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• *CLINICAL RESEARCH* •

A community-based epidemiological study of elevated serum alanine aminotransferase levels in Kinmen, Taiwan

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Abstract

AIM: To explore any gender-related differences in prevalence of and condition-associated factors related to an elevated serum alanine aminotransferase (ALT) level amongst residents of Kinmen, Taiwan.

METHODS: A total of 11 898 of a potential 20 112 regional residents aged 30 years or more completed a related questionnaire that was carried out by the Yang-Ming Crusade between 1991 and 1994 inclusively, with blood samples being collected by public nurses. The overall questionnaire response rate was 59.3% (52.4% for males and 66.0% for females).

RESULTS: The prevalence of an elevated serum ALT level for this sub-population was found to be 7.2%, the prevalence revealing a statistically significant decrease with increasing population age ($P<0.0001$). Males exhibited a greater prevalence of elevated serum ALT level than did females (9.4% *vs* 5.3%, $P<0.0001$). Using multiple logistic regression analysis, in addition to male gender, a younger age, greater waist circumference, presence of type-2 diabetes and hyperuricemia were the significant factors associated with an elevated serum ALT level for both males and females. Gender-related differences as regards associated factors were also revealed. For males, obesity was significantly related to an elevated serum ALT level (OR = 1.28, 95%CI: 1.00-1.66) but this was not so for females (OR = 1.09, 95%CI: 0.84-1.42). Hypertriglyceridemia (OR = 1.80, 95%CI: 1.36-2.39) and hyperuricemia (OR = 1.61, 95%CI: 1.03-2.52) were significantly related to elevated serum ALT levels only for females.

CONCLUSION: Several gender-related differences were noted pertaining to the prevalence of and relationship between obesity, hypertriglyceridemia and hyperuricemia and elevated serum ALT level in the present study.

Key words: Alanine aminotransferase; Prevalence; Community-based study; Gender difference

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INTRODUCTION

Alanine aminotransferase (ALT) has, for some time, been viewed as a sensitive indicator of liver-cell injury[1]. Currently, the determination of serum ALT level constitutes the most frequently applied test for the identification of patients suffering from liver disease, this parameter also acting as a surrogate marker for disease severity and/or as an index of hepatic activity[2]. This cytosolic enzyme is able to be detected in many organs and is able to catalyze the transfer of the α-amino group from alanine to α-ketoglutaric acid[3]. The current understanding is that elevated serum ALT levels are associated with gender, age, obesity, waist-to-hip ratio, serum glucose concentration, serum triglyceride level, use of certain medication and history of viral hepatitis infection[4-6]. The early detection of this disorder by screening, followed by appropriate intervention, may offer a practical way for the prevention of condition-associated hepatocellular damage.

From the viewpoint of preventive medicine, it is not only important to be cognizant of the background prevalence of elevated serum ALT levels regionally, but also to explore the complete spectrum of demographic and biological markers which may be related to elevated serum ALT levels. Further, to the best of our knowledge, some uncertainty still exists as regards whether the prevalence of and the associated risk factors for an elevated serum ALT level reveal gender difference amongst a sub-population. Thus, in order to identify the prevalence of and associated risk factors for an elevated serum ALT level, a community-based screening program for the detection of elevated serum

ALT level was considered necessary. The present study was designed so as to attempt to explore the potential for condition-related gender difference, because it was considered that such difference might underscore important implications for the understanding of the overall pathogenesis of an elevated serum ALT level. The purpose of this study was to explore such gender difference in the context of prevalence of and associated risk factors for elevated serum ALT levels amongst the general population aged 30 years or more, as determined by the application of a community-based screening program to a well-organized, self-contained community-living on Kinmen Island, Taiwan.

MATERIALS AND METHODS

Study design and data resource

Kinmen is an island located around 90 km west of Taiwan in the Straits of Taiwan, close to the Chinese mainland. Based upon this island's population stability, geographical region and local community-support network, Kinmen was selected as a site to conduct various screening programs for chronic-related diseases, in this instance, elevated serum ALT levels. We conducted this community-based mass screening program targeting subjects aged 30 years or more during the period 1991-1994 inclusively. The details of the study design and execution, with respect to the mass-screening program, have been described in full elsewhere[7]. Briefly, according to resident household registration, a total of 20 112 subjects (10 136 males) were eligible to participate in such population screening. A total of 11 898 individuals (5 311 males) of the original 20 112 subjects underwent screening following their response to an invitation letter or telephone call, such individuals completing a questionnaire and providing a blood sample. The overall response rate was 59.2%, including 52.4% for males and 66.0% for females.

