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Association between Asia–Pacific body mass index classification and serum liver enzymes: alanine aminotransferase, aspartate aminotransferase and gamma-glutamyl transferase in healthy individuals

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Abstract

Background Elevated levels of serum liver transaminases are good indicators of liver cell damage, and elevated serum gamma-glutamyl transferase (GGT) level is a good indicator of both bile duct and hepatocellular damage. At early stages, elevated serum levels of these liver enzymes can be mostly prevailed as an asymptomatic condition and therefore in an undiagnosed state. This may be resulted in a number of complications and may lead to chronic hepatic damage that will be more severe and difficult to care. Serum liver enzyme levels are affected by age, gender, body mass index (BMI), ethnicity, drugs and viruses. Obesity has been an epidemic in nearly every country in the world. BMI is the best parameter to assess the magnitude of obesity. Having this background, the present study was designed to investigate the correlation between the levels of serum liver enzymes alanine aminotransferase (ALT), aspartate aminotransferase (AST) and GGT and Asia–Pacific cut-off points of BMI in healthy individuals.

Methods A descriptive cross-sectional study was conducted using 120 Sinhala, Buddhist subjects which belonged to 18–32 years. BMI was calculated according to the standard protocol. The serum ALT and AST concentrations were measured by UV assay according to the IFCC method without pyridoxal phosphate activation, and the serum GGT concentration was measured by UV assay according to Szasz method, using the Mindray BS-240 Full Automatic Biochemistry Analyser.

Results Serum levels of liver enzymes were significantly higher in males than females. In females, serum levels of ALT ($r=0.312$, $p<0.001$), AST ($r=0.138$, $p=0.071$) and GGT ($r=0.212$, $p=0.047$) positively correlated with BMI. In males too, serum levels of ALT ($r=0.431$, $p<0.001$), AST ($r=0.324$, $p=0.013$) and GGT ($r=0.314$, $p=0.031$) were positively correlated with BMI. The minimum values of serum ALT, AST and GGT levels were observed in underweight group, while the maximum values were observed in obese group in both genders.

Conclusions ALT had the strongest correlation with BMI in both females and males. Therefore, ALT can be suggested as the best liver enzyme that can be used in screening purposes by concerning BMI.

Keywords Alanine aminotransferase, Aspartate aminotransferase, Gamma-glutamyl transferase, Body mass index

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Introduction

The liver is an utmost important organ in human body, and it deals with a wide variety of metabolic processes. Liver diseases can lead to a numerous complications, and they can even be life threatening [1]. Most often in many individuals with liver diseases, the hepatic function can be normal. But serum activities of cytosolic, membrane-associated and mitochondrial enzymes of hepatocytes are elevated in various types of liver diseases [2]. Alanine aminotransferase (ALT), aspartate aminotransferase (AST) and gamma-glutamyl transferase (GGT) are clinically important liver enzymes of concerned. Each of these enzymes is being tested as a part of liver function test in diagnosis of liver diseases [3]. Elevated serum levels of these liver enzymes can be mostly prevailed as asymptomatic and therefore in an undiagnosed state. This may be resulted in a number of complications and may lead to chronic hepatic damages that will be more severe and difficult to cure.

ALT, AST and GGT are furthermore affected by other factors such as gender, age, body mass index (BMI), alcohol consumption, viruses such as hepatitis B and C and drugs. "Obesity" has been an epidemic in nearly every country in the world [4]. BMI is the best parameter to assess the magnitude of obesity. Overconsumption of energy-dense foods, sedentary life style, genetic factors and endocrine and neuronal system increase the energy storage in adipose tissue and produce adverse health consequences [5].

There are differences in BMI cut-off values of Asians when compared to Western population [6]. Serum levels of liver enzymes ALT, AST and GGT are highly affected by ethnicity and food habits which mainly vary with culture, religious background and geography. And also, there is a huge deviation related to ethnicity and food habits in between developed and developing countries [7].

According to the Asia–Pacific cut-off points, BMI is categorized as underweight (<18.5 kg/m^2), normal weight (18.5–22.9 kg/m^2), overweight (23–24.9 kg/m^2) and obese (≥25 kg/m^2). Though the cut-off point of underweight is similar, other three cut-off points of Asia Pacific categorization are deviated from the WHO BMI categorization, i.e. according to the WHO categorization normal weight (18.5–24.9 kg/m^2), overweight (25–29.9 kg/m^2) and obese (≥30 kg/m^2) [6].

