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THE RELATIONSHIP BETWEEN ELEVATED ALANINE TRANSAMINASE AND BODY MASS INDEX IN COLLEGE STUDENTS POPULATION: A CROSS-SECTIONAL STUDY

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ABSTRACT

The objective of our study was to evaluate the accuracy of body mass index (BMI) in detecting an elevated alanine transaminase (ALT) level in the college students population. The cross-sectional survey was conducted from 2005 to 2008 based on the health checkup data. A total of 7875 college freshmen were examined. Logistic regression was used to quantify the contribution of BMI to an elevated ALT (40 U/L) level. The Receiver Operating Characteristic (ROC) curve was used to calculate the BMI cut-off points for the risk of elevated ALT. BMI was a significant predictor of elevated ALT in both male (OR=1.30, 95%CI:1.24–1.36) and female (OR=1.21, 95%CI:1.60–1.27). The risk of elevated ALT was 38.79 (95%CI:22.46–67.01) fold higher with obesity in male and 21.96 (95%CI:8.24–58.51) fold in female. According to the data of the ROC curve, the BMI cut-off points for predicting the risk of elevated ALT were 24.1 kg/m^2 in male and 21.7 kg/m^2 in female. BMI is a good predictor of elevated ALT serum activity in the college students population. To identify college students population at high risk of elevated ALT in Taiwan, cut-off points little higher than currently recommended overweight for BMI is needed in male students while lower than overweight for BMI is suggested in female.

Keywords: Alanine transaminase, body mass index, ROC curve, AUC.

INTRODUCTION

With the continual improvement in hygiene and decreasing exposure to health hazards, acute liver damage has become less common. Instead, the growing concern is now for early detection of chronic liver damage (Sia1 *et al*., 2004). Alanine transaminase (ALT) is the most common laboratory tests for the detection of liver diseases. Elevated plasma ALT levels are associated with obesity and metabolic syndrome (Marchesini *et al*., 2005; Oh *et al*., 2006; Shen *et al*., 2005). Body mass index (BMI) is the principal and universal measure of obesity. Studies show that BMI values are associated with elevated ALT levels (Bedogni *et al*., 2003; Lee *et al*., 2001; Okita *et al*., 2001; Pratt and Kaplan, 2000). Overweight and obesity are the most common findings in adolescents with elevated ALT levels (Strauss *et al*., 2000). The prevalence and etiologies of elevated ALT have geographic variations and they are rarely reported in Taiwan, and even fewer reports describing the relationship between BMI and ALT in college students population. In this study, we explored the prevalence of elevated ALT levels and the contribution of BMI to elevated ALT and to determine optimal BMI cut-off points for predicting the risk of elevated ALT in the college students.

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METERIALS AND METHODS

Subjects

This cross-sectional investigation was based on a health checkup data from a university in central Taiwan, conducted from 2005 to 2008. A total of 7875 freshmen were examined. The students of this university were from a wide range of locations throughout Taiwan. ALT was measured by common laboratory methods in hospital. BMI was calculated as weight (kg)/height(m)^2. Subjects were classified as under-weight (BMI <18.5 kg/m^2), normal-weight (18.5 BMI<24.0 kg/m^2), over-weight (24.0 BMI<27 kg/m^2) and obesity (BMI 27 kg/m^2) according to the definition recommended by the Department of Health, Executive Yuan, Taiwan (2002). Blood ALT level was used to screen abnormal liver function with a cut-off values of 40 U/L representing a state of acute liver cell damage (Guzzaloni *et al*., 2000). Therefore, elevated ALT was defined as ALT higher than 40 U/L.

Statistical analysis

Continuous variables were presented as mean values and standard deviation. Categorical variables were presented as frequencies. Associations between categorical variables were tested by using of Chi-square test. Continuous variables were tested using the *t*-test. Logistic regression analysis was used to establish the contribution of BMI to elevated ALT, with elevated ALT serving as the dichotomous outcome variable. Odd ratio (OR) and 95% confidence intervals (CI) were computed. We used the Receiver Operating Characteristic (ROC) analysis to ensure the predictive validity, and to find out the optimal cut-off points (Schouw *et al*., 1992). The sensitivity (SN) and specificity (SP) of each model were calculated and ROC curves were drawn by plotting SN vs. 1-SP to determine the BMI cut-off points for the risk of elevated ALT. We defined the best cut-off points as the value with the highest accuracy that maximizes the Youden's index (sensitivity+specificity-1) (Swets, 1973). Sensitivity and specificity have been calculated at all possible cut-off points to find the optimal cut-off points. The areas under receiver operator characteristic curve (AUC) were calculated to assess accuracy. AUC is a measure of the diagnostic power of a test. A perfect test will have an AUC of 1.0 and an AUC equal 0.5 means the test performs no better than chance. Statistical significance was set to a value of $p<0.05$ for all tests. Statistical analysis was performed using SPSS for Windows.

Table 1. Characteristic of the study subjects.