Data collection

Data pertaining to study participants was collected from them, the process including face-to-face interviews together with the provision of a structured questionnaire (questions pertained to demographic details, lifestyle information, and personal disease history), and the determination of participant blood pressure. All these investigations were carried out by the Yang-Ming Crusade, a group of well-trained and -organized medical students from the National Yang-Ming University, Taipei, Taiwan. During the study period, fasting blood samples were drawn via venipuncture from study participants by public-health nurses. Overnight-fasting serum and plasma (from whole blood preserved with EDTA and NaF) samples were kept frozen (-20 ℃) until ready for analysis. Subjects for whom the serum ALT level was ⩾40 U/L were classified as individuals who featured an elevated ALT level[8]. In addition, the study-used definitions of type-2 diabetes and hypertension derived from 1999 WHO criteria[9] and TNC VI (The Sixth Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure)[10], respectively. Subjects featuring a personal disease history of type-2 diabetes or hypertension and who had received medication to treat such conditions were viewed as "known cases" of such disease. Definitions of the following diseases/conditions were obesity: a BMI ⩾25 kg/m^2, a large waist circumference ⩾90 cm for males and ⩾80 cm for females, hypercholesterolemia ⩾200 mg/dL, hypertriglyceridemia ⩾200 mg/dL, low HDL a level <35 mg/dL, high BUN a level ⩾20 mg/dL, high creatinine ⩾1.4 mg/dL and hyperuricemia ⩾7 mg/dL for males or ⩾6 mg/dL for females.

Statistical analysis

Statistical analysis was performed using SAS for Windows (SAS version 8.1; SAS Institute Inc., Cary, NC). A P value of <0.05 was considered to represent statistically significant difference between two test populations. For the univariate analysis, the two-sample independent t-test method was adopted to assess difference in the mean value of continuous variables between normal and elevated serum ALT levels. Crude and adjusted odds ratios (adjustment for sex and age) were estimated and 95% confidence intervals were used. Multiple logistic regressions were also performed in order to investigate the independence of risk factors associated with a high serum ALT level.

RESULTS

The overall mean of serum ALT level for the test population proved to be 20.85±44.82 U/L, males revealing a greater serum ALT level than was the case for females (respectively, 23.77±50.91 U/L *vs* 18.49±39.06 U/L, P<0.05). Table 1

Table 1 Gender- and age-specific prevalence of elevated serum alanine aminotransferase (ALT) level among subjects aged 30 and above in Kinmen

	Level of ALT (U/L)											
	Male (n = 5 311)				Female (n = 6 587)				Total (n = 11 898)			
Age (yr)	Screened No	⩾40 (U/L) No	Prevalence (%)	P-value for χ^2 test for trend	Screened No	⩾40 (U/L) No	Prevalence (%)	P-value for χ^2 test for trend	Screened No	⩾40 (U/L) No	Prevalence (%)	P-value for χ^2 test for trend
30–39	1 326	173	13.1		2 215	96	4.3		3 541	269	7.6	
40–49	1 255	144	11.5	<0.0001	1 581	94	6.0	0.192	2 836	238	8.4	<0.0001
50–59	1 456	112	7.7		1 224	75	6.1		2 680	187	7.0	
60–69	840	47	5.6		978	60	6.1		1 818	107	5.9	
⩾70	434	24	5.5		589	26	4.4		1 023	50	4.9	
Total	5 311	500	9.4		6 587	351	5.3		11 898	851	7.2	

Table 2 Comparison of characteristics of elevated serum ALT level among subjects aged 30 and over in Kinmen (mean±SD)

