Paediatrica Indonesiana

p-ISSN 0030-9311; e-ISSN 2338-476X; Vol.56 No.6 (2016) p. 351-6; doi: 10.14238/pi56.6.2016.351-6.

Original Article

Comparison of serum aminotransferases in overweight and obese children

Ayu Shintia Shanti, I Gusti Lanang Sidiartha

Abstract

Background Obesity has become a global issue. Non-alcoholic fatty liver disease is a metabolic complication of obesity, and indicated by elevated serum aminotransferases.

Objective To compare serum aminotransferase levels in overweight and obese children.

Methods This cross-sectional study was conducted from August to October 2015. A total of 82 subjects aged 6-10 years met the study criteria. Blood specimens and data concerning lifestyle and family history using questionnaires were collected. Subjects were divided into three groups based on BMI: overweight, obese, and severely obese. Comparisons of serum aminotransferase levels were analyzed by Kruskal-Wallis and post hoc tests, with P values < 0.05.

Results The median serum alanine aminotransferase (ALT) levels in overweight, obese, and severely obese subjects were 14 (IQR 6-42) U/L, 15 (IQR 11-44) U/L, and 23 (IQR 9-59) U/L, respectively (P=0.031). The median serum aspartate aminotransferase (AST) levels in overweight, obese, and severely obese subjects were 22 (IQR 17-36) U/L, 22 (IQR 16-32) U/L, and 24 (IQR 15-41) U/L, respectively (P=0.049). Post hoc analysis revealed that median serum ALT levels were significantly higher in the severely obese group than in the overweight group [-8.982 (95% CI -14.77 to -3.20; P=0.003)], as well as in the obese group [-5.297 (95% CI -10.58 to -0.02; P=0.049)]. In addition, the median serum AST level was significantly higher in the severely obese group than in the obese group [-2.667(95% CI -5.27 to -0.07; P= 0.044)].

Conclusion Median serum ALT and AST levels are significantly higher in severely obese children than in obese and overweight children. **[Paediatr Indones. 2016;56:351-6. doi: 10.14238/pi56.4.2016.351-6]**.

Keywords: *serum aminotransferase, body mass index, obese children*

The global prevalence of overweight and obese children increased from 4.2% in 1990 to 6.7% in 2010. This trend is expected to reach 9.1% or 60 million by 2020.[1] The 2013 Indonesian National Health Survey (*Riset Kesehatan Dasar*, RISKESDAS) revealed that the prevalence of obesity in children aged 5 to 12 years was 11.9%, of whom 19.7% were boys and 32.9% were girls.[2] In Denpasar, Bali, obesity prevalence increased from 11% in 2002 to 21% in 2013.[3,4]

Obesity increases the risk of developing a variety of pathological conditions, including insulin resistance, type 2 diabetes, dyslipidemia, hypertension, and non-alcoholic fatty liver disease (NAFLD).[5] In youth, NALFD is often clinically silent and discovered only upon screening or the incidental testing of serum aminotransferase. Non-alcoholic fatty liver disease increases serum aminotransferase levels and the risk of liver disease, which may lead to fibrosis, cirrhosis, or eventually, hepatocellular carcinoma.[6] Although elevated serum liver enzymes are not an accurate measurement of liver damage, they may be a

From the Department of Child Health, Udayana University Medical School/Sanglah Hospital, Denpasar, Bali, Indonesia.

Reprint requests to: Ayu Shintia Shanti, Departement of Child Health, Udayana University Medical School/Sanglah Hospital, Jl. Pulau Nias, Denpasar 80114, Indonesia. Tel. +62-361-244038, Fax. +62-361-244038; E-mail: ayushintiashanti@yahoo.com.

valuable and non-invasive test to screen and a marker to control NAFLD evolution in obese children and adolescents. To detect NAFLD in obese children and adolescents, serum aminotransferases concentrations should be routinely determined.[5,6]

