Journal of Metabolic Syndrome
ISSN: 2167-0943

Parry et al., J Metabolic Synd 2012, 1:5
DOI: 10.4172/2167-0943.1000118

Research Article Open Access

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

Irshad Ahmad Parry[1], Riyaz Ahmad Bhat[1]* and Imran Khan[1]

[1]Department of Internal Medicine, Sher-i-Kashmir Institute of Medical Sciences, Srinagar, Kashmir, India

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 toll 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.

Corresponding author: Dr. Riyaz Ahmad Bhat, Department of Internal Medicine, Sher-i-Kashmir Institute of Medical Sciences, Srinagar, Kashmir, India, Tel: 9419604468; E-mail: bhatdrriaz@hotmail.com

Received December 01, 2012; **Accepted** January 23, 2013; **Published** January 25, 2013

Citation: Parry IA, Bhat RA, Khan I (2012) The Prevalence of Non-alcoholic Fatty Liver Disease and its Association with Metabolic Syndrome and Obesity in Pediatric Population of North India. J Metabolic Synd 1:118. doi:10.4172/2167-0943.1000118

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-metric 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 16-18 years of age (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 with statistically significant difference (Table 2). BMI had significant impact on the prevalence of fatty liver among various metabolic parameters. Children with abnormal lipids did not show statistically significant difference in the prevalence as compared to normal children (Table 2).

Parameters	Men (n=440)	Women (n=672)	Total (n=1112)
Age (years)	11.06 ± 2.7	15.39 ± 3.5	13.45 ± 3.8
Systolic blood pressure (mm/Hg)	103.41 ± 8.2	108.07 ± 11.3	105.98 ± 10.3
Diastolic blood pressure (mm/Hg)	66.34 ± 5.9	71.37 ± 7.7	69.11 ± 7.4
Waist circumference (cm)	55.69 ± 12.2	70.47 ± 11.4	63.84 ± 13.9
Fasting blood glucose (mmol/L)	4.70 ± 0.71	4.76 ± 0.52	4.73 ± 0.62
Triglycerides (mmol/L)	1.34 ± 0.32	1.38 ± 0.41	1.36 ± 0.37
HDL-cholesterol (mmol/L)	1.06 ± 0.12	1.08 ± 0.14	1.07 ± 0.13

Table 1: Clinical characteristics of studied population.

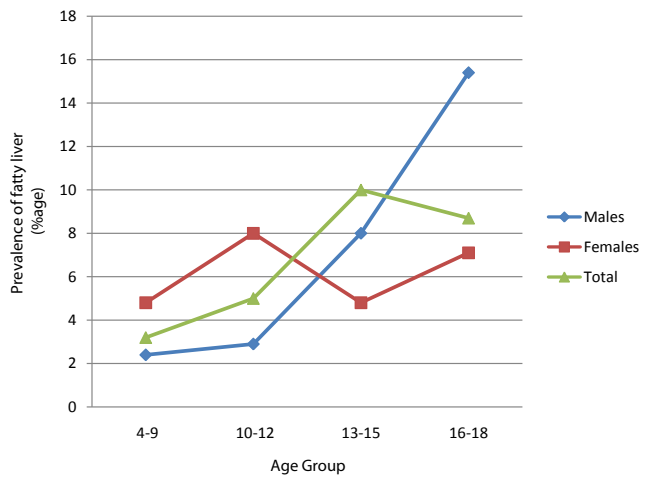

Figure 1: The prevalence of fatty liver increased with age in males with highest prevalence in the age group 16-18 years. Females presented highest prevalence around age group 13-15 years.

Parameters		Ultrasonography			
		Normal	Fatty Liver	Total	P value
WC	Normal	1011 (95 %)	59 (5 %)	1070	P<0.05
	Increased	19 (48 %)	23 (52 %)	42	
Lipids	Normal (total)	299 (94%)	19 (6.0%)	318	p>0.05
	High TG	328 (92.1%)	28 (7.8%)	356	
	Low HDL-c	183 (93.8 %)	12 (6.2%)	195	
	Both High TG and low HDL-c	220 (90.5%)	23 (9.4%)	243	
BMI	Low BMI	16 (100%)	0 (0%)	16	P<0.05
	Normal BMI	966 (94.8%)	52 (5%)	1018	
	Overweight	25 (73.5%)	9 (26%)	34	
	Obese	13 (38.2%)	21 (61%)	34	
MS	Absent	1010 (93.8%)	66 (6.1%)	1076	P<0.05
	Present	20 (55.5%)	16 (44.4%)	36	

WC: Waist Circumference; BMI: Body Mass Index; MS: Metabolic Syndrome; TG: Triglycerides; HDL-c: High Density Lipid Cholesterol.

Table 2: Relationship of metabolic parameters with fatty liver.