Variable	Level of ALT (U/L)			
	<40 (U/L) (n = 11 074)	≥40 (U/L) (n = 851)	Total (n = 11 898)	P-value for t test
Age (yr)	49.7±13.3	47.9±12.2	49.6±13.2	0.0001
BMI (kg/m^2)	23.3±3.4	24.6±3.4	23.4±3.5	<0.0001
Waist circumference (cm)	82.7±10.1	86.6±9.7	83.1±10.2	<0.0001
FPG (mg/dL)	100.3±28.2	105.4±28.8	100.9±28.2	<0.0001
SBP (mmHg)	129.8±21.0	132.7±19.7	129.9±20.9	<0.0001
DBP (mmHg)	80.0±12.4	83.5±12.0	80.3±12.4	<0.0001
Cholesterol (mg/dL)	201.4±39.5	211.3±44.2	202.2±40.0	<0.0001
Triglyceride (mg/dL)	91.8±57.7	120.9±79.2	93.9±60.0	<0.0001
HDL (mg/dL)	56.5±20.0	55.9±23.9	56.5±20.5	0.49
BUN (mg/dL)	16.6±5.5	16.8±5.1	16.6±5.5	0.39
Creatinine (mg/dL)	0.79±0.31	0.84±0.26	0.79±0.31	<0.0001
Uric acid (mg/dL)	5.5±1.6	6.3±1.7	5.6±1.6	<0.0001

presents the gender- and age-specific prevalence of an elevated serum ALT level (≥40 U/L) amongst study-participating subjects aged 30 years and over. The overall prevalence of an elevated serum ALT level for the test population was 7.2%, this parameter revealing a statistically significant decrease with increasing study-subject age by means of the χ^2 trend test (P<0.0001). The prevalence of an elevated serum ALT level proved to be substantially greater for males than for females (respectively, 9.4% *vs* 5.3%, P value for χ^2 test <0.0001). In addition, after stratifying data by age into one of five broad (age) groups, study-participating males exhibited a more-pronounced prevalence of elevated serum ALT level for all age groups apart from the 60-69-years-old age group than was the case for the female group. The age-specified prevalence of an elevated serum ALT level revealed a significant inverse relationship with age when applying the χ^2 trend test (P<0.0001) for male study subjects but not so for females (P = 0.192).

Table 2 illustrates the results of the comparison of a variety of test characteristics and their potential association with the specific (serum ALT) class value (either ≥40 U/L, or <40 U/L) for study-included subjects aged 30 years and over. Using the two-sample independent t-test, the associated factors that were significantly related to elevated serum ALT level included age [≥40 U/L (47.7±12.2 years) *vs* <40 U/L (49.7±13.3 years)], BMI [≥40 U/L (24.6±3.4 kg/m^2) *vs* <40 U/L (23.3±3.4 kg/m^2)], waist circumference [≥40 U/L (86.6±9.7 cm) *vs* <40 U/L (82.7±10.1 cm)], and serum level of FPG [≥40 U/L (105.4±28.8 mg/dL) *vs* <40 U/L (100.3±28.2 mg/dL)], SBP [≥40 U/L (132.7±19.7 mmHg) *vs* <40 U/L (129.8±21.0 mmHg)], DBP [≥40 U/L (83.5±12.0 mmHg) *vs* <40 U/L (80.0±12.4 mmHg)], cholesterol [≥40 U/L (211.3±44.2 mg/dL) *vs* <40 U/L (201.4±39.5 mg/dL)], triglyceride [≥40 U/L (120.9±79.2 mg/dL) *vs* <40 U/L (91.8±57.7 mg/dL)], creatinine [≥40 U/L (0.84±0.26 mg/dL) *vs* <40 U/L (0.79±0.31 mg/dL)], and uric acid [≥40 U/L (6.3±1.7 mg/dL) *vs* <40 U/L (5.5±1.6 mg/dL)].

