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Original Research Article

Prevalence of fatty liver disease in children with obesity- a diagnostic study based on its ultrasound appearance

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ABSTRACT

Background: Non-alcoholic fatty liver disease is an asymptomatic involvement of the liver, can progress to chronic liver disease and must be identified at an early stage for good prognosis. The implementation of the appropriate therapeutic interventions is determinant of the attempts to treat it. For that purpose, early diagnosis and staging of the disease is essential. It seems that diagnostic imaging should be a first-line tool for the staging and monitoring pediatric NAFLD/NASH for appropriate interventions to be implanted in a timely way. This study evaluated the prevalence of fatty liver in relation with body mass index (BMI) by means of ultrasound in children of age group 6-15 years.
Methods: In this cross-sectional study, 83 children aged 6 to 15 years, were selected randomly. The participants were examined by a pediatrician. Liver ultrasound was performed for all children and grade of fatty liver was determined.
Results: There was a significant correlation between grade of fatty liver with BMI, our study showed a strong association between BMI and prevalence of fatty liver on ultrasound.
Conclusions: According to the study hypothesis, based on BMI, the degree of NAFLD in children were predictable. Ultrasound of liver in grading of fatty liver is one of the assessments methods of fatty liver but it is not a diagnostic method; it is useful for prevention to reduce BMI.

Keywords: BMI, Diagnosis, Fatty liver grading, NAFLD/NASH, Obesity, Ultrasound

INTRODUCTION

Fatty liver disease (FLD) is characterized by a spectrum of chronic liver disease, presented with excessive hepatic fat accumulation (steatosis) occurring with or without hepatic inflammation and fibrosis. A percentage of children with hepatic steatosis could progress to a more advanced form of the disease, non-alcoholic steato-hepatitis (NASH) that includes hepatic inflammation and can result in various degrees of fibrosis and cirrhosis, in children. FLD is thought to be a hepatic manifestation of underlying metabolic dysfunction and is very strongly associated with a number of metabolic risk factors, including insulin resistance, dyslipidemia, cardiovascular disease and, most significantly, obesity in adulthood. Fatty liver disease is expected to become the most prevalent cause of liver pathology, liver failure and indication for liver transplantation in childhood and adolescence. Despite this, "paediatric" non-alcoholic FLD (NAFLD) remains under-studied, under-recognized and undermanaged. Major gaps are in our approach to screening, sampling, diagnosis, management and follow-up, particularly during the transition between paediatric and adult clinical services. Accurate epidemiological and pathophysiological data from larger longitudinal cohort studies are needed to better determine the true prevalence and natural history of paediatric NAFLD among different ethnic groups. Recognition of occurrence of NAFLD in the paediatric population and the differences in its clinical presentation, pathophysiology, histology and prognosis

when compared to adult disease, it is of at most importance.[1] In a study among school children in Thiruvananthapuram school district, of age group 10 to 15 years, the prevalence of obesity was 4.99% and that of overweight were 17.73%. However there are very few studies on the prevalence of fatty liver disease, metabolic syndrome and hyper-insulinemia in the obese subjects of paediatric age group in Indian ethnic population. The prevalence of non-communicable or chronic disease is increasing very rapidly in developing countries than in industrialized countries. According to the World Health Organization (WHO) estimates, by the year 2020, chronic diseases will account for approximately three-quarters of all deaths in the developing world.[2] Obesity is the biggest risk factor for chronic diseases including fatty liver disease and plays a central role in the metabolic syndrome (MS), a common pathophysiological condition with implications for the development of many chronic diseases.

According to the International Obesity Task Force (IOTF) report, at least 10% of school children between the age of five and 17 years are overweight or obese, representing a total of 155 million children. Around 30 to 45 million within that figure are classified as obese, accounting for 2-3% of the world's children aged 5-17 and the situation is getting worse.[3] In the United States, for example, the rate of overweight and obesity among children and adolescents aged 6 to 18 years increased to more than 25% in the 1990s from 15% in the 1970s. Until now, most national public health programs and policies, as well as national-level research on children, have focused on under nutrition and its effects on the survival and mortality of parents and children. Calculated global prevalence of overweight in children aged 5-17 years is estimated by International obesity task force (IOTF) to be ~10%, but this is unevenly distributed with prevalence ranging from 30% in United States to <2% in Africa. Obesity beginning in childhood often precedes the hyper insulinemia state. Genetic predisposition or early-life events may contribute to the insulin resistance and adverse body fat-patterning manifested in the metabolic syndrome. However, not much is known about the prevalence of childhood obesity and the Paediatric metabolic syndrome because of very few number of studies, the various definitions used, and the different age groups studied, which makes comparisons difficult.

