Prevalence of non-alcoholic fatty liver disease and its correlation with anthropometric measures and laboratory parameters in overweight and obese children and adolescents

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ABSTRACT

Introduction: Non-alcoholic fatty liver disease (NAFLD) is the most common cause of liver disease in children and its primary cause is obesity. In addition, children with NAFLD may be at increased risk for cardiovascular disease. **Objective:** The objective of this study was to estimate the prevalence of NAFLD in overweight and obese children and to study its correlation with various anthropometric measures and laboratory parameters in overweight and obese children and adolescents. **Materials and Methods:** This cross-sectional observational study was conducted in the Department of Pediatrics of a teaching institution of central India. The study included 30 overweight and obese children and adolescents between 6 and 18 years of age. Subjects' demographic details, anthropometric examination (body mass index [BMI], neck circumference, and waist/hip ratio}, and laboratory parameters such as aspartate transaminase (AST), alanine aminotransferase (ALT), fasting glucose levels, and homeostatic model assessment of insulin resistance (HOMA-IR) were taken. Ultrasonography (USG) abdomen was done to grade fatty liver changes. **Result:** 17 (57%) children were male and 13 (43%) were female. 80% (24/30) of the study population ≥10 years of age. Prevalence of NAFLD in obese children was 28.5% (6/21). The prevalence of NAFLD in overweight children was 11.1% (1/9). Out of seven subjects with AST levels >37 IU/L, 5 (72%) had abnormal liver echotexture findings on USG (p=0.00006). Our study showed a positive correlation of BMI percentile values in patients with normal, Grade I and Grade II liver echotexture finding on USG, respectively. **Conclusion:** Obesity and overweight are associated with increased risk of NAFLD. Abnormal liver function test in overweight and obese children should raise the suspicion of NAFLD. All these children with high AST and ALT need sonography screening.

Key words: *Children, Liver function tests, Non-alcoholic fatty liver disease, Obesity*

Non-alcoholic fatty liver disease (NAFLD) is a condition defined by significant lipid accumulation (5–10%) in hepatic tissue in the absence of significant chronic alcohol consumption [1]. Most of the patients with NAFLD have increased liver fat content alone (simple steatosis), but others may develop increasing hepatic inflammation known as non-alcoholic steatohepatitis, and up to 20% of the patients reveal progressive hepatic fibrosis and may eventually develop cirrhosis or liver failure [1,2]. Estimates from recent epidemiological studies indicate a prevalence rate of 10–30% in the Western adult populations [3-5] as well as in Asian populations [6-9].

NAFLD is the most common cause of liver disease in children and its primary cause is obesity. In children, NAFLD causes a particular pattern of liver damage that is the most severe in children who are non-white, boys, or are especially obese [10]. In addition, children with NAFLD may be at increased risk for cardiovascular disease [11]. A long-term retrospective study conducted by researchers at Mayo Clinic showed that children with NAFLD are more than 13 times as likely to die over a 20-year period or require a liver transplant as kids in the general population [12].

The great interest in diagnosing obesity and intervening as early as possible in children and adolescents derives from the fact that, in this age group, different from adults, the evolution of NAFLD and metabolic syndrome can be prevented or even slowed down since the repair processes in young people may be more active than in adult [13]. We planned this study to determine the prevalence of NAFLD in overweight and obese children and adolescents and to study its correlation of NAFLD with various anthropometric measures and laboratory parameters.

MATERIALS AND METHODS

This cross-sectional observational study was conducted on 30 children, aged 6–18 years attending the outpatient endocrinology clinic at the Department of Pediatrics of a

teaching institution of central India for complaint of increasing weight. Prior approval from the Institutional Ethics Committee was obtained, and informed consent was taken from the study subject and their parents before recruitment. Children, aged 6–18 years with body mass index (BMI) ≥85th percentile for particular age and sex, were included in the study. Children with BMI <85th percentile for the particular age and sex, children <6 years and >18 years of age, and children with a history of use of drugs known to cause fatty changes in the liver were excluded from the study.

Demographic profile was recorded for all the patients. As per the standard methods of measurement, their weight, height, BMI, waist circumference (WC), hip circumference, waist/hip ratio, and neck circumference (NC) were measured. BMI was interpreted as per CDC guidelines (for age <18 years) [14]. WC percentiles were generated according to Kurian's chart [15]. Cutoff value for NC was adopted from the USA study [16]. Waist/hip ratio was interpreted as per Huxley criteria [17]. The study subjects were divided into two groups: Group A included overweight (BMI between 85th and 95th percentiles) and Group B included obese (BMI ≥ 95th percentile) children.