Table 3 presents the crude and adjusted odds ratios for the association between certain relevant associated risk factors and elevated serum ALT level. Compared to individuals who exhibited a normal serum ALT level, subjects featuring an elevated serum ALT level revealed a more-

Table 3 Univariate analysis of associated factors for elevated serum alanine ALT level among subjects aged 30 and over in Kinmen

		Elevated ALT level (≥40U/L)		Crude OR (95%CI)	Adjusted OR[1] (95%CI)
		Yes (n = 851)	No (n = 11 074)		
Gender	Male	500	4 811	1.85	-
	Female	351	6 236	(1.60-2.13)	
Age (yr)	30-39	269	3 272	1.00	-
	40-49	238	2 598	1.11	-
				(0.93-1.34)	
	50-59	187	2 493	0.91	-
				(0.75-1.11)	
	60-69	107	1 711	0.76	-
				(0.60-0.96)	
	≥70	50	973	0.63	-
				(0.46-0.85)	
Smoking	Yes	267	2 941	1.26	0.87
	No	584	8 106	(1.08-1.47)	(0.72-1.04)
Alcohol drinking	Yes	266	2 362	1.67	1.24
	No	585	8 685	(1.44-1.95)	(1.04-1.48)
Obesity	Yes	360	3 032	1.94	2.05
	No	491	8 015	(1.68-2.23)	(1.77-2.37)
High waist - circumference	Yes	471	4 599	1.72	2.41
	No	380	6 388	(1.50-1.98)	(2.07-2.80)
Type-2 diabetes	Yes	134	938	2.01	2.39
	No	717	10 109	(1.66-2.45)	(1.94-2.93)
Hypertension	Yes	366	3 850	1.41	1.54
	No	485	7 197	(1.22-1.62)	(1.32-1.79)
Hypercholesterolemia	Yes	205	1 682	1.77	1.85
	No	646	9 362	(1.50-2.08)	(1.56-2.19)
Hypertriglyceridemia	Yes	99	518	2.66	2.65
	No	745	10 383	(2.12-3.34)	(2.10-3.33)
Low HDL	Yes	138	1 337	1.45	1.34
	No	663	9 324	(1.20-1.76)	(1.10-1.63)
High BUN	Yes	193	2 446	1.03	1.01
	No	658	8 598	(0.87-1.22)	(0.85-1.20)
High creatinine	Yes	7	132	0.69	0.66
	No	843	10 909	(0.32-1.47)	(0.31-1.42)
Hyperuricemia	Yes	342	2 680	2.10	2.08
	No	507	8 355	(1.82-2.43)	(1.79-2.40)

[1]Adjustment for gender and age.

pronounced prevalence of alcohol drinking (adjusted OR = 1.24, 95%CI: 1.04-1.48), in addition to obesity (adjusted OR = 2.05, 95%CI: 1.77-2.37), substantial waist circumference (adjusted OR = 2.41, 95%CI: 2.07-2.80), type-2 diabetes (adjusted OR = 2.39, 95%CI: 1.94-2.93), hypertension (adjusted OR = 1.54, 95%CI: 1.32-1.79), hypercholesterolemia (adjusted OR = 1.85, 95%CI: 1.56-2.19), hypertriglyceridemia (adjusted OR = 2.65, 95%CI: 2.10-3.33), a low HDL level (adjusted OR = 1.34, 95%CI: 1.10-1.63), and hyperuricemia (adjusted OR = 2.08, 95%CI: 1.79-2.40) subsequent to adjustment for gender and age.

The effect of independently associated risk factors upon elevated serum ALT level was examined using the multiple logistic regression models. As is depicted in Table 4, subsequent to adjustment for confounding factors, gender (female *vs* male, OR = 0.21, 95%CI: 0.11-0.39), age (OR = 0.95, 95%CI: 0.93-0.97), interaction between gender and age (OR = 1.02, 95%CI: 1.01-1.03), and the presence of obesity (yes *vs* no, OR = 1.20, 95%CI: 1.00-1.44), a large waist circumference (yes *vs* no, OR = 1.79, 95%CI: 1.48-2.17), type-2 diabetes (yes *vs* no, OR = 1.70, 95%CI: 1.35-2.13), hypercholesterolemia (yes *vs* no, OR = 1.46, 95%CI: 1.22-1.76), hypertriglyceridemia (yes *vs* no, OR = 1.40, 95%CI: 1.06-1.84), and hyperuricemia (yes *vs* no, OR = 1.63, 95%CI: 1.39-1.92) appeared to be statistically significantly related to an elevated serum ALT level. The data presented in Table 4 also show the dramatically different results of multiple logistic regressions of the data as stratified by gender. For males, the statistically significantly associated risk -factors related to an elevated serum ALT level included age (OR = 0.97, 95%CI: 0.96-0.98), and the presence of obesity (yes *vs* no, OR = 1.28, 95%CI: 1.00-1.66), a large waist circumference (yes *vs* no, OR = 1.88, 95%CI: 1.45-2.42), type-2 diabetes (yes *vs* no, OR = 1.74, 95%CI: 1.28-2.37), and hyperuricemia (yes *vs* no, OR = 1.47, 95%CI: 1.19-1.80). For female study participants, the statistically significant associated risk factors related to an elevated serum ALT level included age (OR = 0.98, 95%CI: 0.97-0.99), and presence of a large waist circumference (yes *vs* no, OR = 1.66, 95%CI: 1.24-2.21), type-2 diabetes (yes *vs* no, OR = 1.56, 95%CI: 1.11-2.21), hypercholesterolemia (yes *vs* no, OR = 1.80, 95%CI: 1.36-2.39), hypertriglyceridemia (yes *vs* no, OR = 1.61, 95%CI: 1.03-2.52), and hyperuricemia (yes *vs* no, OR = 1.92, 95%CI: 1.49-2.48).

