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BRIEF ARTICLE

Prevalence and features of fatty liver detected by physical examination in Guangzhou

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Abstract

AIM: To investigate the prevalence of fatty liver discovered upon physical examination of Chinese patients and determine the associated clinical characteristics.

METHODS: A total of 3433 consecutive patients who received physical examinations at the Huangpu Division of the First Affiliated Hospital at Sun Yat-sen University in Guangzhou, China from June 2010 to December 2010 were retrospectively enrolled in the study. Results of biochemical tests, abdominal ultrasound, electrocardiography, and chest X-ray were collected. The diagnosis of fatty liver was made if a patient met any two of the three following ultrasonic criteria: (1) liver and kidney echo discrepancy and presence of an increased liver echogenicity (bright); (2) unclear intrahepatic duct structure; and (3) liver far field echo decay.

RESULTS: The study population consisted of 2201 males and 1232 females, with a mean age of 37.4 ± 12.8 years. When all 3433 patients were considered, the overall prevalence of hyperlipidemia was 38.1%, of fatty liver was 26.0%, of increased alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST) levels was 11.9%, of gallstone was 11.4%, of hyperglycemia was 7.3%, of hypertension was 7.1%, and of hyperuricemia was 6.2%. Of the 2605 patients who completed the abdominal ultrasonography exam, 677 (26.0%) were diagnosed with fatty liver and the prevalence was higher in males (32.5% *vs* females: 15.3%, $P < 0.001$). The overall prevalence of fatty liver increased with age, with the peak prevalence (39.5%) found in the 60 to 70-year-old age group. Among patients between the ages of 18 to 50-year-old, the prevalence of fatty liver was significantly higher in males (20.2% *vs* females: 8.7%, $P < 0.001$); the difference in prevalence between the two sexes in patients > 50-year-old did not reach statistical significance. Only 430 of the patients diagnosed with fatty liver had complete information; among those, increased ALT and/or AST levels were detected in only 30%, with all disturbances being mild or moderate. In these 430 patients, the overall prevalence of hypertriglyceridemia was 31.4%, of mixed type hyperlipidemia was 20.9%, of hypercholesterolemia was 12.3%, of hyperglycemia was 17.6%, of hypertension was 16.0%, of hyperuricemia was 15.3%, and of gallstone was 14.4%. Again, the prevalences of hypertriglyceridemia and hyperuricemia were higher in males (hypertriglyceridemia, 36.0% *vs* females: 12.0%, $P < 0.05$; hyperuricemia, 17.3% *vs* females: 7.2%, $P < 0.05$); in contrast, however, the prevalences of mixed type hyperlipidemia and hypercholesterolemia was higher in females (mixed type hyperlipidemia, 18.7%

vs females: 30.1%, $P < 0.05$, hypercholesterolemia, 9.5% *vs* females: 24.1%, $P < 0.05$). Finally, comparison of the fatty liver group to the non-fatty liver group showed that prevalences of hyperlipidemia, hyperglycemia, hypertension, and hyperuricemia were higher in the former (all $P < 0.01$).

CONCLUSION: A high prevalence of fatty liver is detected upon physical examination in Guangzhou, and the primary associated clinical findings are hyperlipidemia, hyperglycemia, hypertension, and hyperuricemia.

Key words: Fatty liver; Nonalcoholic; Prevalence; Hyperlipidemia; Hyperglycemia; Hypertension

Core tip: This study represents the first published investigation of fatty liver prevalence detected by routine physical examinations of individuals residing in the Huangpu District of Guangzhou, China. A high prevalence of fatty liver (26.0%) was detected among the total physical examinees and was characterized by an age-related increasing trend, with the highest prevalence (39.5%) found among individuals between 60 and 70-year-old. The individuals diagnosed with fatty liver also showed significantly higher prevalences of hyperlipidemia, hyperglycemia, hypertension, and hyperuricemia than their non-fatty liver counterparts (all $P < 0.01$), suggesting a close association between fatty liver and dysmetabolic factors.

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INTRODUCTION

Prevalence of fatty liver in China has risen consistently over recent years, accompanying improvements in people's living conditions and adoption of a more Westernized diet. In Western countries, estimates of fatty liver prevalence in the adult population have ranged from 20% to 33%[1], and the most recent prevalence estimate reported for Shanghai, China is 20.82%[2]. In addition to being the most frequently diagnosed liver disease in Chinese clinics, fatty liver represents a particularly alarming threat to human health and public healthcare systems as it can readily progress to steatohepatitis, cirrhosis, or liver cancer.