Various biochemical tests were performed from all the study subjects including aspartate transaminase (AST) and alanine aminotransferase (ALT) levels. Normal value was taken as ≤37 IU/L for AST and ≤40 U/L for ALT. Fasting blood samples were taken after a minimum fasting of 8 h for estimating plasma glucose and fasting serum insulin levels. Homeostatic model assessment of insulin resistance (HOMA-IR) was estimated using formula [18]: HOMA-IR = fasting blood sugar (mg/dL) × fasting insulin (mmol/L)/405. Two cutoffs were taken to define insulin resistance: (1) HOMA-IR 1 >75th centile and (2) HOMA-IR 2 >90th centile.

Finally, ultrasonography (USG) abdomen of the study subjects was carried out in the Department of Radiodiagnosis to determine the liver size and echotexture (fatty changes). Liver echotexture was graded according to Mottin's criteria [19]. (1) Grade I (mild) - a slight diffuse increase in fine echoes in the hepatic parenchyma with normal visualization of the diaphragm and intrahepatic vessel borders. (2) Grade II (moderate) - a moderate diffuse increase in fine echoes with slightly impaired visualization of the intrahepatic vessels and diaphragm. (3) Grade III (marked) - marked increase in fine echoes with poor or no visualization of the diaphragm, intrahepatic vessel borders, and posterior portion of the right lobe of the liver.

All relevant data collected from the patient were entered in a pre-designed pro forma. Statistical analysis was done using computer software (SPSS version 20). The qualitative data were expressed in proportion and percentages and the quantitative data were expressed as mean and standard deviations. The difference in proportion was analyzed using Chi-square test and the difference in means was analyzed using student *t*-test (unpaired). Significance level for tests was determined as 95%. Test is considered significant if p<0.05.

RESULTS

A total of 30 subjects were included in the study over a period of 1 year. 17 (57%) males and 13 (43%) females were the study subjects. 20% (6/30) of the study population were in the age group of <10 years and 80% (24/30) were ≥10 years of age. In this cohort, overweight males were 3, obese males were 14, overweight females were 6, and obese females were 7. Clinical, anthropometric, and biochemical characteristics are depicted in Table 1.

Out of 30 subjects, seven showed abnormal echotexture on sonography. Out of 13 females, 3 (23%) had abnormal echotexture, and out of 17 males, 5 (23.5%) had abnormal liver echotexture. Prevalence of NAFLD in obese children was 28.5% (6/21) and 11.1% (1/9) in overweight children. Four subjects had Grade I NAFLD and three had Grade II NAFLD. Rising trend of BMI percentile values with increasing echotexture of liver on USG are shown in Table 2. Out of three overweight children with normal NC, all had normal USG, while among six overweight children with NC more than normal, 5 (83.3%) had normal USG, and 1 (16.7%) had Grade I liver echotexture findings.

Out of three males with waist/hip ratio <0.9, all 3 (100%) had normal USG. 14 males had waist/hip ratio >0.9, and out of them, 10 (71.4%) had normal USG, 1 (7.1%) had Grade I, and 3 (21.4%) had Grade II changes on USG (p>0.99). All the three females with waist/hip ratio <0.8 had normal USG. 7 out of 10 (70%) females with waist/hip ratio >0.8 had normal USG and 3 (30%) had Grade I liver changes.

Relationship of USG findings with liver function tests is shown in Table 3. Out of 23 subjects with normal AST levels, 21 (91%) had normal USG, while only 2 (9%) had liver changes. Out of seven subjects with AST levels >37 U/l, 5 (72%) had altered liver echotexture on USG (p=0.00006). Out of 22 subjects with normal ALT levels, 19 (86%) had normal USG, while 3 (14%) had Grade I changes. Out of eight subjects with ALT >40 U/l, 4 (50%) had normal USG, 2 (25%) had Grade I, and 2 (25%) had Grade II changes (p=0.037).

Table 1: Clinical, anthropometric, and biochemical characteristics of the subjects

Parameters	Mean±SD (range) n=30
Age (years)	12.7±3.3 (7–19)
BMI (kg/m^2)	27.7±4.2 (20–35.9)
WC (cm)	92.3±12.7 (67–116)
Waist/hip	0.93±0.09 (0.77–1.17)
NC (cm)	34.1±2.8 (28–40)
Fasting sugar (mg/dL)	87.1±7.6 (73.1–107)
Fasting insulin (mcu/mL)	17.4±13.5 (1.6–61)
AST (U/L)	32.7±9.9 (19–64)
ALT (U/L)	34.2±19.1 (14–100)
HOMA-IR	3.7±3.07 (0.4–14.5)
Liver size in USG (cm)	12.4±1.8 (8.5–15.5)

