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Original Research Article

Non-alcoholic fatty liver disease in obese and overweight children

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ABSTRACT

Background: Childhood obesity is rising alarmingly and approaching an epidemic proportion in many countries. It increases the risk of developing non-communicable disease in adulthood. Non-alcoholic fatty liver disease (NAFLD) is a key co-morbidity associated with obesity and emerged as the leading cause of chronic liver disease in children. This study aimed to see the prevalence of the NAFLD with overweight and obesity among children.
Methods: It was a cross sectional study conducted among children aged 5.5 to 18 years attending in the pediatric endocrinology clinic of department of pediatrics, Bangabandhu Sheikh Mujib medical university over a period of 14 months. Children's weight and height were evaluated and then BMI was calculated for particular age and sex according to center for disease control growth chart. All obese and overweight children were included except those taking systemic steroid, or suffering from genetic, endocrine, liver or renal disease. Patients were advised to do serum alanine aminotransferase (ALT) and ultrasonography of hepatobiliary system.
Results: A total of 90 children were enrolled in the study. Among them majority (93.3%) were obese and the rest were overweight (6.7%). Overall, 40% children had NAFLD including 40.5% among the obese and 33.3% among the overweight ($p>0.05$). Majority (91.6%) had mild NAFLD. Alanine amino transferase (ALT) level was raised significantly among children with NAFLD compared to those without NAFLD (58.3% and 16.7% respectively, $p<0.001$).
Conclusions: More than one-third of the overweight and obese children had NAFLD with a significantly higher level of ALT compared to children without NAFLD. Therefore, NAFLD should be routinely screened among children with increased weight to take timely intervention and prevent further progression of the disease.

Keywords: Obesity, NAFLD, ALT, Children

INTRODUCTION

Childhood overweight and obesity is rising alarmingly and approaching an epidemic proportion in many countries.[1] Over a span of last three decades the worldwide prevalence of childhood overweight and obesity rose by nearly 50%.[2] It is affecting not only the developed countries but also the developing world.[3] Approximately one in ten children of Bangladesh is either obese or overweight.[4]

Childhood obesity works as a risk factor for a number of chronic diseases like hypertension, type 2 diabetes, dyslipidemia, and NAFLD, thereby increasing morbidity

and mortality in later life.[5] NAFLD is the leading cause of chronic liver disease in children. In this disease there is accumulation of fat in the liver in the absence of excessive alcohol consumption or other known liver pathology.[6] It is a spectrum of disease ranging from steatosis (fat infiltration into the liver) to steatohepatitis, which is characterized by hepatocellular inflammation and injury, to fibrosis and eventually cirrhosis.[7] The prevalence of NAFLD in the pediatric population has been estimated to be between 3-12%, but this rate can be as high as 70-80% among the obese children.[8] It shows a significant difference by race and ethnicity with a higher prevalence among the Asian, and white children.[9]

The pathogenesis of NAFLD is complex and not fully understood because of the combination of environmental and genetic factors that contribute to the development of it.[10] Day and James proposed the "two hits" hypotheses in 1998.[11] The first hit is represented by peripheral insulin resistance, leading to fat accumulation in hepatocytes, and an increased lipid peroxidation leading to liver steatosis. The second hit is represented by oxidative stress, that produce reactive oxygen species (ROS) that induce hepatocellular injury by the inhibition of mitochondrial respiratory chain enzymes. ROS further causes lipid peroxidation, cytokine production contributing to hepatocellular injury and fibrosis.

To prevent progression of NAFLD to liver cirrhosis among children early detection and timely intervention is essential. But there is a dearth of literature which explored the prevalence of NAFLD among overweight and obese children of Bangladesh. Therefore, we aimed to explore the prevalence of NAFLD in obese and overweight children attending in a tertiary care center of the country.

METHODS

It was a cross sectional study conducted in Bangabandhu Sheikh Mujib medical university (BSMMU) from August 2017 to October 2018. All children 5.5 to 18 years old attending at the Pediatric Endocrinology outpatient department were approached for inclusion. After measurement of weight and height only obese and overweight children were included in this study. Children taking systemic steroid, suffering from genetic, endocrine, liver or renal disease were excluded from the study. A structured questionnaire was used to collect data regarding history, physical examination and investigations. The weight of the children was measured by an electronic weighing machine to a nearest 100 g and height was recorded using locally made height scale. The height scale was made up of two horizontal flat wooden boards, one for head-end and another for foot-end which were attached with a long vertical scale to the nearest 0.5 cm. To assess overweight and obesity, BMI was calculated and categorized for particular age and sex according to CDC growth chart. Children having BMI between ≥85th to <95th% was considered overweight and children having BMI≥95th% was considered obese. Waist circumference was measured between the iliac crest and lower rib case using an anthropometric tape.