To gain further understanding about the prevalence and presenting features of fatty liver in China, the current study was designed as a single-site retrospective analysis of adult patients who underwent physical examinations in Guangzhou and were diagnosed with fatty liver.

MATERIALS AND METHODS

Study participants

A total of 3433 consecutive adult patients who underwent routine physical examinations at the Huangpu Division of the First Affiliated Hospital of Sun Yat-sen University from June 2010 to December 2010 were retrospectively enrolled in the study.

Physical examination

Patients presented to the hospital for blood sampling after 10 h of fasting; all serological measurements were carried out on-site at the certified laboratory. Automated techniques (Architect C8000 automatic biochemistry analyzer; Abbott Laboratories, Abbott Park, IL, United States) were used to measure plasma concentrations of glucose, total cholesterol (CHOL), triglyceride (TG), serum uric acid, serum creatinine, blood urea nitrogen, alanine aminotransferase (ALT), and aspartate aminotransferase (AST). Direct sandwich enzyme-linked immunosorbent assay was used to measure hepatitis B virus markers.

Abdominal ultrasonography was performed to detect the presence of fatty infiltration in the liver, using standard imaging criteria to assess hepatic fat[3]. Electrocardiography and chest X-ray were performed to rule out serious heart and lung diseases.

Diagnostic criteria and definitions

Hypertension was diagnosed by a systolic pressure of $\geqslant$ 140 mmHg and/or a diastolic pressure of $\geqslant$ 90 mmHg, according to the 2010 Chinese guidelines for the management of hypertension[4]. Hyperglycemia was diagnosed by fasting plasma glucose level of $\geqslant$ 110 mg/dL[5]. Hyperuricemia was diagnosed by blood uric acid level of $\geqslant$ 7 mg/dL in men and $\geqslant$ 6 mg/dL in women[6]. Abnormal serum creatinine level was defined as $\geqslant$ 1.6 mg/dL. The various types of hyperlipidemia were diagnosed by CHOL $\geqslant$ 200 mg/dL and TG $\geqslant$ 150 mg/dL for mixed type hyperlipidemia, CHOL $\geqslant$ 200 mg/dL and TG < 150 mg/dL for hypercholesterolemia, and CHOL < 200 mg/dL and TG $\geqslant$ 150 mg/dL for hypertriglyceridemia[7]. Fatty liver was diagnosed when a patient met any two of the three following ultrasonic criteria: liver and kidney echo discrepancy and presence of increased liver echogenicity (bright); unclear intrahepatic duct structure; liver far field echo decay[3].

Statistical analysis

All statistical analyses were performed by the SPSS statistical software suite, version 13.0 (Chicago, IL, United States). All reported *P*-values were two-sided, and $P < 0.05$ was considered statistically significant. Descriptive data are expressed as mean ± SD. Comparisons between quantitative data were carried out by the Student's *t*-test, and comparisons between categorical variables were carried out by the χ^2 test.

Table 1 Prevalence of dysmetabolic diseases and biochemical abnormalities in the total study population *n* (%)

	Patients examined	Positive patients
Hyperlipidemia	2715	1035 (38.1)
Fatty liver	2605	677 (26.0)
Increased ALT and/or AST levels	3393	405 (11.9)
Gallstone	2605	296 (11.4)
HBsAg	2244	198 (8.8)
Hyperglycemia	2767	203 (7.3)
Hypertension	2938	210 (7.3)
Hyperuricemia	2700	167 (6.2)
Increased Scr levels	2150	10 (6.2)

HBsAg: Hepatitis B surface antigen; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; Scr: Serum creatinine.

RESULTS

Demographic and clinical characteristics of physical examinees

The study population of physical examinees consisted of 2201 males and 1232 females. Three-thousand-two-hundred-and-five of the patients described themselves as employed, with the majority being mental laborers and a small percentage being physical laborers (84.8% and 15.2%, respectively). The mean age of the overall study population was 37.4 ± 12.8-year-old (range: 18-87 years). The overall prevalences of dysmetabolic diseases and perturbed biochemical findings are listed in Table 1.

