Prevalence and Risk Factors of Fatty Liver in Dehui City of Jilin Province of Northeastern China

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The prevalence of fatty liver disease (FLD), a chronic disorder that includes alcoholic liver disease (ALD) and non-alcoholic fatty liver disease (NAFLD) ranges from 1% to 50% and varies with age, gender and occupation in different districts of China. Some studies have shown that FLD especially NAFLD, has a relationship with cardiac disease, metabolic syndrome, dyslipidemia and obesity. To determine the prevalence of FLD and related diseases in the Dehui City of Jilin Province in the Northeastern region of China, we surveyed the population of Dehui City of Jilin Province in China.

The objective of this study was to evaluate the prevalence of FLD in relation to different factors, such as age, location, occupations and educational levels, and analyze the risk factors of FLD.

The study sample was separated into three groups according to alcohol consumption: non-alcoholic fatty liver disease (NAFLD), alcoholic liver disease (ALD) and suspected alcoholic liver disease (SALD) groups. All subjects (18-78 years) completed a standard questionnaire, physical examination and hepatic ultrasound examination. Multivariate logistic regression was used to screen risk factors of FLD.

The study indicated that the prevalence of FLD was 23.1%, stratified by NAFLD 14.5%, SALD 5.5% and ALD 3.0%. This survey showed a lower prevalence of hypertension between NAFLD and other groups ($P<0.001$). As alcohol consumption increased, the prevalence of FLD gradually decreased, when compared with NAFLD. The risk factors of FLD were hypertension, central obesity, alcohol consumption, dyslipidemia fasting blood glucose and being male.

Among groups of FLD, NAFLD has a higher prevalence in the Jilin Province of China. In China, elderly men with high educational levels working in mentally taxing fields are at a high risk of FLD. It is shown that hypertriglyceridemia is a very important risk factor to coronary heart disease, diabetes and hypertension. Generally, FLD was significantly associated with hypertension, drinking, high triglycerides and central obesity.

Introduction

Fatty liver disease (FLD), including alcoholic liver disease (ALD) and non-alcoholic fatty liver disease (NAFLD), is a chronic disorder and is defined as lipid accumulation exceeding the normal range of five percent of wet liver weight. FLD encompasses a pathological spectrum consisting of hepatic steatosis, which is defined as the accumulation of fat in the liver; steatohepatitis occurs when steatosis becomes associated with inflammation, which can further progress to cirrhosis and hepatocellular carcinoma.[1] Currently, FLD has become a common problem both in developed and developing countries.[2] In China, the overall prevalence of NAFLD varies: 15.9% in the north-east of China, 17% in east China, 15% in south China and 41.6% in central China.[2,3,4] A study reported by Fan indicated that the community prevalence of NAFLD was about 15% in the more affluent regions of China.[5] It is 41.64% in a middle-class region and 36.49% in a lower class region.[6,7]

Historically, for FLD, most subjects were related to excessive alcoholic intake, but recently non-alcoholic precipitants of FLD have increasingly received more attention. Notwithstanding alcohol consumption, factors such as oxidative stress, mitochondrial dysfunction, insulin resistance (IR), immune dysregulation and adipokines are considered to play an important role in the pathogenesis of FLD.[8]

In recent years, the prevalence of FLD has increased dramatically in China due to alterations in lifestyle and dietary habits. Factors such as personal income, dietary habits and work surroundings have changed dramatically in the past 20 years. Meat and vegetable consumption has decreased for the majority of Chinese citizens as income has increased. Economic development has inevitably influenced the structure and habits of Chinese society; while there still is a great disparity between the richer and poorer classes, a growing middle class and high-income segment have emerged.[9]

Therefore, it is important to assess the epidemiological features of FLD in our country in order to facilitate its prevention and treatment. To date, there has only been one large population study from Jilin

Figure 1. Queries about drinking

Drinking Questionnaire	
1	Are you a drinker?
2	How often do you drink in a week and for how long?
3	Which type of drink do you consume most of the time?
4	Please write down your history of drinking of the last six months i.e. it should
	contain type of drink, degree of alcohol, volume and frequency of your drink.
5	Have you ever changed your habit of drinking? If yes, please write down your
	history of drinking before the change, it should contain type of drink, degree
	of alcohol, volume and frequency of your drink.
6	Have you ever quit drinking and why?
7	Have you other members in your family with the habit of drinking?

