The Prevalence of Non-alcoholic Fatty Liver Disease and its Association with Metabolic Syndrome and Obesity in Pediatric Population of North India

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Abstract
Background: This study was conducted to evaluate the prevalence of fatty liver and its association with the metabolic syndrome and its components in school children of Kashmir valley of north India.

Methods: In this cross-sectional study, a total of 1112 children aged 4-18 years were selected from different schools of Kashmir valley. Anthropometric assessments, blood pressure measurements and fasting blood samples were obtained after proper consent. Ultrasonography was performed by a single sonologist on prefixed dates. Fatty liver was defined by already established criteria for fatty liver disease. Metabolic syndrome was defined according to Adult treatment panel III criteria. Analysis and inferences were drawn using Student’s test, chi-square test, Man Whitney U test and logistic regression analysis.

Results: The overall prevalence of fatty liver was 7.4%. The Prevalence of fatty liver in children with metabolic syndrome was 44.4% and in obese children it was 61%. Body Mass Index, waist circumference and metabolic syndrome are strongly correlated with the prevalence of fatty liver.

Conclusion: This study is the first study from India on the prevalence of fatty liver disease in children. The estimates of our study are unexpectedly high and immediate attention is needed to address the problem.

Keywords: Fatty liver disease; Metabolic syndrome; Central obesity; Body Mass Index (BMI)

Introduction

The global epidemic of childhood obesity has become a serious public health concern [1]. Recent studies suggest that the prevalence of non-alcoholic fatty liver disease (NAFLD) is increasing in children [2,3] especially in obese children [4,5]. This condition is considered to be the most common form of chronic liver disease in the pediatric population [6]. The clinical presentation of NAFLD ranges from simple steatosis, to steatohepatitis, fibrosis, and even to cirrhosis [2,3]. The prevalence of NAFLD seems to be higher than expected [7].

NAFLD is undoubtedly associated with Insulin resistance and metabolic syndrome (MS) [8]. The liver injury in fatty liver is strongly associated with atherogenicity of lipid profile [9]. In addition of having direct correlations with metabolic abnormalities of MS, fatty liver appears to increase the risk of type 2 Diabetes mellitus and dyslipidemia [10,11].

Abnormalities of fat metabolism lead to increased free fatty acid flux from adipose tissue to non-adipose tissue like liver which in turn participates and propagates many of the fundamental metabolic derangements that are characteristic of the insulin resistance syndrome and type 2 diabetes [12,13]. Being an essential component of MS, obesity and insulin resistance account for high incidence of fatty liver in patients with MS. Liver enzyme elevations have been shown to be directly related with the presence of metabolic components of MS [14].

NAFLD probably is the most common form of liver disease in children. It is likely that it will continue to increase with increasing obesity and MS in childhood [15]. The relationship of NAFLD to the MS and its components needs more investigations [16]. Research is needed to know whether the presence of NAFLD and elevated serum aminotransferases levels in children would predict onset of diabetes in adults.

Although prevalence of obesity in Kashmiri Adult population is known, no data exists on childhood obesity and prevalence of NAFLD from this northern Indian state. We tried to study the prevalence of NAFLD and the impact of metabolic parameters like Waist circumference, Body mass index and dyslipidemia on fatty liver disease in this adolescent population of Kashmir.

Research Design and Methods

A total of 1112 children in the age group 4-18 years were studied in this population based prospective study during September 2009 to September 2011 from different schools of Kashmir valley. After taking proper consent from the parents, following children were included in the study- (a) Children who had consent from parents (b) Children who were not suffering from any metabolic disease (c) Children not on any medication.

We used Ultrasonography (US) [17] abdomen as the diagnostic tool to estimate prevalence in this population based study. Liver biopsy was not found appropriate given the nature of study. Liver enzymes although estimated were not used for diagnostic purposes. US were performed by using Sonoline SL-2 machine of Seimens Ltd. with 7.5 MHz curvilinear probe. All US evaluations were done by the same senior sonologist to decrease interobserver error.

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Anthropometric assessment and laboratory parameters

Body weight was measured by an electronic scale (Filizola®) to the nearest 0.1 kg while the school children were barefoot and wearing light clothes. Height was determined by a portable Seca stadiometer to the nearest 0.1 cm, according to norms proposed by the World Health Organization [18]. BMI (Body Mass Index) was calculated by using the measured height and weight and converted to percentiles for age in months and gender by using the Center for Disease Control and Prevention [19] growth charts and computer software Epi-Info version 3.2 (2004). Indian BMI Percentile were used to classify children under weight if their calculated z-score placed them below the 5th percentile, healthy weight if between 5th and 84.9th and overweight between the 85th and 94.9th and obese if it was above 95th percentile for age and gender [20,21]. Waist circumference was measured midway between the rib cage and the superior border of the iliac crest by using a milli-meter non-extensible and non-elastic measuring tape (Sanny®) after complete expiration. Central obesity was present if waist circumference was >90th percentile for age and gender.

