

Non-Alcoholic Fatty Liver Disease and Steatohepatitis in Taiwanese Children: The Prevalence and Serum Retinol Binding Protein 4 level

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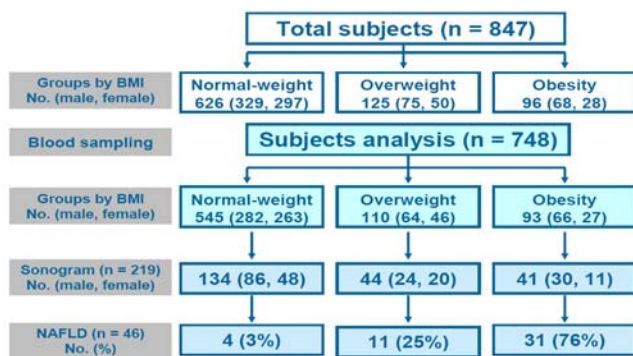
BACKGROUND

Nonalcoholic fatty liver disease (NAFLD) manifests fatty infiltration of the liver in the absence of chronic alcohol use. It is associated with potential serious long-term outcomes. The gold standard for establishing diagnosis of NAFLD is based on performance of a liver biopsy, but this procedure is invasive and not routinely performed in the pediatric population. Studies have suggested that serum retinol binding protein 4 (RBP4) is a major circulating adipokine that is elevated in systemic insulin resistance. The correlations between serum RBP4 levels and NAFLD have not been studied in the pediatric population as yet.

AIMS

The aims of this study were to investigate the prevalence of NAFLD in schoolchildren with various body mass index (BMI). Moreover, the correlation between serum RBP4 level and liver injury was investigated.

Fig. 1. The study flow diagram and the case numbers



METHODS

- 847 schoolchildren aged 4 to 12 years were evaluated by anthropometric measurements.
- The participants were categorized into three groups based on BMI: normal weight (BMI < 85th %), overweight (85th % ≤ BMI < 95th %), and obesity (BMI ≥ 95th %).
- The serum glucose, AST, ALT, triglycerides and cholesterol levels were measured after an 8-hour overnight fast.
- NAFLD was diagnosed as fatty infiltrates of liver in sonogram and NASH was defined as NAFLD with an elevated ALT level.

RESULTS

- The study flow diagram and the case numbers were shown in Fig. 1. A total of 847 healthy children were enrolled. The prevalence of overweight and obesity in schoolchildren was 14.8% and 11.4%, respectively.
- After obtaining the consents, the blood samples from 748 volunteers were drawn. Table 1 shows the mean age and male-to-female ratio were significantly higher in children with obesity than those with normal weight ($P=0.001$). Furthermore, the mean values of AST and ALT were significantly higher in obese children than the other two groups ($P<0.05$).

Table 1. Anthropometric and metabolic characteristics of the study children who have blood sampling (n = 748) by BMI classification

Mean	Normal-weight (n = 545)	Overweight (n = 110)	Obesity (n = 93)
Age (years)	8.4	8.5	8.8 [†]
Sex=male, No. (%)	282 (52%)	64 (58%)	66 (71%) [†]
BMI (kg/m ²)	15.9	20.0 [†]	24.4 ^{††}
AST (IU/L)	24.1	23.6	27.6 ^{††}
ALT (IU/L)	12.2	15.5	31.2 ^{††}

[†]p < 0.05 vs. normal-weight; ^{††}p < 0.05 vs. overweight

BMI, body mass index; AST, aspartate aminotransferase; ALT, alanine aminotransferase

- Among 219 children with ultrasound examinations, NAFLD was identified in 3%, 25%, and 76% of children with normal weight, overweight, and obesity, respectively (Fig. 1). Moreover, NASH was diagnosed of 15% (14/93) in children with obesity.
- Children with NAFLD had significantly higher BMI, triglyceride, insulin, HOMA index, AST, ALT, and RBP4 levels than those age- and gender-matched controls (all $P<0.05$) (Table 2). Furthermore, multiple logistic regression analysis confirmed that BMI and RBP4 level were two independent factors to predict NAFLD in children (Table 3).

Table 2. Difference in the selected variables among the subjects with NAFLD and sex- and age-matched controls

Mean value	No NAFLD (n = 98)	NAFLD (n = 46)	p value
Age (years)	9.3	9.1	0.158
Sex=male, No. (%)	69 (70%)	31 (67%)	0.714
BMI (kg/m ²)	17.2	23.2	< 0.001
Triglycerides (mg/dL)	78.8	113.9	< 0.001
Total cholesterol (mg/dL)	173.4	172.0	0.787
Glucose (mg/dL)	89.3	90.4	0.354
Insulin (mU/L)	4.5	12.3	< 0.001
HOMA index	1.0	2.8	< 0.001
AST (IU/L)	23.1	28.4	< 0.001
ALT (IU/L)	13.0	34.3	< 0.001
RBP4 (mg/L)	22.6	26.6	< 0.001

BMI, body mass index; HOMA, homeostasis model of assessment; AST, aspartate aminotransferase; ALT, alanine aminotransferase; RBP4, Retinol-binding protein 4; NAFLD, nonalcoholic fatty liver disease

Table 3. Multiple logistic regression analysis using NAFLD as a dependent variable with all subjects (n = 144)

Variables	SE	OR (95% CI)	p value
BMI (kg/m ²)	0.164	1.772 (1.285 - 2.445)	<0.001
Triglycerides (mg/dL)	0.010	0.988 (0.968 - 1.008)	0.239
Insulin (mU/L)	0.712	1.676 (0.415 - 6.766)	0.468
HOMA index	3.125	0.185 (0.000 - 84.641)	0.589
AST (IU/L)	0.084	0.947 (0.803 - 1.116)	0.515
ALT (IU/L)	0.063	1.114 (0.984 - 1.260)	0.088
RBP4 (mg/L)	0.069	1.164 (1.017 - 1.333)	0.028

BMI, body mass index; HOMA, homeostasis model of assessment; AST, aspartate aminotransferase; ALT, alanine aminotransferase; RBP4, Retinol-binding protein 4; NAFLD, nonalcoholic fatty liver disease

CONCLUSIONS

A high prevalence of obesity and NAFLD is found in Taiwanese children. Childhood obesity is closely related to the male gender, increase of age, triglycerides, AST, ALT, RBP4 levels, insulin resistance, and NASLD. Moreover, the increase of serum RBP4 level and BMI are two risk factors to develop NAFLD in children.