The most important fact to be considered is that obesity has been identified as a risk factor of liver disease and disease progression. During last few years, it has been reported that in developed countries occurring of liver diseases as a global burden due to obesity [8]. Furthermore, it has been reported that there is a dramatic increase in liver diseases owing to obesity during past decades [9]. So, it has a great importance on screening serum levels of liver enzymes at the early stage of overweight and obese individuals as they are more prone to liver diseases. Thereby, they can obtain proper treatments before falling into risk.

If it is possible to build up a correlation between serum liver enzyme levels and BMI, people can think on screening tests by concerning their BMI. As a majority of chronic liver disease is asymptomatic, this would be very useful in developing a model for disease screening. Overweight and obese subjects can be made aware of the correlation between BMI and serum liver enzyme levels and encouraged to reduce their weight with respect to their height. People can assume their degree of risk for the liver disease with the aid of BMI, and thereby, they can manage their food habits or lifestyle. Physicians can concern about this correlation when interpreting the results of liver enzyme tests especially in overweight and obese patients. Therefore, the objective of present study was to investigate the correlation between the levels of serum liver enzymes ALT, AST and GGT and BMI according to Asia Pacific cut-off points of BMI categorization and to determine the best liver enzyme that can be used in screening purposes by concerning BMI.

Materials and methods

This study was a descriptive cross-sectional study with laboratory investigations. The study was conducted after obtaining ethical approval from the Ethical Review Committee, Faculty of Medical Sciences, University of Sri Jayewardenepura, Sri Lanka.

Study population

The study population included 120 subjects, and they were selected according to the inclusion and exclusion criteria by examining the answers provided to the self-administered questionnaire. Inclusion criteria were healthy Sinhala, Buddhist, males and females within 18–32 age group. The exclusion criteria included individuals who were clinically diagnosed with liver diseases, patients suffering from renal failure, cardiac diseases, type-2 diabetes, hypertension and respiratory diseases, alcoholics, people with routine medication and pregnant and lactating women.

Sample size calculation

Subjects were selected by convenience sampling method, and sample size was calculated according to the following equation ensuring a higher precised sample.

$$n = \frac{Z^2\sigma^2}{e^2}$$

where:

Z: Confidence level = 95%

σ^2: Variance

e: Chance of sampling error

n: Sample size

Thirty subjects from each BMI category were recruited to the study.

Calculation of body mass index (BMI)

Height and weight were measured following the standard protocols, and BMI was calculated according to following formula.

$$\text{BMI} = \frac{\text{Weight}(\text{kg})}{\text{Height}(\text{m}^2)}$$

After that, the BMI value of each individual was included in the appropriate BMI category according to the Asia–Pacific cut-off points: (i) BMI < 0.5 kg/m^2 (underweight), (ii) BMI between 18.5 and 22.9 kg/m^2 (normal weight), (iii) BMI between 23.0 and 24.9 kg/m^2 (overweight) and (iv) BMI ≥ 25.0 kg/m^2 (obese).

Collection of blood specimens and serum separation

Three millilitres of whole blood was drawn from each subject after following venipuncture. All the collected blood specimens were left undisturbed at room temperature for 30 min by keeping the plain tubes with blood in an upright position in a tube rack. All the specimens were observed clotted after 30 min. Then, the tubes were gently tapped in order to detach the clot from the bottom of the tubes. Next, the clotted specimens in plain tubes were centrifuged at 3000 rpm for 5 min. After centrifugation, tubes were carefully observed for haemolysis before serum was separated. Finally, the supernatant was separated and transferred into Eppendorf tube, and the serum specimens were stored at − 20 °C until the analysis.

Determination of serum liver enzyme levels

The levels of three liver enzymes in all the serum specimens were measured using the Mindray BS-240 Full Automatic Biochemistry Analyser. Before the serum specimen analysis, the analyser was calibrated for the serum liver enzymes: ALT, AST and GGT, using the human multi-calibrator from Mindray, and calibration was done according to the manufacturer's instructions. Following the calibration, two quality control (QC) samples (Human Assayed Control from Mindray), one with a known normal value (normal level control) and other with a known abnormal value (pathological level control) for each serum liver enzyme, were run in order to verify the performance of the measurement procedure. The serum specimens were analyzed after obtaining results of the quality control.