In the 1999-2004, the US Centers for Disease Control through the National Health and Nutrition Examination Survey (NHANES) reported that the prevalence of elevated ALT (>30 U/L) was 7.4% among white adolescents, 11.5% among Mexican-Americans, and 60% among black adolescents.[6] Tominaga *et al*. reported a 2.6% prevalence of NAFLD (based on ultrasound) among Japanese children aged 4-12 years old.[7] This threshold also applied to the adolescent participants in the NHANES 1999-2004, for whom a similar prevalence of 3.6% was found. In addition, Schwimmer *et al*.[9] examined liver tissue from autopsies performed on children 2-19 years of age at the time of death in the county of San Diego, California and showed that fatty liver was present in 13% of subjects, but with significantly different percentages by race and ethnicity (Asian: 10.2%, black: 1.5%, Hispanic: 11.8%, and white: 8.6%). The NAFLD prevelances tended to increase with age, ranging from 0.7% for ages 2 to 4 years and up to 17.3% for ages 15 to 19 years.[8] There have been few studies with a focus on pre-adolescent obesity. The aim of this study was to compare serum aminotransferase levels in overweight, obese, and severely obese children.

Methods

This analytic, cross-sectional study was conducted from August to October 2015. Inclusion criteria were childen with a body mass index (BMI) at or above the 85^{th} percentile, aged 6-10 years, and from one of two elementary schools in Denpasar, Bali. Children were excluded for the following conditions: dysmorphic facial features, chronic disease, autoimmune disease, severe liver disease, or refusal to participate in this study. This study was approved by the Ethics Commission of Udayana University Medical School, Sanglah Hospital, Denpasar.

Overweight was defined as a BMI at or above the 85^{th} percentile and below the 95^{th} percentile; obese was defined as a BMI at or above the 95^{th} percentile and below the 99^{th} percentile; and severely obese was defined as a BMI at or above the 99^{th} percentile, for children of the same age and gender. We used the CDC 2000 BMI percentile curves, based on age and gender of the children (aged 2-20 years), using a formula of weight (in kilograms) divided by the square of height (in meters).[5] Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) are liver enzymes which synthesize and break down amino acids and convert energy storage molecules (in U/L). Lifestyle assessments included the amount of exercise in a week during or outside school hours, watching television while eating snacks (hours per day), playing electronic computer games (hours per day), and number of large meals in a day. Familial history included obesity and liver disease in family members.

One examiner measured subjects' body heights and weights using a standard *ZT-120®* scale (precision 0.5 kg and maximum weight 120 kg) and a stature meter of 70-190 cm (precision 0.5 cm). Those scales were last calibrated in 2014. Body heights were measured in subjects without shoes standing on the scale, looking straight ahead. Subjects' parents received information on their children's conditions and provided informed consent.

Blood specimens were taken in the morning and about 5 mL put into serum separator tubes (SST). Tubes containing the blood were gently inverted 5-10 times, then stored in an upright position. The blood specimens were all processed at the same time by centrifuging 3100 rpm for 10 minutes, to separate the serum layer. Serum AST and ALT levels were measured using a *Roche/Hitachi®* (*COBAS C501*) automatic analyzer. The results can be obtained within three hours from the onset of blood sampling.

The minimum required sample size, calculated based on α 0.05, power 80%, and effect size 20%, was 21 subjects for each group. The independent variable was BMI group (overweight, obese, and severely obese children). The dependent variable was serum aminotransferase levels (ALT (5-41 U/L) and AST (5-40 U/L)). The data were analyzed using *SPSS 17* software. Distribution of data was analyzed by Kolmogorov-Smirnov test. Comparison of serum aminotransferase levels between groups was done by Kruskal-Wallis test because the data distribution was not normal. Further analysis was done by post hoc test. Results with P values <0.05 were considered to be statistically significant.

Results

A total of 82 children aged 6-10 years participated in the study. Subjects consisted of 51.2% males and 48.8% females, as shown in **Table 1**. Median age of subjects was 9.2 (IQR 6-10.9) years.

Table 2 shows the bivariate analysis of median serum ALT and AST levels between groups. Median serum ALT levels in the overweight, obese, and severely obese groups were 14 (IQR 6-42) U/L, 15 (IQR 11-44) U/L, and 23 (IQR 9-59) U/L, respectively (P=0.031). Median serum AST levels in the overweight, obese, and severely