WC, BMI and MS showed strong positive correlations with fatty liver. BMI was the single most parameter having strong correlation with 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

		Age Group	SEX	WC	Obesity (BMI)	MS (ATP)	Dyslipidemia#
Fatty liver	Correlation coefficient	.080 (**)	.023	.340 (**)	.399 (**)	.259 (**)	.037
	Significance (2-tailed)	.008	.439	.000	.000	.000	.221

WC: Waist Circumference; ATP: Adult Treatment Panel; BMI: Body Mass Index; MS: Metabolic Syndrome.
WC, BMI and MS have significant positive correlation with fatty liver.
**Correlation is significant at .01 levels (2-tail).
*Correlation is significant at .05 levels (2-tail).
#Dyslipidemia includes hypertriglyceridemia, low HDL-C, and combined abnormalities of both parameters.

Table 3: Correlations of different parameters with Fatty liver.

in females as compared to males. Also an alarmingly high prevalence was observed in children with MS and obesity. This observation proves the relationship which has been observed between fatty liver and metabolic parameters of MS [25,31,32].

The prevalence of obesity in our adolescent population is not known. This high prevalence of NAFLD in our population could be because of the fact that there has been a drastic change in life style and dietary habits over the last decade in addition to sedentary life habits because of the cold weather conditions prevailing in most part of the year.

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 observation 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.

Acknowledgements

The authors are highly thankful to the parents and their children for the cooperation they extended during the study. The support of paramedical staff from the department of Radiodiagnosis, SKIMS, Srinagar Kashmir India is highly acknowledged. The authors are obliged to thank Saba Riyaz, SA, from the department of Statistics for the help and support in statistical analysis.

Source of funding: The study was funded by ethical and grants committee, SKIMS, Srinagar India.

References

1. Kosti RI, Panagiotakos DB (2006) The epidemic of obesity in children and adolescents in the world. Cent Eur J Public Health 14: 151-159.
2. Fraser A, Longnecker MP, Lawlor DA (2007) Prevalence of elevated alanine aminotransferase among US adolescents and associated factors: NHANES 1999-2004. Gastroenterology 133: 1814-1820.
3. Mager DR, Roberts EA (2006) Nonalcoholic fatty liver disease in children. Clin Liver Dis 10: 109-131, vi-vii.
4. Chan DF, Li AM, Chu WC, Chan MH, Wong EM, et al. (2004) Hepatic steatosis in obese Chinese children. Int J Obes Relat Metab Disord 28: 1257-1263.
5. Sagi R, Reif S, Neuman G, Webb M, Phillip M, et al. (2007) Nonalcoholic fatty liver disease in overweight children and adolescents. Acta Paediatr 96: 1209-1213.
6. Sherlock S, Dooley J (2002) Diseases of the liver and biliary system. Oxford: Blackwell Science, UK.
7. Imhof A, Kratzer W, Boehm B, Meitinger K, Trischler G, et al. (2007) Prevalence of non-alcoholic fatty liver and characteristics in overweight adolescents in the general population. Eur J Epidemiol 22: 889-897.
8. Rocha R, Cotrim HP, Carvalho FM, Siqueira AC, Braga H, et al. (2005) Body mass index and waist circumference in non-alcoholic fatty liver disease. J Hum Nutr Diet 18: 365-370.
9. Nobili V, Alkhouri N, Bartuli A, Manco M, Lopez R, et al. (2010) Severity of liver injury and atherogenic lipid profile in children with nonalcoholic fatty liver disease. Pediatr Res 67: 665-670.
10. Sung KC, Kim SH (2011) Interrelationship between fatty liver and insulin resistance in the development of type 2 diabetes. J Clin Endocrinol Metab 96: 1093-1097.
11. Adiels M, Taskinen MR, Borén J (2008) Fatty liver, insulin resistance, and dyslipidemia. Curr Diab Rep 8: 60-64.
12. Day CP, James OF (1998) Steatohepatitis: a tale of two "hits"? Gastroenterology 114: 842-845.
13. Lewis GF, Carpentier A, Adeli K, Giacca A (2002) Disordered fat storage and mobilization in the pathogenesis of insulin resistance and type 2 diabetes. Endocr Rev 23: 201-229.
14. Hultcrantz R, Glaumann H, Lindberg G, Nilsson LH (1986) Liver investigation in 149 asymptomatic patients with moderately elevated activities of serum aminotransferases. Scand J Gastroenterol 21: 109-113.
15. Caprio S (2005) Definitions and pathophysiology of the metabolic syndrome in obese children and adolescents. Int J Obes (Lond) 29: S24-S25.
16. Nonomura A, Mizukami Y, Unoura M, Kobayashi K, Takeda Y, et al. (1992) Clinicopathologic study of alcohol-like liver disease in non-alcoholics; non-alcoholic steatohepatitis and fibrosis. Gastroenterol Jpn 27: 521-528.
17. Saverymuttu SH, Joseph AE, Maxwell JD (1986) Ultrasound scanning in the detection of hepatic fibrosis and steatosis. Br Med J (Clin Res Ed) 292: 13-15.
18. Propst A, Propst T, Judmaier G, Vogel W (1995) Prognosis in nonalcoholic steatohepatitis. Gastroenterology 108: 1607.