NC: Neck circumference, WC: Waist circumference, BMI: Body mass index, ALT: Alanine aminotransferase, AST: Aspartate transaminase, HOMA-IR: Homeostatic model assessment of insulin resistance, USG: Ultrasonography, SD: Standard deviation

Table 2: Relationship between liver echotexture findings on USG and BMI

BMI	Normal	NAFLD Grade I	NAFLD Grade II	p value
Number of cases	23	4	3	0.127
BMI percentile (mean±SD)	95.66±3.6	96.42±2.55	98.66±0.6	

USG: Ultrasonography, BMI: Body mass index, NAFLD: Non-alcoholic fatty liver disease

Table 3: Relationship between liver echotexture finding on USG with AST and ALT

Laboratory tests	Normal USG	Grade I	Grade II	Total	p value
Normal AST levels (<37 U/l)	21	2	0	23	0.0006
AST >37 U/l	2	3	2	7	
Normal ALT levels (<40U/l)	19	3	0	22	0.037
ALT >40 U/l	4	2	2	8	
Total	23	5	2	30	

ALT: Alanine aminotransferase, AST: Aspartate transaminase, USG: Ultrasonography

Table 4: Correlation of HOMA-IR with liver echotexture

HOMA-IR	Normal	NAFLD I	NAFLD II	Total	Chi-square	p value
0–2	11	0	0	11	5.2	0.02
2.1–4	7	2	1	10	0.37	0.54
4.1–6	2	1	0	3	0.18	0.66
6.1–8	1	1	1	3	3.49	0.06
8.1–10	0	0	1	1	3.3	0.06
>10	2	0	0	2	0.65	0.41
Total	23	4	3	30		

HOMA-IR: Homeostatic model assessment of insulin resistance, NAFLD: Non-alcoholic fatty liver disease

Subjects' HOMA-IR was correlated with liver echotexture as shown in Table 4. 11 (36.6%) subjects had normal HOMA-IR, while 19(63.4%) had high HOMA-IR. Higher HOMA-IR was associated with abnormal liver echotexture, although it was statistically not significant (p>0.05).

DISCUSSION

In the present study, the prevalence of NAFLD among obese children was found to be 28.5%, while among overweight children, it was 11.1%. Overall prevalence of NAFLD in those with BMI >85th percentile for the corresponding age and sex was found to be 23.3%. In earlier studies, the prevalence of NAFLD has been reported to range from as low as 20% to as high as 77% in other studies as conducted by Chan *et al.* [20-25]. In our study, the prevalence of NAFLD was almost equal in both the sexes (23.5% in males and 23.1% in females), which is in accordance with other studies [21-25].

Our study has shown positive correlation of BMI percentile values with normal, Grade I and Grade II liver echotexture finding on USG, although this difference was not significant (p=0.127). Tominaga *et al.* showed a strong correlation of NAFLD with BMI in their study [26]. Out of three overweight children with normal NC, all had normal USG, while among six overweight children with NC more than normal, 5 (83.3%) had normal USG, and 1 (16.7%) had Grade I changes. No literature could be found correlating the NC with NAFLD. Further studies are required to establish the relationship between the two.

In our study, we found a significant association between elevated AST and ALT levels with increased echogenicity on USG. Thus, it can be concluded that steatosis has a significant chance of being associated with steatohepatitis. Earlier studies have shown that AST and ALT values are either more than normal or in the high normal range in patients with NAFLD [27].

Pathogenesis of the NAFLD is not completely understood. The first step appears to involve deposition of excess fat in the liver; this is followed in some patients by increased fatty acid oxidation, oxidative stress, and cytokine production, resulting in progression to steatohepatitis and fibrosis. Various pathogenetic mechanisms that pay a role include cytokines (tumor necrosis factor-α, adiponectin, resistin, leptin, interleukins, and transforming growth factor ß) that lead to insulin resistance, and serum and liver iron overload and oxidative stress that lead to necroinflammation and fibrosis [28]. Thus, it becomes important in obese children to assess the liver function tests and extent of changes in liver echotexture for timely intervention.

In the present study, relationship between NAFLD and insulin resistance was not found to be statistically significant. However, earlier studies have shown that chances of NAFLD increase significantly with increasing insulin resistance [13,29]. Small sample size was the main limitation for establishing this fact. However, this study could be used as a base to perform further studies on a larger scale.

CONCLUSION

Obesity and overweight are associated with increased risk of NAFLD. Abnormal liver function test in overweight and obese children should raise the suspicion of NAFLD. All these children with high AST and ALT need sonography screening and regular follow-up and monitoring.

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