Characteristics of the 677 patients diagnosed with fatty liver

Of the 2605 subjects who underwent abdominal ultrasonography, 677 subjects (26.0%) showed imaging signs of fatty liver. The prevalence of fatty liver was significantly higher in males than in females (32.5% *vs* 15.3%, $P < 0.001$). The overall prevalence of fatty liver increased with age, with the 60 to 70-year-old age group representing the peak prevalence (39.5%) and without age bias. However, when the larger age group of 18 to 50-year-old was considered, a significantly higher prevalence was found for males (20.2% *vs* females: 8.7%, $P < 0.001$); this trend did not exist for the > 50-year-old age group (34.6% *vs* females: 38.9%, $P = 0.301$) (Table 2). The overall prevalences of dysmetabolic diseases and perturbed biochemical findings for the 677 patients with fatty liver are listed in Table 3.

Characteristics of the 430 patients with fatty liver and complete physical examination data

In total, 430 of the patients diagnosed with fatty liver also had complete data accounting for all of the physical examination components; this group was comprised of 347 males (80.7%) and 83 females (19.3%), with a mean age of 43.8 ± 12.4-year-old (range: 19-78 years). One-hundred-and-twenty-nine patients (30.0%) showed mildly or moderately increased ALT and/or AST levels (40-200 U/L); however, the amount of patients with increased ALT was significantly higher than of patients with increased AST (29.8% *vs* 7.9%, $\chi^2 = 67.2$, $P < 0.001$). The majority of patients with abnormal ALT and/or AST levels showed a mild increase, and included 102 patients (70.1%) with ALT and/or AST levels < 2-times the upper normal limit and 27 patients (20.9%) with ALT and/or AST levels 2 to 5-times the upper normal limit. Males were more likely to have increased ALT and/or AST levels (32.6% *vs* 19.3%, $P < 0.05$).

The overall prevalences of dysmetabolic diseases and perturbed biochemical findings for the 430 patients with fatty liver and complete data are listed in Table 4. The prevalences of hypertriglyceridemia and hyperuricemia were higher in males than in females, but the prevalences of mixed type hyperlipidemia and hypercholesterolemia were higher in females than in males ($P < 0.05$). The difference in the prevalence of hypertension or hyperglycemia between males and females did not reach statistical significance ($P > 0.05$).

Risk factors associated with fatty liver

Patients with no signs of fatty liver and hepatitis B surface antigen negativity were assigned to a non-fatty liver group, which included 382 males (77.2%) and 113 females (22.8%), with a mean age of 42.5 ± 10.9-year-old. Compared to the fatty liver group, the sex and age distributions were not significantly different ($P > 0.05$). As shown in Table 5, the prevalences of hyperlipidemia, hyperglycemia, hypertension, and hyperuricemia were significantly higher in the fatty liver group than in the non-fatty liver group ($P < 0.01$).

DISCUSSION

Fatty liver is a clinicopathologic syndrome that manifests from hepatic steatosis and excessive fat accumulation caused by a variety of factors. The syndrome spectrum includes simple fatty liver, steatohepatitis, fatty liver cirrhosis, and associated hepatocellular carcinoma. While liver biopsy is the gold standard for diagnosis of fatty liver, ultrasonography is generally used as a non-invasive screening method for the general population. The reported estimates of fatty liver cases diagnosed by ultrasonography have ranged from 17% to 46% in Europe, United States and other Asian countries[8-11]. In the current survey of physical examinees in Huangpu District, Guangzhou, the prevalence of fatty liver detected in physical examination was 26%; this rate is similar to previous estimates made in other Chinese cities[12,13].

It is generally recognized that the prevalence of fatty liver increases with age, with the highest rates found in the age group of 50 to 70-year-old[10,14]. In the present study, the highest prevalence of fatty liver occurred in the age group of 60 to 70-year-old. It is important to note that elderly people harbor significantly more of the known risk factors for fatty liver, such as obesity, hypertension, diabetes, and hyperlipidaemia. Furthermore, aging brings restrictions on physical mobility, which in turn supports or promotes the above risk factors and can eventually lead to a higher prevalence of fatty liver[15].

Table 2 Age and sex distribution of overall fatty liver prevalence

Age (yr)	All patients	Patients with fatty liver	Overall prevalence	Prevalence in males	Prevalence in females	χ^2	*P* value
18-19	17	1	5.80%	7.10%	0.00%	-	-
20-29	1055	55	5.20%	6.40%	2.30%	7.47	0.006
30-39	1003	206	20.50%	26.70%	8.70%	44.80	< 0.001
40-49	799	212	26.50%	34.50%	16.80%	31.78	< 0.001
50-59	331	123	37.20%	35.90%	39.00%	0.32	0.569
60-69	147	58	39.50%	37.80%	42.10%	0.27	0.601
⩾ 70	81	22	27.10%	24.50%	32.10%	0.54	0.464
Total	2605	677	26.00%	32.50%	15.30%	95.18	< 0.001