Classic ultrasound (US) is the most widely used imaging method for the diagnosis of fatty liver filtration due to its high availability, its user-friendliness, its tolerance by the examinees and its low cost. Typical findings are based on the ultrasonographic comparison to the right renal parenchyma, the peripheral attenuation and the presence of areas with focal amplification of the ultrasound beam.[4] The degree of infiltration can be subjectively classified as mild, moderate or severe, or as suggested by some studies, can be classified using absolute ultrasound criteria.[5,6]

A large pediatric cohort study showed a positive correlation between ultrasound degree of fatty infiltration and histologically established severity of the disease.[7] In the same study, a particularly interesting finding was the lack of a positive correlation between transaminase values with either ultrasound or histological findings, suggesting a lower diagnostic value of these markers in pediatric patients. Ultrasound was considered an effective tool for the staging and screening of these patients.[8] Interestingly, there has been a higher incidence of NAFLD/NASH in obese children with steatosis upon biopsy, which makes it a possible risk factor for the disease. Therefore, it is important to note that the combination of fatty liver on ultrasound with a high serum ALT value increased the detection of NAFLD in children in these highly suspected groups.[9] However, there was a remarkable percentage with conspicuous fatty infiltration on ultrasound and unaffected value of ALT in serum.

In addition, it was found that children with fatty infiltration and a normal ALT value did not usually show other manifestations of metabolic syndrome. These studies rendered the ultrasound an effective tool for screening NAFLD/NASH in the suspected pediatric population, in contrast to the measurement of serum aminotransferases, which in the current literature seem to be insufficient.[10]

Aims and objectives

To study the diagnostic accuracy of ultrasound study in the prevalence of fatty liver disease in obese children within the age group of 6-15 years.

METHODS

It was a hospital based study of sample size 83. The study was carried out at the Department of Radiodiagnosis, Government Medical College, Thiruvananthapuram for a period of one year: April 2016 to March 2017.

Inclusion criteria

Obese children of either sex of age group 5-15 years, obesity as defined by BMI>95th centile for age and sex as per CDC charts.

Exclusion criteria

Patients who have a diagnosed secondary cause for obesity. Those who were not willing to participate in the study.

Sample size

83 cases (All the children referred to the department of radiodiagnosis during the study period satisfied the inclusion criteria, except those with the exclusion criteria were included in the study).

Method of study

Research protocol was submitted to Human Ethical Committee, Medical College, Thiruvananthapuram. Study was initiated after getting clearance from both the Human Ethical Committee and Research committee.

Obese children who attended to the department of radiodiagnosis, during the study period, who satisfied the inclusion criteria were recruited for the study. A written informed consent form was signed by the parents of all these children, prior to the induction into the study. Children who were detected to have any secondary cause for obesity were excluded from the study.

Primary details of the patients such as life history, dietary patterns, family history, and daily habits were elicited by interrogation. Height and weight were measured as per standardized methods. Waist circumference (WC) was measured with a non-elastic, flexible tape; measured at the mid-point between the iliac crest and the lower edge of the ribs at the end of normal expiration. Abdominal obesity is defined using the sex and age-specific 90th waist circumference percentile.

Fatty liver grading was measured by using USG machine Siemens Acuson S2000. Using a calibrated scale from 0 to 3, children were stratified based on the severity of fat infiltration into normal liver, mild, moderate and severe fat infiltration. The calibration was based on echogenesis and imaging of the vascular parenchyma and septum. Liver echogenicity was measured in a longitudinal section compared to that of the adjacent right kidney.[11,12] Grading of fatty liver was assessed.

RESULTS

Among 83 participants, males =32 (39%), females =51 (61%) (Table 1).

Table 1: Distribution of study subjects by sex.

Sex	Fatty liver		Total	%
	Present	Absent		
Male	21	11	32	39
Female	27	24	51	61
Total	48	35	83	100

P value <0.255, odds ratio 1.69 (not significant)

Females were 22% more than the male participants.

Chi square test = 1.297. P value <0.255 and odds ratio 1.69. Hence not able to establish association of sex with fatty liver disease.