Table 1. Baseline characteristics of subjects

Characteristics	BMI group			Total
	Overweight (n=21)	Obese (n=29)	Severely obese (n=32)	(n=82)
Gender, n (%)				
Male	9 (42.8)	17 (58.6)	16 (50.0)	42 (51.2)
Female	12 (57.2)	12 (41.4)	16 (50,0)	40 (48.8)
Median age (IQR), years	9.1 (6.9 - 10.6)	9.3 (6.0 - 10.9)	9.3 (6.0 - 10.7)	9.2 (6 - 10.9)
Median weight (IQR), kg	39 (25 - 60)	44 (30 - 65)	46 (35 - 79)	43 (25 - 79)
Median height (IQR), cm,	136 (120 - 160)	135 (118 - 158)	138 (121 - 156)	136 (118 - 160)
Family history of obesity, n (%)	10 (47.6)	15 (51.7)	18 (56.2)	43 (52.4)
Lifestyle, n (%)				
Physical activity ≤ 1 time/week	15 (71.1)	24 (82.7)	29 (90.6)	68 (82.9)
Watching television > 2 hours/day	19 (90.5)	26 (89.6)	30 (93.7)	75 (91.5)
Playing computer games > 2 hours/day	18 (85.7)	24 (82.7)	24 (75.0)	66 (80.5)
Eating habits > 3 times/day	10 (47.6)	15 (51.7)	24 (75.4)	49 (59.8)
Having fizzy drinks > 1 bottle/day	13 (61.9)	20 (68.9)	25 (78.1)	58 (70.7)

Kolmogorov-Smirnov test; IQR=interquartile range

Table 2. Serum aminotransaminase levels based on BMI group

Variables	BMI group			P value
	Overweight	Obese	Severely obese	
Median ALT, U/L (IQR)	14 (6 - 42)	15 (11 - 44)	23 (9 - 59)	0.031*
Median AST, U/L (IQR)	22 (17 - 36)	22 (16 - 32)	24 (15 - 41)	0.049*

Kruskal-Wallis analysis; ALT=alanine aminotransferase, AST=aspartate aminotransferase, BMI=body mass index, *P value < 0.05

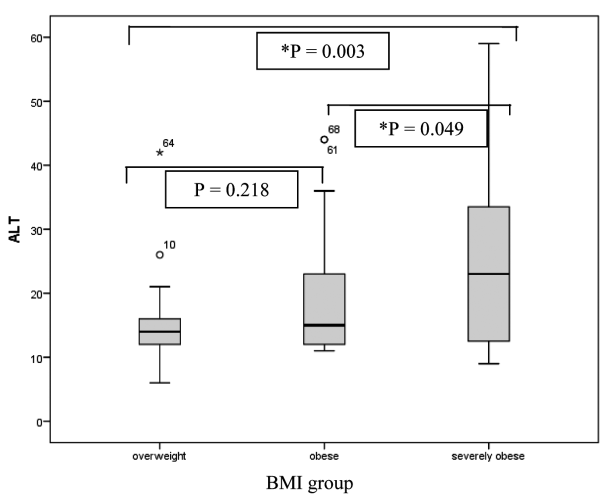

Figure 1. Post hoc analysis of serum ALT among BMI groups (*P value < 0.05)

(Note: 10, 61, 64, 68 indicate number of samples with AST level above upper limit)

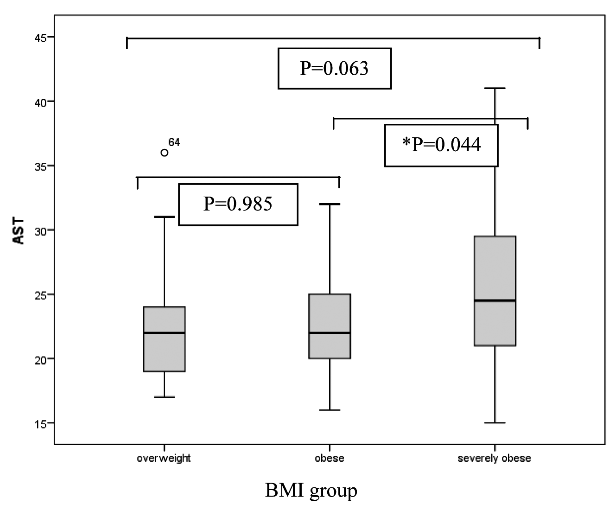

Figure 2. Post hoc analysis of serum AST among BMI group (*P value < 0.05)

(Note: 64 indicates number of samples with AST level above upper limit) obese groups were 22 (IQR 17-36) U/L, 22 (IQR 16-32) U/L, and 24 (IQR 15-41) U/L, respectively (P=0.049).