Province, located in northeast of China, published in 2008.[10] It was the result of a three-year investigation that focused on the overall prevalence of FLD and NAFLD. However, data from rural and city areas is still lacking, as well as data on ALD and SALD. This situation prompted our more detailed study of FLD epidemiology in the Jilin Province.

Subjects and Methods and Materials

Design

Approval from the institutional ethic committee of the First Hospital of Jilin University was obtained. This cross-sectional, population-based study was conducted in the city of Dehui, a city-level division of the Jilin Province in northeast China. Dehui has a population of 807,000, corresponding to 14 towns (urban) and 308 villages (rural). The economic status of the city is relatively affluent compared to other areas in Jilin Province. Therefore, to some extent, Dehui may be considered representative of the majority of the population of Jilin province and reflect the epidemiology of FLD there. The city has a moderate economic status among Jilin Province.

The sampling was random and multi-staged. Firstly, nine cities in Jilin Province were selected and numbered from one to nine. The city of Dehui was selected by simple randomization sampling (lottery method). In the second stage, nine villages and eleven towns were selected from 308 villages and 14 towns in the city of Dehui by random sampling, and in the third stage, cluster sampling was used in the areas selected above. The third stage was divided into two phases. In phase one, every participant was asked to participate in a questionnaire by door-to-door interviews. Phase two was of comprised of a physical examination and an ultrasound examination of the liver.

The sample size (N) was calculated based on a 10.0% prevalence (p) of fatty liver with a 1% uncertainty level (d), using the formula $N = t^2p(1-p)/d^2$ (where t^2 is defined by 95% confidence). We therefore estimated that this study would necessitate enrollment of 3,600 subjects. A total of 6,043 eligible subjects were selected from the district, all of whom should be permanent residents. Eventually, a total of 3,850 subjects accepted the questionnaire and physical and ultrasound examinations. A total of 3,815 subjects were included in this study, with 35 subjects being excluded due to their drinking history. Every participant signed the Informed Consent.

The selection criteria required the participants to be permanent residents of the city to control for sampling error. Before the study, a media-driven campaign was conducted in order to achieve a high level of participation. Risk screening for fatty liver was estimated by a questionnaire, via door-to-door interview. The survey was based on standardized interviews performed by trained health professionals. The survey data was collected and loaded using a personal computer within 24 hours after the interview. The questionnaire included self-reported age, gender, education, working hours, physical activity, smoking habits, family history of heart attack, hypertension, diabetes mellitus, alcohol consumption, awareness of arterial hypertension, drug prescription and two control measurements of systolic and diastolic blood pressure (BP). BP was measured by physicians before the interview under standard conditions (in an upright position, after about five minutes of resting time). Queries about drinking included seven items (Figure 1).

Ultrasound (US) examination of the liver was conducted by a total of 15 medical doctors of the hepatology department

Definitions and Preferred Cut-off Values

The diagnosis of FLD was based on ultrasonography, in accordance with the guidelines for diagnosis and treatment of non-alcoholic and alcoholic FLDs issued by Fatty Liver and Alcoholic Liver Disease Study Group of the Chinese Liver Disease Association.[11] These were adapted from the American Gastroenterological Association's medical position statement: nonalcoholic fatty liver disease from 2002.[12] Generally, the diagnosis of NAFLD and ALD was based on a combination of medical history, clinical symptoms, laboratory and ultrasound (US) findings. Viral hepatitis and other chronic liver diseases were excluded.

ALD was diagnosed when a subject fulfilled the FLD criteria and drank more than 40 g (male) or 20 g (female) alcohol per day over the course of five years. Suspected ALD (SALD) was defined when alcohol consumption was between 20-40 g (male) or 10-20

Characteristic	**Male (n = 1824)**	**Female (n = 1991)**	**P-value**
Age	45.68±12.94	46.53±11.66	NS
Height	167.93±7.13	158.10±40.95	P <0.001
Weight	68.93±18.92	59.44±16.00	P <0.001
BMI	24.20±3.59	23.91±3.73	P <0.05
WC	83.78±10.83	79.21±10.44	P <0.001
SBP	130.52±20.34	128.34±22.17	P <0.001
DBP	85.00±12.99	81.73±12.80	P <0.001
FBG	5.24±1.35	4.96±1.31	P <0.001
CHOL	4.41±0.96	4.32±0.94	P <0.001
LDL	3.04±0.88	3.00±0.80	NS
TG	1.75±1.76	1.50±1.25	P <0.001
HDL	1.37±0.46	1.43±0.41	P <0.001