Variables	Total (*n*=7,875)	Male (*n*=5,586)	Female (*n*=2,289)	*P* value
	Mean ± SD	Mean ± SD	Mean ± SD	
Height (cm)	168.22 ± 8.18	171.77 ± 6.23	159.55 ± 5.46	<0.001
Weight (kg)	62.30 ± 13.98	67.06 ± 13.38	53.01 ± 9.81	<0.001
BMI (kg/m^2)	22.15 ± 4.16	22.71 ± 4.27	20.80 ± 3.54	<0.001
ALT(U/L)	21.66 ± 22.95	24.48 ± 25.52	14.79 ± 12.53	<0.001
	Frequencies (%)	Frequencies (%)	Frequencies (%)	
Obesity (BMI 27.0 kg/m²)	957 (12.2)	810 (14.5)	147 (6.4)	<0.001
Over-weight (24.0<BMI 27.0 kg/m²)	1076 (13.7)	913 (16.3)	163 (15.1)	<0.001
Elevated ALT (ALT>40 U/L)	796 (9.6)	690 (12.4)	69 (3.0)	<0.001

Continuous variables are given as mean ± standard deviation and tested using the *t*-test.
Categorical variables were presented as frequencies (percentage) and tested using Chi-square test.
Abbreviations: BMI, body mass index; ALT, alanine aminotransferase

Table 2. Odds ratios and 95% confidence intervals for the relationship between BMI and elevated ALT.

Elevated ALT	Male			Female		
	OR	95% CI	*P* value	95%CI		*P* value
BMI all	1.30	1.24- 1.36	<0.001	1.21	1.60- 1.27	<0.001
Under- weight	1			1		
Normal-weight	3.05	1.76- 5.29	<0.001	2.91	1.14- 4.81	<0.001
Over-weight	12.52	7.20-21.77	<0.001	4.81	1.51-15.36	<0.001
Obesity	38.79	22.46-67.01	<0.001	21.96	8.24-58.51	<0.001

under-weight (BMI<18.5 kg/m^2); normal-weight (18.5 BMI<24.0 kg/m^2); over-weight (24.0 BMI<27 kg/m^2); obesity (BMI 27 kg/m^2)

Table 3. The AUC and optimal cut-off point of BMI for prediction elevated ALT.

	AUC (95% CI)	*P* AUC	Cut-off (Sen,%; Spec,%)
BMI male	0.81(0.80 - 0.83)	<0.001	24.1 (72.9, 75.8)
BMI female	0.72(0.66 - 0.79)	<0.001	21.7 (62.7, 71.6)

Abbreviations: AUC=area under the curve; Sen=sensitivity; Spec=specificity

RESULTS

The characteristics of the study subjects are given in table 1. A total of 7875 college freshmen (5586 male students, 2289 female students) attending the university were included in this study. The average BMI of the students was 22.71±4.27 kg/m^2 for male and 20.80±3.54 kg/m^2 for female. The average ALT of the students was 24.48±25.52 U/L for male and 14.79±12.53 U/L for female. ALT level higher than 40 U/L was found in 9.6% (796/7875) of all students (12.4% in male and 3.0% in female). The prevalence of elevated ALT was significantly ($p<0.001$) higher in male than in female. The prevalence of obesity (BMI 27.0 kg/m^2) was 12.2% (14.5% in male and 6.4 % in female).

Odds ratio (OR) of elevated ALT was calculated according to BMI classification compared to the reference group (Table 2). The results show that BMI was a significant predictor of elevated ALT in both male (OR=1.30, 95%CI:1.24–1.36) and female (OR=1.21, 95%CI: 1.60–1.27). In male students with over-weight and obesity had 12.52 times (95%CI:7.20–21.77) and 38.79 times (95%CI:22.46–67.01) for elevated ALT. In female students with over-weight and obesity had 4.81 times (95%CI:1.51–15.36) and 21.96 times (95%CI:8.24–58.51) for elevated ALT.

In table 3 shows that AUC was 0.81 (95%CI:0.80–0.83) for male and 0.72 (95%CI:0.66–0.79) for female ($p<0.001$) which were significantly higher than what would be expcted by chance (AUC > 0.5). Thus, as determined by ROC curves, BMI was a good predictor of elevated ALT. ROC curve analysis by sex suggested that BMI is a more sensitive and specific measure of elevated ALT in male than in female (Fig. 1). The ROC curves achieved a maximum Youden's index at BMI cut-off points of 24.1 kg/m^2 in male (sensitivity 72.9%, specificity 75.8%) and 21.7 kg/m^2 in female (sensitivity 62.7%, specificity 71.6%) (Table 4).

Table 4. Statistical indices for a range of cut-off value of BMI.