DISCUSSION

Prevalence of an elevated serum ALT level

One of the important benefits of the ALT screening program was the chronic liver disease which was often identified by the detection of an (asymptomatic) elevated serum aminotransferase level and as such, a screening test was commonly included in the serum chemistry panels conducted on healthy individuals[11]. Further, the relative significance of such results was often ignored when the serum ALT level was deemed to be only just slightly abnormal[11]. However, it would appear that only few community-based studies have been published, attempting to determine the prevalence and possible etiology of an elevated serum ALT level for the general population of Taiwan[12], that also faced to the burden of liver disease. In the present study, an elevated serum ALT level appeared to be fairly common for the test population, the condition affecting an estimated 7.2% of the general population in Kinmen. The prevalence of an elevated serum ALT level amongst different test populations appears to vary according to the results of different studies conducted in different countries[6,11-13]. In addition to the differences in the specifics of diagnostic criteria for such an elevated serum ALT level, this disparity would likely be largely due to differences between different population stocks. The prevalence of an elevated serum ALT level for our study population (7.2%) was slightly lower than the corresponding figure presented in a previous population-based study conducted in A-Lein, Taiwan which was reported to be 7.5%[12]. The apparent slightly lower prevalence rate in our study may have been due to differences between the predominantly rural lifestyle of residents of Kinmen and the more urban lifestyle of

Table 4 Multiple logistic regression of associated factors for elevated serum ALT level among subjects aged 30 and above in Kinmen

Variable	ALT (≥40 (U/L) *vs* <40 (U/L))					
	Male		Female		Total	
	OR	95%CI	OR	95%CI	OR	95%CI
Gender (female *vs* male)	-	-	-	-	0.21	0.11-0.38
Age (yr)	0.97	0.96-0.98	0.98	0.97-0.99	0.95	0.93-0.97
Interaction between gender and age	-	-	-	-	1.02	1.01-1.03
Smoking (yes *vs* no)	0.93	0.76-1.14	0.68	0.33-1.38	0.90	0.74-1.10
Alcohol drinking (yes *vs* no)	1.14	0.93-1.40	1.48	0.85-2.59	1.17	0.96-1.41
Obesity (yes *vs* no)	1.28	1.00-1.66	1.09	0.84-1.42	1.20	1.00-1.44
High waist circumference (yes *vs* no)	1.88	1.45-2.42	1.66	1.24-2.21	1.79	1.48-2.17
Type-2 diabetes (yes *vs* no)	1.74	1.28-2.37	1.56	1.11-2.21	1.70	1.35-2.13
Hypertension (yes *vs* no)	1.12	0.91-1.38	1.18	0.90-1.55	1.14	0.97-1.34
Hypercholesterolemia (yes *vs* no)	1.26	0.98-1.61	1.80	1.36-2.39	1.46	1.22-1.76
Hypertriglyceridemia (yes *vs* no)	1.30	0.91-1.85	1.61	1.03-2.52	1.40	1.06-1.84
Low HDL (yes *vs* no)	0.96	0.74-1.25	1.12	0.79-1.60	1.02	0.82-1.25
High BUN (yes *vs* no)	0.92	0.73-1.16	1.10	0.82-1.48	0.99	0.82-1.19
High creatinine (yes *vs* no)	0.55	0.22-1.40	0.25	0.03-1.89	0.46	0.20-1.06
Hyperuricemia (yes *vs* no)	1.47	1.19-1.80	1.92	1.49-2.48	1.63	1.39-1.92