Blood sample had taken for estimation of ALT. High ALT was defined as: ≥35U/L. Ultrasonography was, performed by same radiologist for all participants by using a 4D ultrasound machine (Model: GE voluson-730). Fatty liver was classified as mild, moderate, and severe according to hepatic echogenicity. Mild NAFLD was characterized by minimal diffuse increase in hepatic echogenicity with normal visualization of diaphragm and intrahepatic vessel borders. Moderate NAFLD was characterized by moderately diffuse increase in echogenicity with slightly impaired visualization of intrahepatic vessels and diaphragm. Severe NAFLD was characterized by marked increase in echogenicity with poor penetration of posterior segment of right lobe of liver, and poor or no visualization of hepatic vessels and diaphragm.

Informed consent was taken from parents and/or guardians of the children. Qualitative data were analyzed by chi-square test. Quantitative data were analyzed by Student's t test. Descriptive data was analyzed by frequency distribution table. Statistical analysis was performed by using SPSS version 22.0 for windows. P value less than 0.05 was considered significant.

RESULTS

A total of 90 obese and overweight children were enrolled in the study among them 84 (93.3%) were obese and 6 (6.7%) were overweight. Mean age, weight, height, BMI and waist circumference of the participants were 10.8±2.3 year, 59.4±17.1 kg, 144.6±13.5 cm, 27.8±4.5 kg/m^2, and 90.1±12.4 cm, respectively. It was observed that 67.8% belonged to age group 10-18 years, 32.2% belonged to age group 5.5 to <10 years. Of all, 62.2% were male, 57.8% had family history of obesity and 61.1% lived in urban area (Table 1).

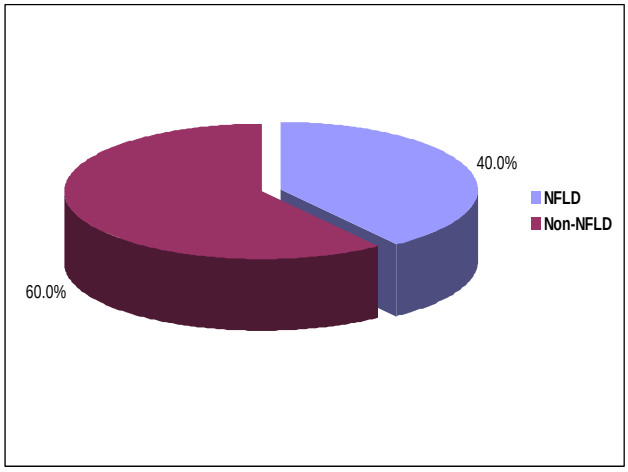

Figure 1: Distribution of study population according to presence of NAFLD (n=90).

Table 1: Socio-demographic profile of the participants, (n=90).

Characteristics	Frequency	Percentage (%)
Age (years)		
5.5-<10	29	32.2
10-18	61	67.8
Mean±SD, Range	10.8 ±2.3, 6.0-16.00	
Sex		
Male	56	62.2
Female	34	37.8
Male:female ratio	1.6:1	
Positive family history of obesity		
Yes	52	57.8
No	38	42.2
Residence		
Urban	55	61.1
Rural	35	38.9
Weight (kg), Mean±SD (kg/m^2)	59.4±17.1	
Height (cm), Mean±SD (cm)	144.6±13.5	
Weight circumference (cm), Mean±SD	90.1±12.4	
BMI category (kg/m^2)*		
Mean±SD	27.8 ±4.5	
Obese (≥ 95th percentile)	84	93.3
Overweight (>85-<95th percentile)	6	6.7

*According to CDC growth chart

Overall, 40% obese and overweight children had non-alcoholic fatty liver disease (Figure 1), 91.6%, 5.6% and 2.8% had mild, moderate, and severe non-alcoholic fatty liver disease, respectively (Table 2). There was no statistically significant difference in mean age (p=0.45), weight (p=0.38), height (p=0.70), BMI (p=0.15) and waist circumference (p=0.58) between non-alcoholic fatty liver disease and non-NAFLD children (Table 3). 40.5% obese children had non-alcoholic fatty liver disease and 33.3% overweight children had Non-alcoholic fatty liver disease and the difference wasn't statistically significant (p=0.73) (Table 4). Serum ALT was raised in 58.3% of non-alcoholic fatty liver disease children, and 16.7% of non-NAFLD children and raised ALT was significantly associated with non-alcoholic fatty liver disease (p≤0.001) as shown in the Table 5.

Table 2: Grading of fatty liver disease among the NAFLD group, (n=36).

Grading	Number	Percentage (%)
Mild	33	91.6
Moderate	2	5.6
Severe	1	2.8
Total	36	100

Table 3: Age and anthropometric measures of obese and overweight children in relation to presence of NAFLD, (n=90).