Data analysis

Data analysis was done using IBM Statistical Package for Social Sciences (SPSS) software version 25. Mann–Whitney *U*-test was used to compare the statistical significance of differences in median ALT, AST and GGT levels between two subgroups. Kruskal–Wallis test was used to compare the median values of ALT, AST and GGT levels among more than two subgroups. Spearman correlation was used to evaluate the correlation between serum liver enzyme levels and BMI.

Results

Distribution of serum liver enzyme levels in the study population

The distribution of serum ALT, AST and GGT levels in the whole study population was a skewed distribution as shown in Figs. 1, 2 and 3, respectively. Furthermore, the distribution of above-mentioned enzymes in males and females separately was also a skewed distribution. On account of this skewed distributions, we considered the median values for serum ALT, AST and GGT levels in the study population.

Association between serum liver enzyme levels and gender

The distribution of serum liver enzyme levels in the study population according to the gender is given in Table 1. Median ALT, AST and GGT levels of males were higher by 15.4, 4.5 and 9.9 U/L, respectively, compared to females. As a result, males showed a statistically significant higher median ALT, AST and GGT levels compared to females ($p < 0.05$).

Distribution of serum liver enzyme levels according to BMI

The distribution of minimum, maximum and median serum liver enzyme levels and IQR according to the BMI in male and female study populations is indicated in Table 2. The distribution of median and IQR serum liver enzyme levels in the study population within four BMI groups is indicated in Table 3.

Comparison of median ALT, AST and GGT levels across BMI categories

Kruskal–Wallis test was used to compare the median values of ALT, AST and GGT levels separately across categories of BMI in female and male study populations. In the female study population, there was a significant difference in ALT and GGT level across BMI categories ($p < 0.05$). However, there was no significant difference in AST level across categories of BMI in females ($p > 0.05$).

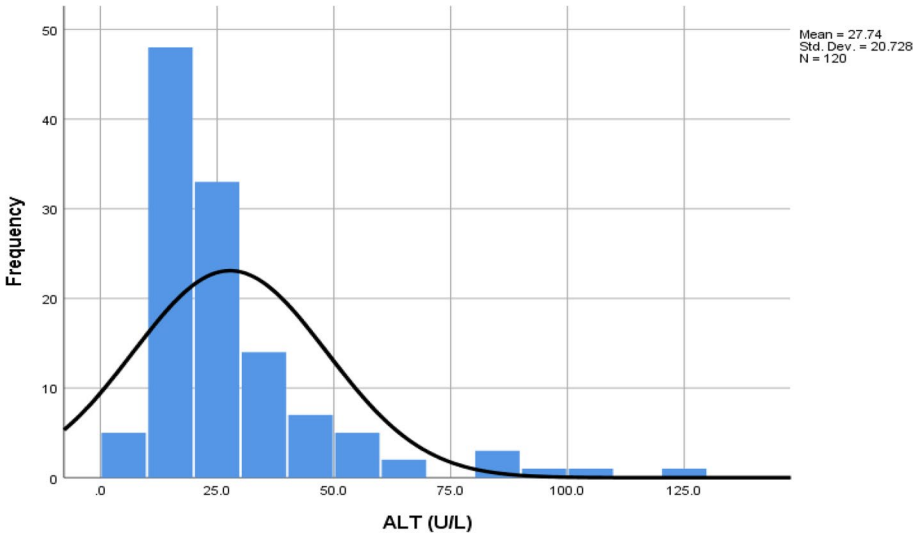

Fig. 1 Distribution of serum ALT level in the study population. Skewness: 1.432. Kurtosis: 3.213. *p*-value: < 0.001