residents of A-Lein, Taiwan. The incidental finding in our study that approximately 47.6% of study-included males had not undergone any form of health screening previously might also partially explain the apparently low prevalence of elevated serum ALT level observed in our study. Further, another possible reason for such difference between the results of the A-Lein study and our results may simply have been related to the different age cut-off point for the two study populations.

Implications of gender difference as regards associated risk factors for elevated serum ALT level

Our results have revealed that male gender and a younger age both represented significant risk factors related to the likelihood of an elevated serum ALT level. Such a finding would appear to be consistent with the results of other hospital and community-based studies conducted elsewhere[6,11,14]. This apparent concentration of liver injury amongst predominantly younger adults remained unexplained at the time of publishing of these (overseas-based) studies, as is the case here, and clearly deserves further attention[6]. In addition, males exhibited a higher prevalence of elevated ALT level than did females (OR = 1.85, 95%CI: 1.60-2.13), such gender difference being consistent with a larger waist-to-hip circumference ratio for males, the latter possibly explaining the former[6].

A growing body of evidence appears to indicate that significant liver disease may accompany (seemingly) mild serum aminotransferase level elevations[15,16]. Consistent with the results of other studies[11,13], our results revealed that a larger BMI and a more-substantial waist circumference were both highly associated with an elevated serum ALT level. Previous studies have indicated that most obese individuals who featured an elevated serum ALT level did suffer from steatosis without any associated hepatic fibrotic reactions or sites of inflammation upon liver biopsy[17,18]. Further, approximately 30% of obese adults, who exhibited an elevated serum aminotransferase level, exhibited steatohepatitis associated with fibrosis or cirrhosis as demonstrated upon liver biopsy[17,18], approximately 40% of these cases revealed progressive liver disease[19]. In addition to such a finding, a larger waist circumference was also reported to be more strongly related to an elevated serum ALT level than was the case for an elevated BMI level for this last-mentioned study[19]. The possible mechanism for such a finding may relate to the observation that waist circumference is typically associated with visceral adipose tissue build-up, such a source of adipose tissue possibly providing a over-supply of potentially hepatotoxic fatty acids to the liver[20]. Further, it has been reported previously that visceral adipose tissue lipolysis was also less sensitive to insulin suppression than was the case for other fat deposits[21]. The present study has further demonstrated that a larger BMI is significantly related to an elevated serum ALT level for males but not so for females subsequent to adjusting for confounding factors. Further epidemiological and etiological investigations are clearly needed in order to clarify the pathophysiological mechanisms of gender difference between obesity and elevated serum ALT level.

In a previous study, type-2 diabetes has been reported to be associated with mild (asymptomatic) elevations in the serum levels of certain enzymes including serum ALT[22]. Elevated ALT levels have been reported as more frequently observed for diabetics than for the general population[23]. The Third National Health and Nutrition Examination Survey (NHANES III) reported that the likelihood of an individual featuring an elevated serum ALT level was greater amongst persons afflicted with type-2 diabetes than it was for non-diabetic individuals[11]. The Hispanic Health and Nutrition Examination Survey also reported that abnormal serum ALT levels were statistically significantly more common amongst Mexican Americans suffering from diabetes as compared to their non-diabetic counterparts[24]. Due to the liver playing an important role in the maintenance of glucoregulation, carbohydrate homeostasis and insulin degradation, it seems logical to conclude that the liver's normal functions might be significantly affected as a consequence of glucose intolerance and/or diabetes mellitus[6,24-26].