Variables	NAFLD, (n=36), Mean±SD	Non-NAFLD, (n=54), Mean±SD	P value
Age (years)	11.02±2.32	10.63±2.36	0.450
Weight (kg)	61.35±15.36	58.15±18.13	0.386
Height (cm)	145.29±12.72	144.18±14.17	0.706
WC (cm)	93.08±14.97	88.02±9.92	0.058
BMI (kg/m^2)	28.64±4.28	27.26±4.54	0.150

P value was determined by Independent samples t test

Table 4: Association of NAFLD with overweight and obese children, (n=90).

Variables	Obese, (n=84), n (%)	Overweight, (n=6), n (%)	Total, (n=90), n (%)	P value
NAFLD	34 (40.5)	2 (33.3)	36 (40)	0.730
Non-NAFLD	50 (59.5)	4 (66.7)	54 (60)	
Total	84 (100)	6 (100)	90 (100)	

P value was determined by Chi-square test

Table 5: Comparison of ALT level between NAFLD and non-NAFLD study population, (n=90).

ALT	NAFLD, (n=36), n (%)	Non-NAFLD, (n=54), n (%)	Total, (n=90), n (%)	P value
Normal (<35U/L)	15 (41.7)	45 (83.3)	60 (40)	<0.001
Increased (≥ 35U/L)	21(58.3)	9 (16.7)	30 (60)	
Total	36 (100)	54 (100)	90 (100)	

P value was determined by Chi-square test.

DISCUSSION

NAFLD is the most important comorbidity of obesity and the most common cause of chronic liver disease in children. It may progress to end stage liver disease. So early diagnosis of NAFLD is important. There is a paucity of literature on the prevalence of NAFLD in overweight and obese children in Bangladesh. Hence this study aimed to explore that gap in knowledge.

We found NAFLD in 40% of all children who participated in this study. This is concordant with a previous study which found NAFLD in 36% of obese Bangladeshi children.[12] While Chinese obese children were found to have hepatic steatosis in 77% cases by Chan et al and in 68.18% cases by Fu et al.[13,14] In India a

study by Pawar et al found that prevalence of non-alcoholic fatty liver disease in obese and overweight children was 62%.[15] NAFLD is classified as mild, moderate, and severe. We found more than ninety percent of participants in our study had mild NAFLD. This corresponds with other studies conducted in Bangladesh, China and Iran which showed that NAFLD among children were mostly mild.[12,16,17]

A comparison of age and anthropometric measurements between children with NAFLD and non-NAFLD in our study showed statistical similarly. In contrast, Rong et al found that BMI in NAFLD group was significantly higher than non-NAFLD group, and Rafeey et al and Chan et al showed in their studies, that NAFLD was positively correlated with BMI and waist circumference.[13,15,17] This difference in findings could be due to the differences in sample size, ethnic variation, and design of these studies.

The NAFLD prevalence was higher in obese children (40.5%) than that of overweight children (33.3%) in our study. However, the difference was not statistically significant ($p>0.05$). This finding is comparable to other studies. The American national health and nutrition survey found that 6% of overweight and 10% of obese adolescents had NAFLD in 2011 showing that the NAFLD burden among obese children is relatively higher than that of overweight children.[18] This is also evident in a Chinese study by Rong et al.[16] where the prevalence of NAFLD in overweight and obese boys were reported to be 25.5 and 75.5% respectively. The same study found the prevalence to be 6.2 and 29% in overweight and obese girls respectively.

ALT is considered to be the most specific marker of liver damage, and NAFLD is one of the most common causes of liver disease worldwide. Serum ALT activity is most available and inexpensive test for initial evaluation of NAFLD. In this study serum ALT was raised significantly in NAFLD group (58.3%) in comparison to non- NAFLD group (16.7%) ($p<0.001$). This is supported by result of Shelim et al who found high ALT in NAFLD group than non-NAFLD group ($p=0.04$).[12] A raised ALT level was also noted among 47.1 and 30% children with NAFLD in studies by Rafeey et al and Pawer et al respectively.[15,17] These indicates a raised ALT among otherwise apparently healthy overweight and obese children should raise concern about presence of NAFLD among them. The study was limited in that it had a small non-randomized sample and was a single center study. However, the strength of this study was that it was one of the few reports regarding non-alcoholic fatty liver disease among overweight and obese children of the Bangladesh.

CONCLUSION

The present study showed a high prevalence of NAFLD in overweight and obese children. In addition, a significant rise in ALT was noted among children with NAFLD. Early diagnosis of the disease with timely intervention is necessary to protect children from progression of NAFLD to cirrhosis. So, ultrasonography and liver function test should be utilized in overweight and obese children for early detection of NAFLD.

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