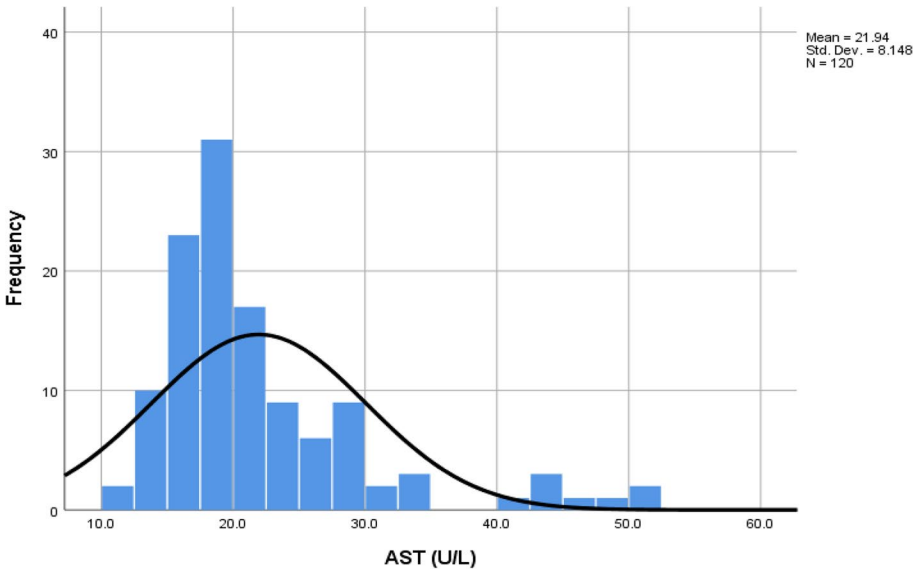

Fig. 2 Distribution of serum AST level in the study population. Skewness: 1.461. Kurtosis: 3.145. *p*-value: < 0.001

In the male study population, there was a significant difference in ALT and AST levels across categories of BMI ($p < 0.05$). But there was no significant difference in GGT level across BMI categories in males ($p > 0.05$).

Identification of statistically significant BMI groups with respect to serum liver enzyme levels in males and females

Following Kruskal–Wallis test, Mann–Whitney *U*-test was performed to compare the statistical significance of differences between two groups. The test was used to compare the median values of ALT and GGT levels separately between BMI groups in the female study population and to compare the median values of ALT and AST levels separately between BMI groups in the male study population in order to identify the BMI groups which are having significantly different median values of ALT and GGT levels in female study population and having significantly different median values of ALT and AST levels in male study population.

There was a significant difference between median ALT levels of underweight and normal weight females ($p < 0.05$). Median ALT level of normal weight females was 5.6 U/L higher than that of underweight females.

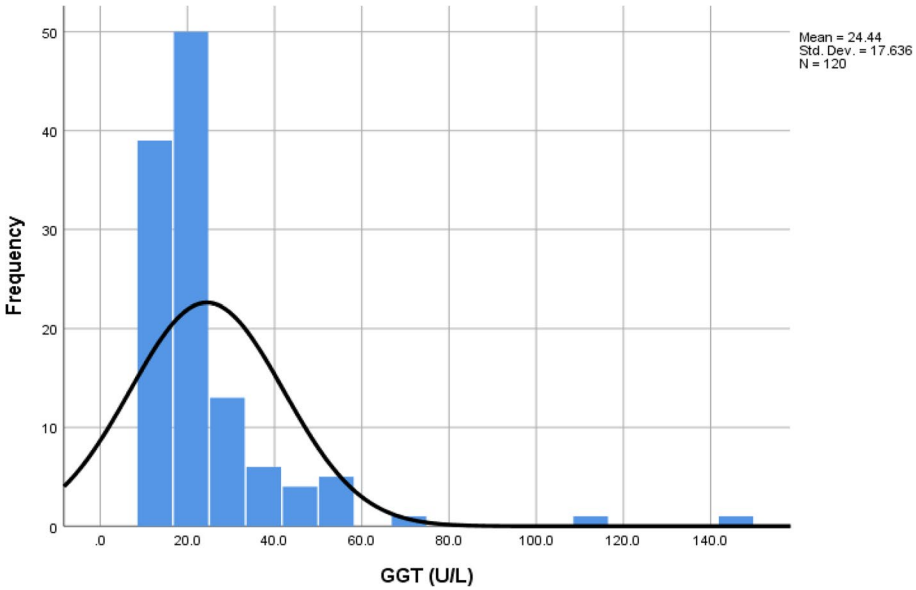

Fig. 3 Distribution of serum GGT level in the study population. Skewness: 2.541. Kurtosis: 4.232. *p*-value: < 0.001

Table 1 Distribution of serum liver enzyme levels in the study population according to the gender