On prefixed dates, a 10 ml fasting non heparinized venous blood sample was drawn from non dominant arm without using tourniquet. Serum was separated within 2 hours of venipuncture, and analysis was done within 24 h. Blood samples were analysed for blood glucose and lipid profile with commercially available enzymatic reagents (Audit Diagnostics, Ireland) adapted to the Hitachi 912 auto analyzer. Metabolic syndrome was defined according to Adult Treatment Panel III criteria [22].

Entire data was subjected to suitable standard statistical technique. Uni-variate analysis was done applying Chi-square test, t test. The analysis were performed using SPSS statistical package 11.17.

Results

The studied population of 1112 children consisted of 672 females and 440 males. The mean age was 13.4 ± 3.8. The basic distribution and clinical characteristics of study population is shown in table 1.

Overall Prevalence of fatty liver was 7.4%. It was more in females as compared to males (7.8% and 6.6% respectively). This difference was statistically insignificant. The prevalence increased with age in male children with highest prevalence around age group 13-15 years (Figure 1). However females did not show similar relationship with age (Figure 1).

Centrally obese children showed significantly high prevalence of fatty liver as compared to normal children (52% vs. 5%, p<0.05). High prevalence was seen among children with MS and high BMI (44.4% and 61% respectively) as compare to normal children (52% vs. 5%, p<0.05). High TG and low HDL-c were the most common constituent of metabolic syndrome (Table 3). Both High TG and low HDL-c showed significantly high prevalence of fatty liver (Table 3).

Discussion

A constant link has been demonstrated between central obesity, insulin resistance and MS both in children and adults [23,24]. NAFLD has been shown to be the new and important hepatic correlate of insulin resistance and the metabolic syndrome [25,26]. The prevalence of fatty liver in the general population of western countries is 20-30%. The prevalence of NAFLD among United States children is 3-10%, rising up to 40-70% among obese children [27]. Taken together, the prevalence of fatty liver in obese children in China, Italy, Japan, and the United States has been reported to be between 10% and 77% [28-30]. Our study is the first study from India which was designed to evaluate the prevalence of fatty liver in children and to know its association with MS and its metabolic parameters. The prevalence estimates in our study are comparable to those found in most western studies. High prevalence was observed in normal children with females being more commonly affected as compared to males. This difference though statistically insignificant could be because of high prevalence of obesity.
been carefully studied, the impact of fatty liver in the natural history of Adipose Tissue, in the pathophysiology of metabolic diseases such as Metabolic Syndrome (MS) has been shown to predict the development of fatty liver. This observation is obvious considering fatty liver as one of the prevalent causes in children and adolescents. Int J Obes Relat Metab Disord 28: 1257-1263.


Nonomura A, Mizukami Y, Unoura M, Kobayashi K, Takeda Y, et al. (1992) Liver histology is required as the gold standard for precise diagnosis of fatty liver. US is sensitive in diagnosing steatosis; however, it cannot distinguish between steatohepatitis and other types of NAFLD [33]. Most studies have used US for the diagnosis because of simplicity in usage, ease of administration and non-invasiveness. US can be useful in prevalence studies and large epidemiological studies. Liver biopsy nevertheless is considered as the gold standard for diagnosis of NAFLD.

There exists a strong relationship between obesity, MS and fatty liver [34,35]. We found a strong correlation of fatty liver with BMI. A similar association was observed in a study from Japan [24]. We estimate the prevalence of fatty liver in centrally obese children as 52% as compared to normal children (5%). Also the observation that prevalence significantly increased with increase in BMI percentiles from underweight to obesity confirms the role of obesity in defining the prevalence of fatty liver.

The age and sex related trends observed in the prevalence of fatty liver are same as observed in adults in different prevalence studies of MS [36,37]. This observation is obvious considering fatty liver as one of the metabolic surrogate of MS presenting as hepatic insulin resistance [38,39]. Given the relationship of metabolic parameters with fatty liver, MS has been shown to predict the development of fatty liver [40].

This unexpected prevalence of fatty liver in Northern Indian adolescent population particularly in obese children and its association with metabolic parameters of MS is of great concern which needs immediate attention and intervention.

**Conclusion**

Although the role of adipose tissue, and particularly Visceral Adipose Tissue, in the pathophysiology of metabolic diseases such as obesity, dyslipidemia, metabolic syndrome and atherosclerosis have been carefully studied, the impact of fatty liver in the natural history of these diseases and vice versa has long been underestimated. There is strong support indicating that different aspects of fatty liver exist and are associated with severe or merely moderate metabolic disturbances.

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**References**