Hyperlipidemia is frequent amongst subjects who feature abnormal serum activities for certain liver enzymes[11,27]. Our findings have demonstrated that both hypercholesterolemia and hypertriglyceridemia are significantly related to the presence of an elevated serum ALT level. Recent studies have suggested that a considerable proportion of moderately obese individuals who feature hyperlipidemia might develop extensive fibrosis and cirrhosis, with a subsequent marked increase in mortality as a consequence of liver-related diseases[28]. Such observations imply that subjects suffering from obesity and hyperlipidemia should receive screening for liver function more regularly than normal individuals in order to avoid serious liver injury. Furthermore, previous study has shown that hypertriglyceridemia was related to serum ALT levels for both males and females, whilst an elevated serum cholesterol level only appeared to be related to an elevated serum ALT level for males[29]. A possible reason for such apparent discordant findings when compared to the results of the present study is that our study population was constituted by a slightly greater proportion of females who were post-menopausal (44%), such a post-menopausal subgroup likely featuring more-elevated serum total cholesterol and triglyceride levels than would be the case for pre-menopausal females[30]. At the time of study execution, we did not have any information pertaining to study participant hepatitis B surface antigen (HBsAg) and anti-HCV status, such that our failure to exclude positive such individuals from the study may also have confounded the results.

Previous clinical study has revealed that a fructose load might lead to a more substantial increase in serum uric-acid level amongst patients suffering from chronic hepatitis than would be the case for normal individuals[31]. In addition, serum uric-acid level has been reported to be elevated amongst subjects suffering from chronic liver lesions, especially those of a non-infectious origin. Further, the extent of such serum-level elevation appears to be dependent upon the specific severity of the hepatic lesions[32], although the previous results relating to the quite significant association between hyperuricemia and elevated serum ALT level appears to be similar to that proffered by other studies[32].

From the cross-sectional nature of our study design, we were not able to determine the degree to which could have occurred or to what extent the increase in serum uric acid level had arisen prior to liver disease having developed.

Although cigarette smoking and alcohol drinking might constitute important risk factors as regards liver-function abnormalities and/or specific liver diseases as inferred by the results of a number of previous studies[24,29], for the current study, habits such as smoking or alcohol consumption did not appear to be significantly related to elevated serum ALT level following multivariate adjustment. Such a result was not really surprising because we found it somewhat difficult to accurately identify the actual duration of such behavior as also the daily intake of alcohol and the number of cigarettes smoked daily in the context of such a large epidemiological study.

Perceived limitations

One of the major limitations to the present study was potential selection bias due to a relatively lower response rate. The potential impact on the prevalence and the study-observed elevated level-associated risk factors were, in our estimation, inevitable. Nevertheless, given the rather large sample size of this study, we still did retain sufficient statistical power to be able to effectively evaluate the presence of any gender differences between the various associated risk factors for an elevated serum ALT level subsequent to adjustment for confounding factors. Secondly, because it would appear that no standard cut-off level for serum ALT level elevation has yet been internationally accepted to constitute abnormality, different studies may elect to set slightly different normal *vs* abnormal cut-off levels, such that our estimation of what constituted an abnormal elevation of serum ALT level could have suffered from some level of misclassification-bias identification. Thirdly, since Kinmen is an offshore island from Taiwan and lacking in medical resources, the screening program involved a lot of difficulties such as mobilization of manpower and facility. For the cost consideration, we did not collect the information of hepatitis B and hepatitis C, tissue samples for histology and ultrasonography results as a part of our study, such that the "true" causes of observed elevated serum ALT levels for study-participating individuals were not able to be determined. Finally, our measurements were conducted at only a single point in time and, by clear inference, would not be able to be used to reflect long-term exposure to various demographic or biochemical aspects or factors, which might be important influencers of (an elevated) serum ALT level. The solution to such a quandary would best be accomplished by conducting a number of prospective longitudinal analogous studies, the results of which would be expected to complement the community-based (cross-sectional) findings of this study.

Conclusions

In conclusion, as a consequence of the conduct of this study, several gender-related dissimilarities were noted as regards the relationship between obesity, hypertriglyceridemia, and hyperuricemia and an elevated serum ALT level for study-included individuals, as also in regard to the actual prevalence of such level elevation. Further studies are not only needed in order to elucidate the temporal sequence of events that typically lead to elevated serum ALT levels and thus develop more satisfactory non-invasive indicators of liver pathology, but also to further explore the realm of gender-related differences that appear to be involved with elevated serum ALT levels.

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