Gender	ALT (U/L)	AST (U/L)	GGT(U/L)
Female			
Minimum	8.5	10.0	10.6
Maximum	102.7	49.8	142.1
Median	17.8	18.1	17.3
IQR	13.0	14.3	22.4
Q1	14.3	16.1	15.4
Q3	27.3	30.4	37.8
Male			
Minimum	10.0	16.1	13.4
Maximum	126.7	52.1	116.0
Median	33.2	22.6	27.2
IQR	23.0	20.1	24.0
Q1	25.3	20.8	22.5
Q3	48.3	40.9	46.5

The difference between median ALT levels of normal weight and overweight females ($p > 0.05$) and overweight and obese females ($p > 0.05$) was not significant. However, there was a significant difference between median ALT levels of underweight and overweight females ($p < 0.05$) and underweight and obese females ($p < 0.05$). Median ALT level of overweight females was 9.0 U/L higher than that of underweight females, while the median ALT level of obese females was 13.1 U/L higher than that of underweight females. Also, there was a significant difference between median ALT levels of normal weight and obese females ($p < 0.05$). Median ALT level of obese females was 7.5 U/L higher than that of normal weight females.

The difference between median GGT levels of underweight and normal weight females ($p > 0.05$), normal weight and overweight females ($p > 0.05$) and overweight and obese females ($p > 0.05$) was not significant. However, there was a significant difference between median GGT levels of underweight and overweight females ($p < 0.05$) and underweight and obese females ($p < 0.05$). Median GGT level of overweight females was 4.0 U/L higher than that of underweight females, while the median GGT level of obese females was 5.4 U/L higher than that of underweight females. Also, there was a significant difference between median GGT levels of normal weight and obese females ($p < 0.05$). Median GGT level of obese females was 4.4 U/L higher than that of normal weight females.

There was a significant difference between median ALT levels of underweight and normal weight males ($p < 0.05$). Median ALT level of normal weight males was 15.2 U/L higher than that of underweight males. The difference between median ALT levels of normal weight and overweight males ($p > 0.05$) and overweight and obese males ($p > 0.05$) was not significant. However, there was a significant difference between median ALT levels of underweight and overweight males ($p < 0.05$) and underweight and obese males ($p > 0.05$). Median ALT level of overweight males was 18.6 U/L higher than that of underweight males, while median ALT level of obese males was 35.5 U/L higher than that of underweight males. Also, there was a significant

Table 2 Distribution of minimum, maximum, median and IQR serum liver enzyme levels in the study population according to the BMI

BMI group	Gender		ALT (U/L)	AST (U/L)	GGT (U/L)
Underweight	Female	Minimum	8.5	13.4	10.6
		Maximum	26.1	22.7	20.8
		Median	11.7	17.8	15.8
		IQR	6.2	4.3	4.7
	Male	Minimum	10.0	16.1	14.4
		Maximum	29.1	19.1	28.1
		Median	14.1	18.1	18.4
		IQR	5.6	1.6	5.6
Normal weight	Female	Minimum	10.0	10.4	12.6
		Maximum	29.6	27.6	37.7
		Median	17.3	19.2	16.8
		IQR	7.2	8.7	7.1
	Male	Minimum	17.5	18.0	13.4
		Maximum	59.2	31.3	71.2
		Median	29.3	21.9	26.3
		IQR	12.8	5.5	17.4
Overweight	Female	Minimum	11.2	10.0	11.7
		Maximum	102.7	49.8	142.1
		Median	20.7	18.1	19.8
		IQR	19.5	17.2	22.3
	Male	Minimum	22.6	16.8	16.9
		Maximum	84.6	45.3	50.2
		Median	32.3	23.5	27.0
		IQR	13.2	13.2	8.8
Obese	Female	Minimum	11.4	14.2	14.5
		Maximum	47.6	27.2	45.4
		Median	24.8	20.1	21.2
		IQR	16.4	5.6	12.5
	Male	Minimum	19.7	18.6	13.9
		Maximum	126.7	52.1	116.0
		Median	49.6	28.2	31.2
		IQR	49.0	7.6	30.4

difference between median ALT levels of normal weight and obese males ($p < 0.05$). Median ALT level of obese males was 20.3 U/L higher than that of normal weight males.