Figures 1 and **2**, and **Table 3** and **4** shows the post hoc analysis results. Median serum ALT was significantly higher in the severely obese group than in the overweight group [P=0.003; -8.982(95% CI -14.77 to -3.20)], and than in the obese group [P=0.049; -5.297(95% CI -10.58 to -0.02)]. Median serum AST was significantly higher in the severely obese group than in the obese group [P= 0.044; -2.667(95% CI -5.27 to -0.07)].

absence of significant alcohol consumption. According to the *American Association for the Study of Liver Diseases*, NAFLD is defined as fat accumulation in the liver exceeding 5% to 10% by weight, as determined from the percentage of fat-laden hepatocytes by light microscopy.[10] Several factors may collectively stimulate inflammation, apoptosis, and fibrosis that ultimately lead to progressive liver disease, which then can elevate serum aminotransferases such as ALT and AST to the upper level of normal limits.[10]

High serum ALT concentrations have been associated with increased hepatic fat fraction and increased intra-abdominal visceral adipose tissue. Elevation of this enzyme is quite sensitive as an indicator of liver injury. Epidemiological studies reported that ALT is the most useful biomarker of NAFLD because this liver enzyme is most closely correlated to liver fat accumulation, although a definitive diagnosis and determination of severity require a liver biopsy.[11] To screen for NAFLD especially in the population of obese children and adolescents, serum aminotransferase concentrations should be routinely measured.[5,11]

Table 3. Mean difference level of serum ALT between BMI group

BMI group	ALT (U/L)		
	Mean difference	95% CI of difference	P value
Overweight – obese	-3.685	-9.9 to 2.22	0.218
Overweight – severely obese	-8.982	-14.77 to -3.20	0.003*
Obese – severely obese	-5.297	-10.58 to -0.02	0.049*

Alanin aminotransaminase (ALT), aspartat aminotransaminase (AST), body mass index (BMI), significant *Pvalue < 0.05

Table 4. Mean difference level of serum AST between BMI group

BMI group	AST (U/L)		
	Mean difference	95% CI of difference	P value
Overweight – obese	-0.028	-2.93 to 2.88	0.985
Overweight – severely obese	-2.695	-5.54 to 0.15	0.063
Obese – severely obese	-2.667	-5.27 to -0.07	0.044*

Alanin aminotransaminase (ALT), aspartat aminotransaminase (AST), body mass index (BMI), significant *P value < 0.05

Discussion

Obesity is caused by a caloric imbalance between food intake and energy expenditure, which leads to an excessive accumulation of adipose tissue. As such, low physical activity in daily life and more screen time, such as watching television and playing computer games, increases the risk of obesity.[5-9] In our study, most subjects watched television more than 2 hours/day (91.5%), played computer games more than 2 hours/day (80.5%), and engaged in physical activity less than once/week (82.9%).

Increased obesity has led to increased comorbidities, such as NAFLD. In youth, NAFLD is often clinically silent and discovered only upon screening or the incidental testing of serum aminotransferase.[7,9] Non-alcoholic fatty liver disease is defined as an accumulation of fat in the cytoplasm of hepatocytes, in the

We found significantly different median serum ALT and AST levels in overweight, obese, and severely obese children. Post hoc analysis revealed that median serum ALT was significantly higher in the severely obese group than in the obese and overweight groups. Also, median serum AST was significantly higher in the severely obese group than in the obese group. Franzese *et al*. revealed a similar elevation of aminotransferases in a sample of 75 obese, prepubertal children (25%), as in our study.[12] Engelmann *et al.* performed a prospective study of 224 healthy overweight and obese children aged 1-12 years, and showed that obese children had significantly higher ALT levels than overweight children (0.9 *vs.* 0.7 times the upper limit of normal; P=0.04).[10,]

The reason for differences in serum ALT concentration and NAFLD prevalence between sexes and puberty remains unclear. A previous study reported that in adolescents with NAFLD, mean increased serum ALT levels were significantly higher in boys [52.06 (SD 34.13) U/L] than girls [25.29 (SD 8.70) U/L].[1]Another study found a 3.2% prevalence of NAFLD among Korean adolescents 10-19 years old, using ALT with a cut-off value of 40 U/L. They reported a significant, positive association between serum ALT level and obesity indices in male adolescents.[15]? Another study found a higher level of serum ALT in boys (13.4%) than girls (4.9%), and higher AST level in boys (9.8%) than girls (3.7%), in children aged 6-10 years.[15] These results were similar to those of our study.