Table 3 Prevalence of dysmetabolic diseases and biochemical abnormalities in the 677 patients diagnosed with fatty liver *n* (%)

	Patients examined	Positive patients
Increased ALT and/or AST levels	676	199 (29.4)
Hypertriglyceridemia	635	197 (31.0)
Mixed type hyperlipidemia	635	135 (21.3)
Hypercholesterolemia	635	92 (14.5)
Hyperglycemia	640	116 (18.1)
Hypertension	636	102 (16.0)
Gallstone	677	97 (14.4)
Hyperuricemia	627	87 (13.9)
HBsAg	506	39 (7.7)
Increased Scr levels	507	3 (0.6)

HBsAg: Hepatitis B surface antigen; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; Scr: Serum creatinine.

Table 4 Sex distribution of prevalence of dysmetabolic diseases and biochemical abnormalities in the 430 subjects with fatty liver *n* (%)

	All patients	Male patients	Female patients	χ^2	*P* value
Increased ALT and/or AST levels	129 (30.0)	113 (32.6)	16 (19.3)	5.63	0.018
Hypertriglyceridemia	135 (31.4)	125 (36.0)	10 (12.0)	17.87	< 0.001
Mixed type hyperlipidemia	90 (20.9)	65 (18.7)	25 (30.1)	5.25	0.022
Hypercholesterolemia	53 (12.3)	33 (9.5)	20 (24.1)	13.19	< 0.001
Hyperglycemia	76 (17.6)	59 (17.0)	17 (20.5)	0.56	0.455
Hypertension	69 (16.0)	53 (15.3)	16 (19.3)	0.80	0.372
Hyperuricemia	66 (15.3)	60 (17.3)	6 (7.2)	5.22	0.022
Gallstone	62 (14.4)	50 (14.4)	12 (14.4)	0.00	0.991
HBsAg	34 (7.9)	27 (7.9)	7 (7.9)	0.04	0.843
Increased Scr levels	3 (0.7)	3 (0.9)	0 (0.0)	-	-

HBsAg: Hepatitis B surface antigen; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; Scr: Serum creatinine.

Most studies have shown that men are more likely to develop fatty liver than women before the age of 50 years, but both sexes face a similar likelihood of developing the condition after 50[16,17]. Similarly, a study involving 26527 Chinese subjects who underwent routine health check-ups showed that the prevalence of fatty liver was 31% in men and 16% in women[18].

The significant difference in the prevalence of fatty liver between men and women before the age of 50 is probably a result of the clear differences in the amount and distribution of body fat between the sexes. Men usually store fat in the abdomen whereas women tend to store fat in the subcutaneous tissue. While the reasons for this differential fat accumulation in men and women remain unclear, evidence from cell research have suggested that lipid metabolism pathways may play important roles. Moreover, molecular studies have uncovered distinctions between men and women in the activity and metabolism of lipids. A Japanese study showed that the triglyceride and cholesterol particles were larger in men than those in women, and both of these factors are associated with risk for fatty liver[15,19].

The fact that the significant difference in prevalence of fatty liver among men and women is lost after the age of 50 is intriguing. Women of this age have decreased adiponectin levels, as a result of the lower estrogen and higher androgen that occur after menopause[20,21]; the resetting of postmenopausal women's physiology to that which more closely resembles the male physiology may account for the similar prevalence of fatty liver between the sexes at this age. The Chinese study mentioned above also showed that the mean ALT levels in men were significantly higher than those in women before 50; yet, the peak levels of ALT were observed in women older than 50 years, which might be related to menopause changes and the decreased physical exercise that frequently accompanies this period of life[18]. Nonetheless, these previously published findings, along with ours presented herein, highlight the importance of prevention and screening of fatty liver in men and postmenopausal women.

Most patients with fatty liver are diagnosed without or with mild clinical symptoms. In a study of fatty liver clinical characteristics by Powell *et al*[22], 79% of diagnosed patients were shown to have normal serum transaminase levels. In the current study, 30% of the patients diagnosed with fatty liver presented with mildly increased ALT and/or AST levels, and most of those were accounted for by ALT increase. Thus, the most common type of fatty liver was nonalcoholic fatty liver disease (NAFLD). Moreover, the fatty liver group showed higher prevalences of hyperlipidemia, hyperglycemia, hypertension, and hyperuricemia as compared to patients without fatty liver, suggesting that fatty liver may be closely associated with these disorders.