There was a significant difference between median AST levels of underweight and normal weight males ($p < 0.05$). Median AST level of normal weight males was 3.8 U/L higher than that of underweight males. But the difference between median AST levels of normal weight and overweight males ($p > 0.05$) and overweight and obese males ($p > 0.05$) was not significant. However, there was a significant difference between median AST levels of underweight and overweight males ($p < 0.05$) and underweight and obese males ($p < 0.05$). Median AST level of overweight males was 5.4 U/L higher than that of underweight males, while median AST level of obese males was 10.1 U/L higher than that of underweight males. The difference between median AST levels of normal weight and obese males ($p > 0.05$) was not significant.

Table 3 Distribution of median and IQR serum liver enzyme levels within BMI groups

BMI group	ALT (U/L)	AST (U/L)	GGT (U/L)
Underweight			
Median	12.1	17.9	16.0
IQR	6.7	5.2	6.3
Normal weight			
Median	21.0	19.7	18.3
IQR	15.4	9.8	19.5
Overweight			
Median	22.9	19.8	20.7
IQR	22.3	19.9	25.1
Obese			
Median	34.0	24.3	26.0
IQR	51.6	55.7	37.5

Correlation between serum liver enzyme levels and body mass index (BMI)

Spearman correlation (r) and *p*-values obtained from statistical analysis are given in Table 4.

Association between serum liver enzyme levels and gender

There was a significant association between serum ALT, AST and GGT levels and gender ($p < 0.05$).

Discussion

According to the results of the present study, it was found that serum levels of liver enzymes are significantly higher in males than females, and it is directly in line with the findings of the previous studies [10–13]. This disparity in serum ALT, AST and GGT levels could be due to higher median BMI in the males (24.61 kg/m^2) compared to females (20.50 kg/m^2) in our study population and differences in sex hormones between males and females Table 5.

We obtained a statistically significant positive moderate linear correlation between serum ALT level and BMI which was stronger for males (r = 0.431) than females (r = 0.312). This finding is supported by the previous studies [14–17]. Ahn et al. stated that there is a significant positive association between serum ALT level and BMI in male adolescents [14]. Kim and Jo reported that BMI had a strong positive relationship

Table 4 Correlation between serum liver enzyme levels and BMI in males and females

Gender	ALT (U/L)		AST (U/L)		GGT (U/L)	
	r	*p*-value	r	*p*-value	r	*p*-value
Female						
BMI	0.312**	< 0.001	0.138	0.071	0.212*	0.047
Male						
BMI	0.431**	< 0.001	0.324**	0.013	0.314*	0.031

Correlation is significant at $^{**}p < 0.01$. Correlation is significant at $^{*}p < 0.05$. In the female study population, since $p < 0.05$, there is a significant positive moderate (0.312) linear correlation between ALT level and BMI for females. Since $p < 0.05$, there is a significant positive weak (0.212) linear correlation between GGT level and BMI for females. Since $p > 0.05$, there is no significant linear correlation between AST level and BMI for females. In the male study population, since $p < 0.05$, there is a significant positive moderate (0.431) linear correlation between ALT level and BMI for males. Since $p < 0.05$, there is a significant positive moderate (0.324) linear correlation between AST level and BMI for males. Since $p < 0.05$, there is a significant positive moderate (0.314) linear correlation between GGT level and BMI for male

Table 5 Association between serum liver enzyme levels and gender

	ALT *p*-value	AST *p*-value	GGT *p*-value
Gender	< 0.001	0.017	< 0.001

with an elevated serum ALT level in nondiabetic Korean adults [15]. Bilal et al. stated that there is a strong positive significant correlation between serum ALT level and BMI in apparently healthy individuals [16]. Qureshi et al. reported that ALT was positively correlated with BMI in both females and males [17].

We received a significant moderate positive linear correlation between serum AST level and BMI for males, while no significant linear correlation observed between serum AST level and BMI for females. Sull et al. investigated the association between BMI and serum aminotransferase levels in the Korean population and found that serum aminotransferase levels are strongly associated with BMI [18]. The results from this study are consistent with our findings with regard to serum ALT level in both genders and serum AST level in males but contrast with our finding with regard to serum AST level in females. Loomba et al. reported a significant linear association between BMI and serum ALT in both sexes, but it was seen with AST only in men, and no statistically significant association was observed between serum AST and BMI in women [19]. The results from this study substantially agree with our finding. However, a direct comparison of this study is impossible due to different conditions used, mainly the different BMI cut-off values, age and also the mean values of serum liver enzyme levels considered in this study.

