Research Paper

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Ultrasonographic Prevalence of Non-Alcoholic Fatty Liver Disease (Nafld) in Kashmir Valley School Children

Medical Science

KEYWORDS: NAFLD, BMI, Metabolic syndrome.WW

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ABSTRACT

Background: The problem of obesity in children has grown considerably in recent years globally as well as in India. This rise in obesity prevalence has resulted in marked increase in the magnitude of non-alcoholic fatty liver disease (NAFLD) in the pediatric age group. Therefore, NAFLD is currently the most common hepatic disorder in pediatric hepatology practice. Objective: To evaluate the prevalence of NAFLD in school children from Kashmir valley using transabdominal ultrasonography.Methods: In this cross-sectional study 1115 children in the age group of 4-18yrs from four different schools of the Kashmir Valley were examined. All subjects underwent detailed clinical evaluation including history, anthropometric assessment and blood pressure measurements. Fasting blood glucose, lipids and transabdominal ultrasonography was done in the fasting state. Results: Mean age of children was 13.4 ± 3.8 years with range of 4-18 years. Out of 1115 children, 675 were girls and 440 boys. Overall ultrasound suggestion of NAFLD in children was 7.43% and among whom 82 (7.5%) were girls and 29(6.5%) were boys. On the basis of socioeconomic stratification 7.4% belonged to upper socio-economic status and 7.3% to lower socio-economic status. Prevalence of NAFLD in children with metabolic syndrome was 56% while as prevalence of NAFLD in obese children was 26%. Body mass index and waist circumference were significant predictors of metabolic syndrome and NAFLD.Conclusion: Our study shows body mass index and waist circumference measurements have significant impact on the prevalence of NAFLD in school children of Kashmir valley

INTRODUCTION

The global epidemic of childhood obesity has become a serious public health concern 1, and recent studies suggest that the prevalence of NAFLD is increasing in children 2, 3, especially in obese children 4, 5. NAFLD probably is the most common form of liver disease in children and seems likely to increase with increasing obesity and the metabolic syndrome in childhood 6. Insulin resistance7 with the concomitant presence of abdominal adiposity, dyslipidemia, hypertension or type 2 diabetes mellitus is regarded as the main risk factor for cardiovascular diseases. Reaven (1988) 7 described syndrome X as a cluster of factors such as abdominal adiposity, dyslipidemia, hypertension and insulin resistance, emphasizing the role played by the latter as a possible precursor factor for the other diseases. The term syndrome initially was used by a group of researchers whose main focus was diabetes mellitus 8 while as other researchers concentrating on diabetes mellitus and hyperinsulinemia as possible causal factors disregarded overweight 9, 10. Later on the Adult Treatment Panel III -National Cholesterol Education Program (ATPIII-NCEP) began to refer the syndrome as the metabolic syndrome (MS), with the purpose to use the term in the more global context and consider other causal factors related with abdominal fat excess 11.

The underlying pathophysiology of the metabolic syndrome remaining elusive insulin resistance is considered to play an important role in the background of genetic predisposition. Obesity is the central factor in the pathogenesis of insulin resistance and factors such as hypertension, dyslipidemia, and subclinical inflammation are more likely its consequences rather than the cause. Thereby insulin resistance may play any substantive role in the pathophysiology of the MS in children 12. Interestingly, apart from these factors, there is evidence that NAFLD may play a critical role in the determination of hepatic insulin resistance 13. NAFLD, sometimes resulting in non-alcoholic steatohepatitis (NASH) and occasionally cryptogenic cirrhosis 14, has been shown to be the new and important hepatic correlate of insulin resistance and the MS.

RESEARCH DESIGN AND METHODS

Subjects

This cross-sectional study was undertaken by departments of Gastroenterology, Clinical biochemistry and Endocrinology of our Institute from October 2008 to October 2010. A total of 1115 children in the age-group of 4-18 years from four different schools of the Valley of Kashmir were studied. The study was approved by Ethics committee of our Institute and prior permission was obtained from directorate of School Education Kashmir and the respective school principals. Schools were selected by simple random method and an informed consent from parents of children was obtained for purposes of examination and drawing blood sample. By systematic random sampling method section A of each class was selected. Children included in the study were: (a). Children who had consent from parents. (b). Children who were not suffering from any metabolic disease. (c). Children who were not taking any hypolipidemic or hypoglycemic drugs or any form of medication. All the children who did not meet the above criteria were excluded from the study.