Among 83 participants, 35 participants (42%) were in age group 6 years to 10 years and 48 10 years to ≤15 years =48 (56%). 10 years to ≤15 years were 14% more than the 6 years to 10 years participants. Chi square test =1.297 and p value <0.155. Hence not able to establish association of age with fatty liver disease (Table 2).

Table 2: Distribution of study subjects by age group.

Age in years	Fatty liver		Total	%
	Present	Absent		
6-10	22	13	35	42
10-15	32	16	48	58
Total	54	29	83	100

P value <0.155, odds ratio 1.32 (not significant)

Table 3: Distribution of study subjects by fatty liver grading versus sex.

Sex	Fatty liver				Total
	Present			Absent	
	FLG 1	FLG 2	FLG 3		
Male	14	2	5	11	32
Female	13	8	6	24	51
Total	48			35	83
Total%	58%			42%	100%

P value=0.2547, p value >0.05 and hence association cannot be established

Calculated p value =0.2547. As p value was more than 0.05, this study cannot establish association of fatty liver grading with sex. This category was not conclusive.

Table 4: Distribution of study subjects by fatty liver grading.

Total participants 83		
Fatty liver grading (FLG)	**Frequency**	**Percent**
FLG 1	27	32.5
FLG 2	10	12.0
FLG 3	11	13.3
Fatty liver not present	35	42.2
Total	83	100.0

Of the 83 participants, 27 participants had FLD grading 1 (32.5%), 10 participants had FLD grading 2 (12.0%), 11 participants had FLD grading 3 (13.3%) and in 35 participants FLD grading was absent.

Table 5: Distribution of study subjects by BMI.

Fatty liver			
BMI	**Grad 1**	**Grade 2**	**Grade 3**
25-30	17	3	2
>30	10	7	9

Out of 83 participants grade 1 FLD was found in 10 (12%), grade 2 FLD in 7 (8.4%) and grade 3 FFD in 9 (10.8%) with BMI 25-30. Out of 83 participants grade 1 FLD was found in 10 (12%), grade 2 FLD in 7 (8.4%) and grade 3 FFD in 9 (10.8%) with BMI >30.

Operational definitions

Obesity is defined by body mass index (BMI) >95th centile for age and sex as per IAP charts.

Measurement of obesity

Body mass index (BMI)

Body weight is related to body fat and is highly dependent on height. Thereby BMI is defined as the weight adjusted to height squared is an index to assess overweight and is a reliable indicator of adiposity.

$$\textbf{Body mass index (BMI)} = \frac{\textbf{Weight in Kg}}{(\textbf{Height in meter})^2} = \text{kg/m}^2$$

With the above formulae, BMI can be calculated by measuring height and weight. BMI correlates with other measures of body fat in children and adolescents. BMI is also an indicator of secondary complications of obesity including current blood pressure, body lipids and long-term mortality.[18] As per WHO classification (for adults): BMI>25 = overweight, BMI >30 = obesity.

Grading of fatty liver disease

Grade 1- diffusely increased hepatic echogenicity but periportal and diaphragmatic echogenicity is still appreciable

Grade 2- diffusely increased hepatic echogenicity obscuring periportal echogenicity but diaphragmatic echogenicity is still appreciable

Grade 3- diffusely increased hepatic echogenicity obscuring periportal as well as diaphragmatic echogenicity.

Figure 1: Ultrasound of grade 1 fatty liver with increased liver echogenicity.

Figure 2: Ultrasound of grade 2 fatty liver with echogenic liver obscuring the echogenic walls of portal venous branches.

Figure 3: Ultrasound of grade 3 fatty liver in which diaphragmatic outline is obscured.

DISCUSSION

In our study, 61% of study subjects were female, 31% were male with p value<0.255 showing insignificance of sex in determination of fatty liver disease (FLD). 58% of the study subjects were in the age group 10 to 15 years. Even though the numbers of female participants were more than that of the male, higher percentage of male participants tested positive for FLD. A recent study by Cherian et al on obesity and overweight in urban school children of Kerala did not show any age-related trend. Prevalence of obesity was 3% for boys and 5.3% for girls.[13] The disparity may be due to small sample size and being a hospital-based study.