We obtained a significant moderate positive linear correlation between GGT level and BMI for males while a significant but a weak positive linear correlation between GGT level and BMI for females. Al-Sultan reported that serum ALT, AST and GGT levels are significantly correlated with BMI [20]. Puukka et al. stated a significant positive correlation between GGT and BMI [13]. The results from these two studies were consistent with our findings.

From the results of the present study, ALT has the strongest positive linear correlation with BMI compared to AST and GGT in both males and females. Accordingly, ALT might be a better marker of hepatic pathology associated with obesity, and ALT can be proposed as the best liver enzyme that can be used in screening purposes by concerning BMI.

The median serum ALT levels in females of underweight, normal weight, overweight and obese group were 11.7, 17.3, 20.7 and 24.8 U/L, respectively, while in males 14.1, 29.3, 32.7 and 49.6 U/L, respectively. Therefore, according to the results of the present study, underweight group had the minimum median value, and obese group had the maximum median value for serum ALT level in both genders. Furthermore, in each BMI category, males had higher median serum ALT levels than females. Sull et al. investigated the association between BMI and serum aminotransferase levels in Korean population and found that serum aminotransferase levels increased progressively from the lowest to the highest category of BMI across the range of BMI from < 18.5 to ≥ 32 kg/m^2 [18]. This finding supports our finding for serum ALT level. Strauss et al. stated that overweight and obesity are the most common findings in adolescents with higher serum ALT levels [21]. This study also supports our findings. We obtained a statistically significant difference in median ALT levels across BMI categories in both females and males. Furthermore, there was a significant difference between median ALT levels of underweight and normal weight, underweight and overweight and underweight and obese BMI groups in both females and males. Similarly, there was a significant difference between median ALT levels of normal weight and obese groups in both

genders. However, we did not receive a statistically significant difference in median ALT levels between any of the other two BMI groups (normal weight and overweight, overweight and obese) in both females and males.

The median serum AST levels in females of underweight, normal weight, overweight and obese were 17.8, 19.2, 18.1 and 20.1 U/L, respectively, while in males 18.1, 21.9, 23.5 and 28.2 U/L, respectively. Accordingly, underweight group had the minimum median value, and obese group had the maximum median value for serum AST level in both females and males. Also, in each BMI category, males had higher median serum AST levels than females. Al-Sultan stated that obese individuals showed higher serum ALT and AST levels than non-obese [20]. Marchesini et al. reported that median serum ALT and AST levels increased with increasing obesity classes [22]. Also, Tasneem et al. stated that ALT and AST levels get increased in overweight obese and morbid obese in both genders when compared to normal group [23]. Therefore, results from previous studies substantially agree with our findings of serum ALT levels in both males and females and serum AST level in males but contradictory with our finding of serum AST level in females. However, a direct comparison of these studies is impossible due to different conditions used, mainly the differing BMI cut-off values from our Asian cut-off points of BMI. We obtained a statistically significant difference in median AST levels across BMI categories in males but not in females. There was a significant difference between median AST levels of underweight and normal weight, underweight and overweight and underweight and obese BMI groups in males. However, we did not obtain a statistically significant difference in median AST levels between any of the other two BMI groups in males.

The median serum GGT levels in females of each BMI category obtained were 15.8, 16.8, 19.8 and 21.2 U/L for underweight, normal, overweight and obese group, respectively, whereas for males were 18.4, 26.3, 27.0 and 31.1 U/L, respectively. Therefore, according to the results of the present study, underweight group had the minimum median value, and obese group had the maximum median value for serum GGT level in both genders. Also, males had higher median serum GGT levels than females in each BMI category. Al-Sultan reported that obese individuals (BMI $\geq$ 30 kg/m^2) showed higher serum GGT levels than nonobese (BMI < 25 kg/m^2) individuals [20]. The results from this study substantially support our findings. But a direct comparison of this study is impossible because BMI cut-off points used were significantly deviated from our Asian cut-off points. Puukka et al. stated that serum GGT activities were higher in subjects with higher BMI [13]. This study also supports our findings. We received a statistically significant difference in GGT levels across BMI categories in females but not in males. Furthermore, there was a significant difference between GGT levels of underweight and overweight females and underweight and obese females. Similarly, there was a significant difference between GGT levels of normal weight and obese females. However, we did not obtain a statistically significant difference in GGT levels between any of other two BMI groups in females.