On the day of study a medical team including a sonologist visited the school at a prefixed date and children were advised to come fasting on the day. A fasting (8-10 hours) blood sample was obtained from antecubital vein using a vacoutainer. The samples were centrifuged and immediately stored at -200C for assay of plasma glucose, lipid profile (triglycerides, HDL, and LDL). Clinical assessment included detailed information about the medical facts, any sicknesses, drug intake etc. and a brief examination. All children were subjected to anthropometric measurements including height, body weight and waist circumference (WC). Body weight was measured while the children were barefoot and wearing light clothes by an electronic scale to the nearest 0.1 kg. Height was determined by a portable stadiometer to the nearest 0.1 cm, according to norms proposed by the World Health Organization, 1995 15. Height and weight measurements were taken twice and the mean of two measurements was used to calculate BMI, which was defined as the ratio

of body weight to body height squared, expressed in Kg/m2. Every morning, the scale and stadiometer were calibrated with standard weight and height respectively. The inter-observer and intra-observer variations of the values obtained was <3%. WC was measured midway between the rib cage and the superior border of the iliac crest by using a mill metric non-extensible and non-elastic measuring tape in complete expiration. Ultrasonographic examination was performed on the same day using using a portable ultrasound machine (Sonosite Titan, Germany) with a 7.5 MHz transducer. The USG diagnostic patterns of NAFLD were based on the presence of a 'bright' liver (brightness and posterior attenuation) with stronger echoes in the hepatic parenchyma than in the renal parenchyma, vessel blurring and narrowing of the lumen of hepatic veins in the absence of findings suggestive of other chronic liver diseases. The degree of NAFLD evaluated by USG reflected the degree of steatosis. A liver displaying increased but homogenous dot reflection, blurred but still discernible vascular profiles and weak portal vein echogenicity was defined as early-stage. A medium-stage fatty liver disease was characterized by disappearance of the portal vascular wall and slightly increased liver volume. Patients with nebulous optical appearance in the liver, little portal vein echogenicity in more than 1/3-1/2 of the liver area and increased liver volume were considered to be in the advanced stage16. The definition of MS for children was derived from modified cut-off for children. Participants had to meet three of the following criterion: fasting blood glucose of ≥ 110 mg/dl, serum triglycerides ≥ 150 mg/dl, HDL≤40 mg/dl, systolic blood pressure or diastolic blood pressure ≥ 90th percentile for age and gender, and waist circumference ≥ 90th percentile for age and gender 17. International Diabetes foundation (IDF) and WHO criterion were also used for definition of MS18 .

Data was analysed using SPSS statistical package 14.0. Continuous variables were expressed as mean+SD. A significance level of p=0.05 was selected for all statistical tests. Chi-square was used to examine whether there was any difference in the prevalence of NAFLD according to sex. Selected anthropometric and metabolic risk factors for NAFLD were analysed by univariate logistic regression

RESULTS

Mean age of children was 13.4 ± 3.8 years and the studied population mostly comprised of girls (60.5%) than boys (39.5%). Out of 1115 children 675 were girls and 440 were boys. Out of them 615(55.2%) belonged to lower socio-economic status and 500(44.8%) belong to upper socio-economic status. In the subcategory of upper socio-economic status minimum age was five years and maximum was 18 years with a mean age of 11.06±2 while as mean age was 15.39±3.5 years in the lower socio-economic status subgroup with a range of 4 to 18 years. The age distribution showed that 41.4% belonged to age group of 16-18 and as per sex distribution girls accounted for 60.5% of total population studied. Table 1 shows the basic distribution of subjects according to demographic variables.

Overall prevalence of NAFLD was 7.2% with the highest prevalence in the age group of 16-18 (table 2). Data of three children was not available. There was significant difference in the prevalence of NAFLD between normal children and with MS. In 52% boys and 33% girls with metabolic syndrome had NAFLD as compared to 5% boys and 6.4% girls had NAFLD in absence of MS (table 3). Similarly NAFLD on USG was noted in 52% of children with high waist circumference as compared (5%) to children with normal waist circumference (table 4). The prevalence of fatty liver was higher in overweight and obese children as 26% and 61% respectively (table 5).

DISCUSSION

NAFLD, sometimes results in non-alcoholic steatohepatitis (NASH) and occasionally cryptogenic cirrhosis19. It has been shown to be the new and important hepatic correlate of insulin resistance and the metabolic syndrome. NAFLD probably is the most common form of liver disease in children and is likely to continue to increase with increasing obesity and metabolic syndrome in childhood 20. Often NASH may be the first clinical indicator of insulin resistance21. In a study conducted in children and adults with muscle-liver-brain-eye nanism, NAFLD was present in all adolescents and adults, and 46% of prepubertal children and 70% of adults fulfilled the NCEP criteria for the MS 22. Early development of NAFLD in non-obese prepubertal children suggests that accumulation of fat in the liver may be the crucial step in the development of insulin resistance 23. The prevalence of NAFLD has been reported to be about 2.6% of urban children in Japan 22. Manco et al 24 conducted a cohort study and concluded that metabolic syndrome, insulin resistance, and NAFLD in children were interrelated. In their cohort study, Hamaguchi et al 25 showed that metabolic syndrome is a predictor for NAFLD. Despite these studies, the relation of NAFLD to the metabolic syndrome in children needs more investigation25.