Table 1. Basic characteristics stratified by gender

Table 2. Prevalence of ALD, SALD, NAFLD and FLD in different groups

Age	n	ALD	SALD	NAFLD	FLD
18-44	1222	2.70%*	5.89%	8.02%*	16.61%*
45-59	2022	3.51%†	5.73%	16.62%†	25.87%
≥60	571	2.10%	4.03%	21.02%	27.15%
Total	3815	3.04%	5.53%	14.52%	23.09%
P-value		P<0.001	P>0.05	P<0.001	P<0.001
Gender					
Male	1797	6.12%	11.41%	8.79%	26.32%
Female	2018	0.30%	0.30%	19.62%	20.22%
Total	3815	3.04%	5.53%	14.52%	23.09%
P-value		P<0.001	P<0.001	P<0.001	P<0.001
Area					
Rural area	2215	3.84%	7.18%	15.26%	26.28%
Urban area	1600	1.94%	3.25%	13.50%	18.69%
Total	3815	3.04%	5.53%	14.52%	23.09%
P-value		P=0.001	P<0.001	P>0.05	P<0.001
Occupation					
Mental work	1451	4.62%	7.58%	13.99%	26.19%
Physical work	2364	2.07%	4.27%	14.85%	21.19%
Total	3815	3.04%	5.53%	14.52%	23.09%
P-value		P<0.001	P<0.001	P>0.05	P<0.001
Education					
low-level	2770	2.17%	3.90%	15.78%	21.84%
high-level	1045	5.36%	9.86%	11.20%	26.41%
Total	3815	3.04%	5.53%	14.52%	23.09%
P-value		P<0.001	P<0.001	P<0.001	P=0.001
Monthly income					
low-level	2854	1.86%	3.54%	15.00%	20.39%
high-level	961	6.56%	11.45%	13.11%	31.11%
Total	3815	3.04%	5.53%	14.52%	23.09%
P-value		P<0.001	P<0.001	P>0.05	P<0.001

Compared with age group of 45-59: * P <0.05; ** P <0.001

Compared with age ≥ 60: † P <0.05.

g (female). NAFLD was diagnosed when alcohol consumption was less than these amounts.

Participants were classified as hypertensive, as defined by the World Health Organization (WHO) criteria, if their two control measurements of systolic blood pressure (SBP) were at or above 140 mmHg, or if their diastolic blood pressure (DBP) was at or above 90 mmHg, or if they were currently taking anti-hypertensive medications. Current cigarette smoking status was classified into three categories according to the number of cigarettes smoked per day: non-smokers, light smokers (1-20 cigarettes/day) and heavy smokers (>20 cigarettes/day).

For the dietary habit, the 'vegetable group' was defined as those eating more than 0.5 kilogram a day of vegetables or fruits and the 'meat group' was defined as those eating over 0.3 kilogram of meat a day.

Education level was classified into two groups: low-level and advanced. Low level of education group included no education, primary school, or middle school education (Grade One to Grade Nine). Advanced education levels included senior schools or colleges.[13]

Monthly incomes were classified into two categories: low-level (< 799 Yuan) and high-level (≥ 800 Yuan). In our study, professional occupations included farmers, workers, teachers, cadres, managers and self-employers. These occupations were separated into mental work and physical work performing groups. Brainwork group corresponded to teachers, cadres and managers, while physical work group includes farmers, factory workers and those who were self-employed.

We calculated the body mass indices (BMI=weight (kg)/height (m^2)). In accordance with the World Health Organization's Asian BMI criteria, overweight was defined as a BMI ≥ 23 kg/m^2 and obesity as BMI ≥ 25 kg/m^2. Central obesity was defined as waist circumference (WC) ≥ 90 cm in men and ≥80 cm in women.

With regard to alcohol consumption, participants were classified into three groups according to their estimated reported weekly intake: NAFLD (none), light (less than 40 g alcohol per day), moderate (40 – 80 g alcohol per day) and heavy (more than 80 g alcohol per day).