From the results of the present study, we received an increase trend in the median values of serum ALT and GGT levels from normal to obese BMI categories in both females and males. Also, we received an increase trend in median values of serum AST levels from normal to obese BMI categories for males but not for females.

Das et al. reported that there is an increase trend in the ALT, AST and GGT values from normal to obese groups [4]. Results from this study substantially agree with our findings relevant to serum ALT, GGT levels for both genders and AST levels for males only. But the result from this study on serum AST level is contradictory with our finding of serum AST levels in females. However, a direct comparison of this study is not possible because of using BMI cut-off values significantly deviate from our Asian cut-off points.

Utzschneider and Khan reported that obesity leads for liver fat accumulation by decreasing adiponectin levels, thus resulting in inadequate fatty-acid oxidation. The authors also stated that insulin resistance or hyperinsulinemia induced by obesity results in increasing de novo lipogenesis in the liver and increasing free-fatty acid flow to the liver by decreased inhibition of lipolysis, accounting for fat accumulation in the liver [24]. Parekh and Anania reported that insulin resistance is associated with impairing the biosynthesis of ApoB-100 leading to hepatocyte triglyceride accumulation and long-term injury from triglyceride storage in the hepatocytes results in developing oxidative injury, apoptosis of hepatocytes, inflammation and defects in mitochondrial function mainly by expression of uncoupling protein-2 (UCP-2). The authors demonstrated that free fatty acids can cause the direct induction of hepatocellular apoptosis and stimulation of the adipocytokine tumour necrosis factor-α (TNF-α), and free fatty acids can also impair mitochondrial or peroxisomal β-oxidation of free fatty-acid stores of hepatocytes leading for the production of hydrogen peroxide and other lipid peroxidation products that lead to both apoptosis and necrotic injury to hepatocytes affecting hepatocellular membranes and organelles [25]. Thus, destruction of hepatocytes by these mechanisms may lead for elevated serum liver enzyme levels with obesity or with increasing BMI.

Popko et al. stated that overweight and obesity induce increased serum levels of inflammatory mediators or cytokines, mainly IL-6 and TNF-α which are secreted by adipocytes [26]. Also, Campo et al. reported that these cytokines can lead for apoptosis of hepatocytes [27]. Accordingly, a combination of these two studies reveal that increased levels of cytokines in obesity lead to hepatocyte apoptosis, and this might be an another cause for elevated serum liver enzyme levels with increasing BMI or with obesity.

Aubert et al. reported that obesity induces hepatic CYP2E1 which is present in significant amounts within liver mitochondria, and free fatty acids in obesity lead to increase CYP2E1 mRNA and/ or protein levels in human hepatocytes. The authors stated that increased expression of CYP2E1 in obesity leads to oxidative stress due to the production of reactive oxygen species (superoxide anion and hydrogen peroxide) which may result in mitochondrial membrane damage inducing hepatocellular death [28]. Thus, damaged hepatocytes may release liver enzymes, and this might be another cause for elevated serum liver enzyme levels in obese.

According to the results of the present study, we suggest that clinicians should concern about this correlation between serum levels of liver enzyme and BMI when interpreting the results of liver enzyme tests especially in overweight and obese patients.

Conclusions

There is a significant positive moderate linear correlation between ALT level and BMI for both females and males. Although there is a significant positive moderate linear correlation between AST level and BMI for males, there is no significant linear correlation between AST level and BMI for females. Though there is a significant positive moderate linear correlation between GGT level and BMI for males, there is a significant positive but a weak linear correlation between GGT level and BMI for females. Higher serum liver enzyme levels are associated with the obese group, while the lower serum liver enzyme levels are associated with the underweight group. ALT had the strongest correlation with BMI in both females and males. ALT can be suggested as the best liver enzyme that can be used in screening purposes by concerning BMI.

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Authors' contributions
Research idea, D, P and P; study designing, P, D, P and D; acquisition of data, D and P; analysis of data, D, P and D; interpretation of data, D, D, P and P; study supervision, P; drafting the manuscript, P.

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Declarations

Ethics approval and consent to participate
The study was conducted after obtaining ethical approval from the Ethical Review Committee, Faculty of Medical Sciences, University of Sri Jayewardenepura, Sri Lanka.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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