The first case of paediatric NAFLD was reported in 1983 by Moran et al.[6,7] It is now the most prevalent form of chronic liver disease in childhood and adolescence, affecting approximately 10-20% of the general paediatric population. In our study fatty liver present in 58% of the participants. A number of studies now suggest the

prevalence of NAFLD in overweight and obese youth to be up to 70%, compared to 7% in those of normal weight.[14,15] Severe obesity is also associated with more adverse clinical outcomes and greater risk of progression of FLD to NASH and cirrhosis in childhood.[16] Although possessing limited sensitivity, abdominal USG and liver function tests remain the first choice in diagnosing NAFLD in children. Children and adolescents with higher BMI have higher degrees of fatty liver seen on ultrasound. A highly significant relationship was observed between BMI and fatty liver (p=0.000). A Chinese study reported that 77% of obese children had evidence of hepatosteatosis on ultrasound but further investigations proved that only 24% of these individuals had fatty liver disease.[13] Younesian et al showed that high prevalence of obesity and anthropometric measurements are independent predicting factors for non-alcoholic fatty liver disease (NAFLD).[16] In 2015, Ardakani et al proved a high prevalence of fatty liver on ultrasound in obese children aged 5 to 15 years.[15] Adibi showed that the prevalence of fatty liver on ultrasound in obese children was 54.4%. Kruger et al reported that fatty liver could be seen on ultrasound of half of overweight or obese people.[17] In our study, the rate of ultrasound reports of fatty liver in children and adolescents with higher BMI were significantly higher. Most epidemiological studies, similar to ours showed a strong association between BMI and fatty liver on ultrasound.[18] Nowadays, due to the rise in global prevalence of over weightiness and obesity, fatty liver is seen more frequently. Panah believed that the risk of steatohepatitis was positively non-linearly correlated with BMI so that with every five-unit increase in BMI, the risk of developing steatohepatitis increased more than four folds.[17] Bahrami proposed that BMI is a strong indicator for steatohepatitis.[18] The results of the above-mentioned studies are consistent with our findings. In our study, the gender distribution in the samples was identical and there was no significant relation in terms of BMI between boys and girls. Fatty liver was found in 40% of girls and 59.2% of boys in these three groups, and this difference was statistically highly significant. In our study, waist circumference was higher in boys, and its size increased with age. There was no significant correlation between waist size and the degree of fatty liver on ultrasound. The number of cases of fatty liver on ultrasound increased with age. According to our findings, there was an association between overweightness and/or obesity and fatty liver. It is recommended to study the relationship between fatty liver, overweightness and obesity, especially in patients with definitive diagnosis of fatty liver. To reduce the risk of fatty liver disease, physical activity, reasonable diet and weight loss, should be recommended.

There are some limitations of the study. Ultrasound may be technically challenging to perform in patients with significant central obesity. In the presence of morbid obesity, the sensitivity and specificity of ultrasound fall to 49% and 75%, respectively, possibly due to technical problems in performing ultrasound in such patients. Furthermore, ultrasound is operator-dependant, and the sonographic evaluation of the liver is based mainly on the subjective visual assessment of hepatic echogenicity and posterior attenuation of the ultrasound beam, with consequent substantial observer variability.

CONCLUSION

The current study was conducted in 83 obese children of age group 6 to 15 years, to find out the prevalence of fatty liver and factors associated with it. The prevalence of fatty liver was found to be 57.8% indicating the fact that more than half of obese children in this age group may suffer from this clinical condition. Most of the children, who are suffering from fatty liver were associated with modifiable risk factors; particularly obesity. Immediate interventions should be initiated to control this problem. Due to the “western” lifestyle, obesity, metabolic syndrome and, consequently, NAFLD/NASH have reached epidemic proportions in the vulnerable pediatric population around the world. This fact should greatly concern the medical community. Pediatric NAFLD is a disease which progressively develops to NASH and cirrhosis of the liver, with several intermediate stages of fibrosis. Each of these stages is a unique clinical situation that demands specific corresponding treatment. Consequently, the need for accurate diagnosis and staging of this disease is of paramount importance. Additionally, screening methods in risk populations such as children with non-intervention tools are essential in order to balance the risk-benefit ratio. In this context, the current literature considers the classic ultrasound as the most suitable screening method and the first-choice diagnostic tool. According to our findings, there was an association between overweightness and/or obesity and fatty liver and grading was higher with increased BMI. It is recommended to study the relationship between fatty liver, overweightness and obesity, especially in patients with definitive diagnosis of fatty liver. To reduce the risk of fatty liver disease, physical activity, reasonable diet and weight loss, should be recommended.

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