The levels of fasting blood glucose (FBG), total cholesterol (TC), high-density cholesterol (HDL-C), low-density cholesterol (LDL-C) and triglycerides (TG) were measured with a Synchron LX20 auto analyzer (Beckman Coulter, Brea, CA, USA). According to the Chinese guidelines on prevention and treatment of dyslipidemia in adults, hypercholesterolemia was defined as TC ≥ 5.18 mmol/L, high LDL-C as LDL-C ≥ 3.37 mmol/L, hypertriglyceridemia as TG ≥ 1.7 mmol/L and low HDL-C as HDL-C < 1.04 mmol/L.[14] Dyslipidemia was defined as the presence of one or more abnormal serum lipid concentrations. The ratio of TC to HDL-C (TC/HDL-C) was considered abnormal if the ratio was over 4.5.

Statistical Analysis

Descriptive statistics were utilized to analyze data consisting of numerical parameters: age, weight, BMI and BP, and all categorical parameters: physical activity, alcohol consumption, fat intake, cigarette smoking, family history of hypertension, educational level and occupation.

Table 3. Prevalence of diseases in NAFLD, SALD and ALD groups (n=3815)

	NAFLD (n=2700)	SALD (n=772)	ALD (n=343)
Hypertension	37.6%	43.5%**	48.7%**
Diabetes Mellitus	5.5%	3.9%	1.7%*
MS	18.9%	19.3%	22.4%
dyslipidemia	94.7%	93.0%†	97.1%
obesity	42.4%	26.7%†**	21.3%**

NAFLD is compared with SALD and ALD: * P <0.05; ** P <0.001

SALD is compared with ALD: † P <0.05.

To identify differences between the above-mentioned risk factors in the hypertensive and normotensive groups, Pearson x^2-test and rank sum test were used. The x^2-test was used for the rate and rank sum test use for measurement data. Relationships between risk factors were investigated by estimating the odds ratio (OR) using a logistic regression model. Separate univariate analyses were used to identify those variables associated with FLD. Because of interrelated between variables, multivariate logistic regression was performed to analysis the risk factors of FLD. Only probability values p<0.05 were considered to indicate statistical significance. The analysis software used was SPSS 18.0 for Windows.

> "The main results of this qualitative study reveal that regardless of language barriers, cultural differences, inability to afford medical care and even absence ofdiplomatic relations, refugees in need of medical attention were provided care and UN, EU and WHO policies are upheld."

Results

Basic Characteristics Stratified by Gender

Anthropometric characteristics including height, weight, WC, SBP and DBP, blood pressure recordings and blood glucose levels of participants are presented in Table 1 to analyze significance between genders. There were no significant differences in the mean age and LDL-c between males and females. All the remaining variables were statistically significantly higher in men than in women with the exception of HDL, which was statistically significantly higher in women.

Overall Prevalence of FLD, NAFLD, ALD and SALD, and Their Relationship with Age, Gender and Way of Life

As shown in Table 2, 881 (23.1%) of the study's sample (3815) were diagnosed as having FLD. The overall prevalence of NAFLD, SALD and ALD was 554 (14.5%), 211 (5.5%) and 116 (3.0%), respectively. FLD prevalence was statistically associated with age (P<0.001), with no statistically significant increase over age 40 years (P>0.05). For ALD, age prevalence increased to the peak of 3.5% in the 44-59 years group but decreased over the age of 60 years (P<0.05); NAFLD prevalence increased with aging (P<0.001); the prevalence of SALD was not statistically different among age groups (P>0.05). When considering the subgroups of areas, type of work, educational levels and monthly income, ALD and SALD were statistically significantly (P<0.001). However, the prevalence of NAFLD was not statistically different between areas (P>0.05), occupations (P>0.05) and monthly income (P>0.05). The only statistically significant difference concerned educational levels (P<0.001).

Comparative Prevalence of Diseases Between NAFLD, SALD and ALD

Table 3 shows that the prevalence of hypertension in NAFLD was lower than in SALD (P<0.001) and ALD (P<0.001), without any statistically significant difference between SALD and ALD. As alcohol consumption increased, the prevalence of obesity gradually decreased (P<0.05), but there was no statistically significant difference in metabolic syndrome (MS) prevalence between the three groups. Dyslipidemia was significantly less prevalent in SALD than in NAFLD. Diabetes mellitus was statistically more prevalent in NAFLD than in ALD (P<0.05).

FLD and its Risk Factors

Table 4 shows the relationship between FLD and risk factors, determined by logistic regression. FLD was positively associated with male gender, hypertension, central obesity, drinking, hypercholesterolemia, high LDL-c, low HDL-c, high TG and high FBG. There was no correlation between FLD and education level.