Risk factors known to be associated with NAFLD include metabolic syndrome, diabetes, and obesity. Prevalence estimates of NAFLD have ranged from 40% to 70% in patients with type 2 diabetes mellitus (T2DM)[23],

Table 5 Distribution of prevalence of risk factors in patients with and without fatty liver

	Patients with fatty liver (n = 430)		Patients without fatty liver (n = 495)		χ^2	P value
	All patients	Prevalence	All patients	Prevalence		
Hypertriglyceridemia	135	31.40%	45	9.10%	73.04	< 0.001
Mixed type hyperlipidemia	90	20.90%	33	6.70%	40.61	< 0.001
Hypercholesterolemia	53	12.30%	95	19.20%	8.07	0.004
Hyperglycemia	76	17.70%	25	5.00%	37.70	< 0.001
Hypertension	69	16.00%	32	6.50%	21.72	< 0.001
Hyperuricemia	66	15.30%	14	2.80%	45.66	< 0.001

57%-74% in individuals with obesity, and 27%-92% in patients with hyperlipidemia[24,25]. Donati *et al*[26] showed that the prevalence of NAFLD in the patients with hypertension but without obesity or T2DM was 2 to 3-times higher than that in the general population. Assy *et al*[25] showed that up to 50% of the patients with fatty liver were dyslipidemic, and that this dysmetabolic condition was chiefly characterized by high serum TG levels, which itself is an important risk factor for cardiovascular disease.

NAFLD is closely related to incidence of cardiovascular disease. In fact, the most common causes of death in patients with NAFLD are atherosclerotic cardiovascular disease and hepatic cirrhosis[27]. Therefore, clinicians should not only consider central obesity, type 2 diabetes, dyslipidemia and hypertension as risk factors for NAFLD, but also pay more attention to them as high risk factors for cardiovascular, kidney and liver diseases. A key strategy for clinical treatment of NAFLD is to reduce the above risk factors, and this can be accomplished by applying the existing knowledge to generate effective public health policies for the prevention of this disease.

In summary, a high prevalence of fatty liver was discovered in physical examinees in Guangzhou. Some of the cases presented with mild or moderate increase in ALT or AST levels, but many had concomitant hyperlipidemia, hyperglycemia, hypertension, or hyperuricemia. Clinicians should pay attention to the intervention and modification of these risk factors. It is important to note, however, that the retrospective nature of this study limits the risk factors that were available for analysis; for example, data on waist circumference, body mass index, dietary habits, and alcohol consumption - all potential risk factors - were lacking. In addition, the single-site population may limit generalization of our results. More studies of larger Chinese populations are needed to gain more detailed information on fatty liver in the general population and to better guide clinical treatment.

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COMMENTS

Background

The incidence of fatty liver is relatively high and on the rise in urban populations of China; however, consultation rates are low due to a lack in adequate knowledge of fatty liver. To date, no study has examined the prevalence and clinical features of fatty liver in urban Chinese who receive routine physical examinations. Thus, this study was designed to retrospectively investigate the prevalence and presenting features of fatty liver in physical examinees of Guangzhou.

Research frontiers

Public health programs of screening, education, and treatment of fatty liver should start with employed urban Chinese, who are generally characterized as relatively well-educated, financially secure, and compliant. The results of this study may offer guidance for clinical treatment by analyzing the presenting features of fatty liver in this population.

Innovations and breakthroughs

This study is the first to assess the presenting features of fatty liver in urban Chinese who received routine physical examinations in Guangzhou. The disease was found to be closely associated with concomitant hyperlipidemia, hyperglycemia, hypertension, or hyperuricemia. The results from this study, which itself is part of a continuous clinical research effort for determining fatty liver diagnostic and prognostic factors, are applicable to the development of new programs for screening and education of fatty liver targeting urban Chinese.

Applications

This study was undertaken mainly for practical purposes, *i.e.*, to raise public awareness of fatty liver and support performance of screening in the general population, which are expected to improve consultation rates and timely initiation of treatment for fatty liver.

Peer review

This study represents the first published investigation of fatty liver prevalence detected by routine physical examinations of individuals residing in the Huangpu District of Guangzhou; the results suggest a close association between fatty liver and dysmetabolic factors. This study was undertaken mainly for practical purposes, such as to raise public awareness of fatty liver and the benefits of screening the general population for this disease so that cases may be diagnosed and treated in a timely manner.

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