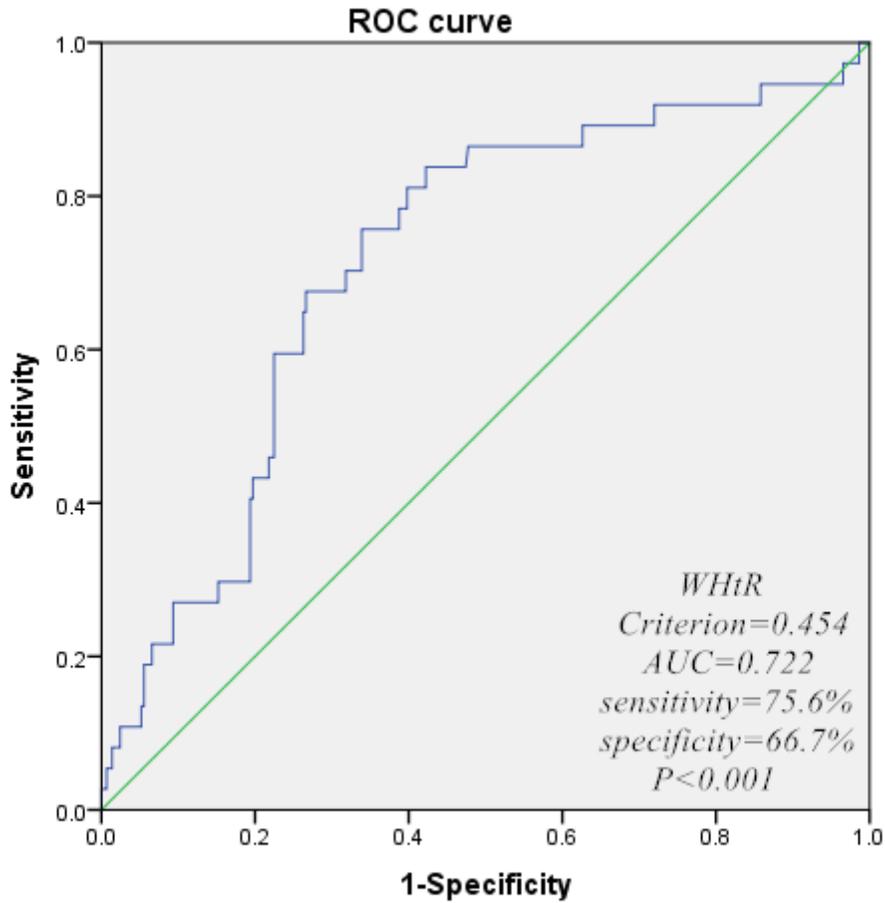


Figure 2

ROC curve of WHtR in predicting NAFPD in children.