Discussion

FLD—especially NAFLD—is the most common liver disease globally, with 3-24% of the general population affected.[15] Moreover, in the general population, 2-3% of fatty liver disease develops into liver cirrhosis and hepatocarcinoma.[16,17]

The prevalence of FLD is even higher in persons with type 2 diabetes (50%), obesity (76%) and morbid obesity (nearly 100%).[18] It was reported that that the prevalence of FLD in individuals with type 2 diabetes mellitus was 69.4% in Brazil and 55.8% in Tehran.[19,20] It is possible that different methods of sample selection, diagnostic criteria, dietary habits and life styles resulted in heterogeneous findings. For our purposes, we select the most accurate diagnostic criteria and take randomized methods to control the sample error, which may result in different findings. Different nations or racial groups and different dietary habits and lifestyles, such as large fat consumption, could also contribute to different findings.

Since China is a developing country, the lifestyle habits of the people are different from those living in more developed countries. Therefore, it is not unexpected that the prevalence of NAFLD in China is much lower (15.9%) than in developed countries. In accordance with reported data, this study showed that FLD was more frequent in males and increased with age.[21] However, some studies suggest that there may be a different relationship between NAFLD and age or gender.[22] Bedogni, et al. found that NAFLD prevalence increased with age in both genders and then significantly decreased for persons over 66 years. The variations between studies can be attributed to differences in social, cultural and environmental backgrounds among the study participants.

Our study shows that the prevalence of FLDF increased with age among residents of the Jilin Province, however, prevalence of FLD remained the same among age groups older than 40 years old. FLD prevalence was significantly higher in males than in females. The prevalence of NAFLD and ALD was higher in the north-east of China than in southern China. Regarding this last finding, there may be two explanations. First, the characteristically long winter in Northeast China may result in individuals partaking in fewer outdoor activities. Second, dietary habits could be another cause since anecdotally those in the north-east are reported to drink highly concentrated wine and consume more meat to keep warm. This study also showed that there is a summit rate of ALD at the 44-59 age group, but a decline in the 60 and up age group. This phenomenon could be explained as a result of type of occupation, but we fail to complete association with occupation in each age group.

This study also showed that the prevalence of hypertension in NAFLD was significantly lower than in SALD or ALD. This might be related to the known relationship between hypertension and drinking. Because drinking raises blood pressure to unhealthy levels, people with hypertension tend to drink less alcohol, which may result in fewer hypertension cases in people with NAFLD compared to SALD and ALD. As alcohol consumption increased, obesity decreased. The precise mechanisms underlying this relationship are not yet fully understood. Inhibition of normal *de novo* lipogenesis in the liver due to alcohol consumption might result in a lower prevalence of obesity. Multivariate logistic regression revealed that FLD was positively correlated with gender (males vs. females), hypertension, central obesity, alcohol consumption, hypercholesterolemia, high LDL-c, low HDL-c, high TG and FBG. No significant relationship with geographical areas or educational level was found. This contrasts with the results of a study conducted in Guangdong Province, which concluded that a high level of education and living in urban areas were found to be protective factors.[23] People with a low level of education in rural areas may be less aware of the risk of FLD and consequent unhealthy lifestyles may elevate the prevalence of FLD. In western countries, alcohol consumption, obesity and diabetes mellitus are the most common causes of FLD. Alcohol consumption has been reported to play an important role in contributing to ALD risk, but this study found that only 3.0% of the participants suffered from ALD.[24] Diabetes mellitus—a common disorder in developed countries—has become a severe problem in China due to alterations in lifestyles and dietary habits, including less physical activity and a diet with heavy consumption of fat and sugar. In this study, FBG was a major risk factor for FLD.

There are several limitations for this study: firstly, the cross-sectional nature of our study precludes us from determining cause-effect relationships. Secondly, we have to face the fact that our data were obtained from a few villages and towns in Dehui City of Jilin Province, so our results may not be generalizable to other localities. A potential concern is that we measured height, weight, waist circumference, fasting blood glucose, CHOL, triglycerides, HDL-c and LDL-c only once, which might have led to random error.

Conclusion

The prevalence of NAFLD was higher than SALD and ALD in Dehui City of Jilin Province of northeastern China. NAFLD was significantly associated with metabolic risk factors such as hypertension, high TG and central obesity, especially for males who regularly consumed alcohol.

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Conflicts of Interest

No potential conflicts of interest relevant to this article are reported.

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