19. Ogden CL, Kuczmarski RJ, Flegal KM, Mei Z, Guo S, et al. (2002) Centers for Disease Control and Prevention 2000 growth charts for the United States: improvements to the 1977 National Center for Health Statistics version. Pediatrics 109: 45-60.

20. Raj M (2012) Obesity and cardiovascular risk in children and adolescents. Indian J Endocrinol Metab 16: 13-19.

21. Marwaha RK, Tandon N, Ganie MA, Kanwar R, Shivaprasad C, et al. (2011) Nationwide reference data for height, weight and body mass index of Indian schoolchildren. Natl Med J India 24: 269-277.

22. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (2001) Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). JAMA 285: 2486-2497.

23. Wieckowska A, Feldstein AE (2005) Nonalcoholic fatty liver disease in the pediatric population: a review. Curr Opin Pediatr 17: 636-641.

24. Tominaga K, Kurata JH, Chen YK, Fujimoto E, Miyagawa S, et al. (1995) Prevalence of fatty liver in Japanese children and relationship to obesity. An epidemiological ultrasonographic survey. Dig Dis Sci 40: 2002-2009.

25. Steinberger J, Moorehead C, Katch V, Rocchini AP (1995) Relationship between insulin resistance and abnormal lipid profile in obese adolescents. J Pediatr 126: 690-695.

26. Manco M, Marcellini M, Devito R, Comparcola D, Sartorelli MR, et al. (2008) Metabolic syndrome and liver histology in paediatric non-alcoholic steatohepatitis. Int J Obes (Lond) 32: 381-387.

27. Bellentani S, Scaglioni F, Marino M, Bedogni G (2010) Epidemiology of non-alcoholic fatty liver disease. Dig Dis 28: 155-161.

28. Franzese A, Vajro P, Argenziano A, Puzziello A, Iannucci MP, et al. (1997) Liver involvement in obese children. Ultrasonography and liver enzyme levels at diagnosis and during follow-up in an Italian population. Dig Dis Sci 42: 1428-1432.

29. Tazawa Y, Noguchi H, Nishinomiya F, Takada G (1997) Serum alanine aminotransferase activity in obese children. Acta Paediatr 86: 238-241.

30. Strauss RS, Barlow SE, Dietz WH (2000) Prevalence of abnormal serum aminotransferase values in overweight and obese adolescents. J Pediatr 136: 727-733.

31. Dixon JB, Bhathal PS, O'Brien PE (2001) Nonalcoholic fatty liver disease: predictors of nonalcoholic steatohepatitis and liver fibrosis in the severely obese. Gastroenterology 121: 91-100.

32. Angulo P, Keach JC, Batts KP, Lindor KD (1999) Independent predictors of liver fibrosis in patients with nonalcoholic steatohepatitis. Hepatology 30: 1356-1362.

33. Ong JP, Younossi ZM, Speer C, Olano A, Gramlich T, et al. (2001) Chronic hepatitis C and superimposed nonalcoholic fatty liver disease. Liver 21: 266-271.

34. Matteoni CA, Younossi ZM, Gramlich T, Boparai N, Liu YC, et al. (1999) Nonalcoholic fatty liver disease: a spectrum of clinical and pathological severity. Gastroenterology 116: 1413-1419.

35. Powell EE, Cooksley WG, Hanson R, Searle J, Halliday JW, et al. (1990) The natural history of nonalcoholic steatohepatitis: a follow-up study of forty-two patients for up to 21 years. Hepatology 11: 74-80.

36. Mujica V, Leiva E, Icaza G, Diaz N, Arredondo M, et al. (2008) Evaluation of metabolic syndrome in adults of Talca city, Chile. Nutr J 7: 14.

37. Bhat RA, Laway BA, Zargar AH (2010) Prevalence of metabolic syndrome in Kashmir valley of Indian subcontinent. Indian J Med Sci 64: 259-264.

38. Angulo P (2007) GI epidemiology: nonalcoholic fatty liver disease. Aliment Pharmacol Ther 25: 883-889.

39. DeFronzo RA (2004) Dysfunctional fat cells, lipotoxicity and type 2 diabetes. Int J Clin Pract Suppl 9-21.

40. Hamaguchi M, Kojima T, Takeda N, Nakagawa T, Taniguchi H, et al. (2005) The metabolic syndrome as a predictor of nonalcoholic fatty liver disease. Ann Intern Med 143: 722-728.