Previous studies on puberty and obesity suggested the estrogen-testosterone ratio as a potential reason for this sex-based difference. Sex hormones affect both fat and muscle distribution. Globulin, which binds sex hormones and is produced in the liver, is strongly correlated with insulin sensitivity and higher ALT level.[10,16] In our study, subjects were children aged 6-10 years. We excluded pubertal children in order to avoid hormonal influences on fat accumulation that would affect liver fuction. The limitations of the study were that we did not perform complete liver function tests or use another test modality to define NAFLD.

In conclusion, serum ALT and AST levels are significantly higher in severely obese children than in obese and overweight children. This results suggest that increased severity of childhood obesity may increase the risk of liver damage that leads to fatty liver disease.

Conflict of Interest

None declared.

References

1. de Onis M, Blossner M, Borghi E. Global prevalence and trends of overweight and obesity among preschool children. Am J Clin Nutr. 2010;92:1257-64.
2. Badan Penelitian dan Pengembangan Kesehatan Kementerian Kesehatan Republik Indonesia.Riskesdas. Laporan Nasional 2013. Jakarta: Kementerian Kesehatan Republik Indonesia; 2013. p1-20
3. Adhianto G, Soetjiningsih. Prevalence and risk factors of overweight and obesity in adolescents. Paediatr Indones. 2002;42:206-11.
4. Ratna MD, Sidiartha IGL. Prevalensi dan faktor risiko obesitas anak sekolah dasar di daerah urban dan rural. Medicina. 2013;44:15-21.
5. Damayanti RS, Lanny CG, Aryono H, Endang DL, Lanang SIG, Maria M. Rekomendasi Ikatan Dokter Anak Indonesia: diagnosis, tata laksana dan pencegahan obesitas pada anak dan remaja. 1st ed. Jakarta: Ikatan Dokter Anak Indonesia; 2014. p. 1-14.
6. Fraser A, Longnecker MP, Lawler DA. Prevalence of elevated alanine aminotransferase (ALT) among US adolescents and associated factors: NHANES 1999-2004. Gastroenterology. 2007;133:1814–20.
7. Ahn MB, Bae WR, Han KD, Cho WK, Cho KS, Park SH, *et al*. Association between serum alanine aminotransferase level and obesity indices in Korean adolescents. Korean J Pediatr. 2015;58:16571.
8. Tominaga K, Kurata JH, Chen YK, Fujimoto E, Miyagawa S, Abe I, Kusano Y. Prevalence of fatty liver in Japanese children and relationship to obesity. An epidemiological ultrasonographic survey. Dig Dis Sci. 1995;40:2002–9.
9. Schwimmer JB, Deutsch R, Kahen T, Lavine JE, Stanley C, Behling C. Prevalence of fatty liver in children and adolescents. Pediatrics. 2006;118:1388–93.
10. Engelmann G, Hoffmann GF, Grulich-Henn J, Teufel U. Alanine aminotransferase elevation in obese infants and children: a marker of early onset non alcoholic fatty liver disease. Hepat Mon. 2014;14:e14112.
11. Rodríguez G, Gallego S, Breidenassel C, Moreno LA, Gottrand F. Is liver transaminases assessment an appropriate tool for the screening of non-alcoholic fatty liver disease in at risk obese children and adolescents? Nutr Hosp. 2010;25:712-7.
12. Franzese A, Vajro P, Argenziano A, Puzziello A, Iannucci MP, Saviano MC, *et al*. Liver involvement in obese children. Ultrasonography and liver enzyme levels at diagnosis and during follow-up in an Italian population. Dig Dis Sci. 1997;42:1428-32.

13. Lin YC, Chang PF, Yeh SJ, Liu K, Chen HC. Risk factors for liver steatosis in obese children and adolescents. Pediatr Neonatol. 2010;51:149-54.
14. Grotti Clemente AP, Molin Netto BD, Ganen Ad, Tock L, Arisa Caranti D, de Mello MT, *et al*. Cut-off values of visceral adiposity to predict NAFLD in Brazilian obese adolescents. J Nutr Metab. 2013;724781.
15. Park HS, Han JH, Choi KM, Kim SM. Relation between elevated serum alanine aminotransaminase and metabolic syndrome in Korean adolescents. Am J Clin Nutr. 2005;82:1046-51.
16. Xanthakos SA, Kohil R. Pediatric nonalcoholic fatty liver disease: prevalence, diagnosis, risk factor, and management. Clin Liver Dis. 2012;1:125-8.