In our study, we observed that there is a strong relationship between waist circumference and non-alcoholic fatty liver disease and we also noticed a linear trend and high odd ratio between clustering metabolic syndrome components and NAFLD. Kunihiko Tominaga et al also carried a study in which they showed a strong relationship between waist circumference and non-alcoholic fatty liver disease and they also noticed a linear trend and clustering metabolic syndrome components and NAFLD in agreement with our results 22. These findings support the importance of an ultrasonographic examination of NAFLD in children as a simple and useful tool to detect the insulin-resistant condition as well as metabolic syndrome because NAFLD may be a hepatic symptom of insulin resistance and/or metabolic syndrome. Thus, our cross-sectional, case–control study revealed a relationship between fat accumulation in the liver and the magnitude of insulin resistance and metabolic syndrome in the pediatric population.

A number of studies have shown that obesity per se is not always related to the development of NAFLD. Nobili et al 26 reported that children with NAFLD are almost always insulin resistant regardless of BMI. Conversely, in our population-based study, WC was an independent risk factor for NAFLD. We conclude that WC should be recognized as a simple and variable parameter to estimate liver fat accumulation. The results of a cohort study carried by Hamaguchi et al in which those participants with NAFLD and metabolic syndrome at baseline developed cardiovascular disease faster than their control counterparts. These researchers concluded that NAFLD—but not metabolic syndrome—retained a statistically significant correlation with cardiovascular disease27.

NAFLD in children and adolescents has a very close relationship with metabolic syndrome, insulin resistance, and WC. Ultrasonographic examination can be considered reliable procedure in any population-based screening for NAFLD. Among the anthropometric indices the most sensitive, simplest, and cost-effective index for the pediatric NAFLD is a WC measurement.

Table 1: Age and Gender distribution of the studied subject

Age	Female	Male	Total
4-9	87 (7.8%)	129 (11.5%)	216 (19.3%)
10-12	112 (10.0%)	106 (9.5%)	218 (19.5%)
13-15	106 (9.5%)	113 (10.1%)	219 (19.6%)
16-18	370 (33.2%)	92 ((8.3%)	462 (41.4%)
Total	675 (60.5%)	440 (39.5%)	1115(100%)

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Age Group	Ultra-sonography	SEX		Total	P value
		Male	Female		
4-9	Normal	126 (97.6%)	83 (95.0%)	209	P>0.05
	Fatty	3 (2.4%)	4 (4.8%)	7 (3.2%)	
10-12	Normal	103 (97.1%)	104 (92.0%)	207	P>0.05
	Fatty	3 (2.9%)	8 (8.0%)	11 (5.0%)	
13-15	Normal	104 (92.0%)	91 (85.0%)	195	P>0.05
	Fatty	9 (8.0%)	15 (4.8%)	24 (10.0%)	
16-18	Normal	76 (84.5%)	343 (92.9%)	419	P<0.05
	Fatty	14 (15.5%)	26 (7.1%)	40 (8.7%)	

Table 3: Effect of Metabolic syndrome on Prevalence of Fatty liver

Metabolic Syndrome	Ultra-sonography	Gender		Total	P value
		Male	Female		
Absent	Normal	399	611	1010	P< 0.05
	Fatty liver	24 (5.0%)	42 (6.4%)	66	
Present	Normal	10	10	20	
	Fatty liver	5 (33.0%)	11 (52.0%)	16	

Table 4: Effect of waist circumference on prevalence of Fatty liver

Ultra Sonography	Obesity Central		Total	P value
	Normal	Obese		
Normal	1011 (95.0%)	19 (48.0%)	1030 (93.0%)	<0.05
Fatty liver	59 (5.0%)	23 (52.0%)	82 (7.0%)	
Total	1070 (94.3%)	42 (3.7%)	1112 (100%)	

Table 5: Effect of BMI on prevalence of fatty liver

Ultra Sonography	Obesity CDC				Total	P value
	Under wt.	Normal wt.	Over wt.	Obese		
Normal	16	966	25	13	1112	P< 0.05
Fatty%	0	52 (5.0%)	9 (26.0%)	21 (61.0%)		
Total	16	1028	34	34	1112	

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