Male			Female		
Cut-off	Sensitivity (%)	Specificity (%)	Cut-off	Sensitivity (%)	Specificity (%)
20.0	95.4	31.6	19.0	85.3	33.4
21.0	92.1	45.0	20.0	74.7	49.7
22.0	86.7	56.5	21.0	66.7	64.3
23.0	80.1	67.3	21.3	66.7	68.0
23.5	76.0	71.8	21.5	65.3	7.03
23.7	75.1	73.5	**21.7***	62.7	71.6
24.1*	72.9	75.8	22.0	58.7	74.8
24.3	69.6	77.9	22.5	53.3	79.1
24.5	68.2	79.6	23.0	49.3	82.1
25.0	62.8	82.5	24.0	42.7	87.6
26.0	55.0	87.1	26.0	34.7	93.2

* maximum *J*, *J*= Sensitivity+Specificity-100

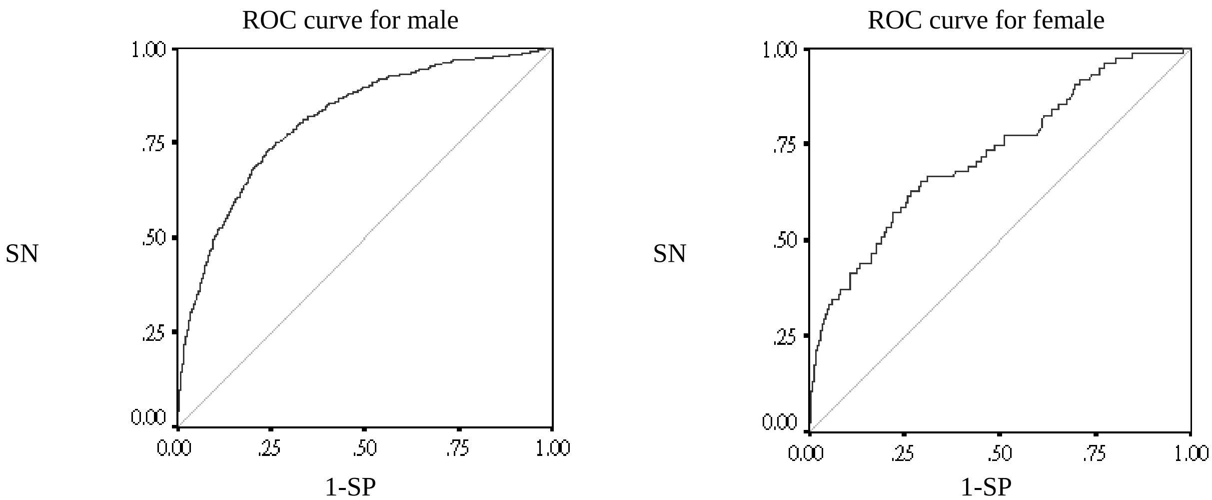

Fig. 1. Accuracy in detecting elevated ALT (40 U/L) by body mass index, Abbreviations: SN=sensitivity; SP=specificity

DISCUSSION

In our study the prevalence of elevated ALT was 9.6 %, and was more common in male students compared to female students (12.4% vs. 3.0%, $p<0.001$). There was 11.4% of elevated ALT in an adult population in Taiwan and was more common in men compared to women (17.3% vs. 6.1%, $p<0.05$) (Chen *et al.*, 2007). It is obvious that the prevalence of elevated ALT was more common in adult population compared to college students in Taiwan.

The present study aimed to establish the relative contribution of BMI to elevated ALT in the college students population. ROC curve analysis has been a useful tool in the study of BMI cut-off points (Do1 *et al.*, 2004; Lin *et al.*, 2002). In the study, we want to clarify the best BMI values for elevated ALT predicting, and want to balance the sensitivity and specificity, so we use ROC curve to determine the best BMI cut-off points. Our study shows that the BMI cut-off points for the risk of elevated ALT were 24.1kg/m^2 in male students which were little higher than overweight cut-points (BMI 24 kg/m^2); and 21.7 kg/m^2 in female students which were lower than overweight cut-points, recommended by the Department of Health, Executive Yuan, Taiwan (2002). Therefore, BMI was a significant predictor for the risk of elevated ALT in both genders. The main strength of the present study is that we quantified the association between BMI and ALT in the college students population. Our findings were very similar to recent studies that BMI was strongly associated with ALT (Adsms *et al*., 2007; Bedogni *et al*., 2003) and a good predictor for the risk of elevated ALT in adolescents (Bedogni *et al*., 2004). The accuracy of the prediction in our study (AUC 0.81 for male and 0.72 for female) was higher than the study in Italy adolescents (AUC 0.71) proposed by Bedogni *et al*. (2004). Potential limitation with the present study is that our sample is from a university so the study subjects do not fully reflect the general college population in Taiwan, an issue that can be addressed by a country-wide study in the future. In addition, we did not consider the influence of physical activity, ethanol intake, tobacco use, HbsAg status on elevated ALT.

In conclusion, prevalence of elevated ALT was more common in adult population compared to college students in Taiwan. BMI was a significant predictor for the risk of elevated ALT which was more accurate in male than in female. To identify college students population in Taiwan at risk of elevated ALT, BMI cut-off points little higher than currently recommended overweight is needed in male students while lower than overweight is suggested in female.

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