Risk Factors for Non-alcoholic Fatty Liver Disease in a Chinese Population

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Abstract

Background : **Non-alcoholic fatty liver disease (NAFLD) is a serious health concern in China. The goal of this cross-sectional study was to determine the prevalence of NAFLD and identify the risk factors associated with this disease in Northern China.**

Methods : **In 2007, a total of 6063 adults from Dehui, a city in Northern China, were surveyed and demographic and social-economic characteristics, life behaviors, and medical history were recorded. Among them, 3850 subjects were randomly selected for physical examination, fasting plasma glucose (FPG) test, fasting lipid and liver function profiles, hepatitis B and C infection screening, and ultrasound examination. The frequency of NAFLD in this population was analyzed by the Chi-square test and the association of potential risk factors was analyzed by logistic regression.**

Results : **The prevalence of NAFLD was 15.9% in this population and the prevalence in females was significantly higher than that in males, particularly for the elderly subgroup. Obesity, hypertension, FPG, diabetes, and metabolic syndrome (MS)-related hyperlipidemia were significantly associated with NAFLD. The data indicate that MS-related multiple risk factors synergistically increase the risk for NAFLD.**

Conclusion : **The prevalence of NAFLD is high in Northern China, which may be associated with the high incidence of diabetes, hypertension, and MS in this area.** (Acta gastroenterol. belg., **2011**, 74, **503-508**).

Key words : Non-alcoholic fatty liver disease (NAFLD), prevalence, risk factors.

Introduction

Non-alcoholic fatty liver disease (NAFLD) is a major health issue throughout the world and is characterized pathologically by accumulation of fat in hepatocytes that is unrelated to consumption of alcohol (1). NAFLD is commonly thought of as a "Western" disease because the prevalence of NAFLD is associated with the level of industrialization. The prevalence of NAFLD in Western countries is estimated to be 20% to 40% of the population (2,3). Although the prevalence of NAFLD in Asian countries is slightly lower than that in Western countries, the incidence of NAFLD in China is increasing due to improved social economic status and advances in diagnostic technology (4,5). Previous studies have shown that the prevalence of NAFLD is 42.6% in Taiwan (6) and 11.7% in Southern China (7). Notably, the people of Northern China are on average taller than people elsewhere in China and have a unique lifestyle, which may affect the development of NAFLD. However, the incidence and prevalence of NAFLD in Northern China has not yet been investigated.

During the process of NAFLD development, affected people usually develop hepatic steatosis and non-alcoholic steatohepatitis. Some cases of NAFLD progress to moderate/severe liver fibrosis and cirrhosis, and even liver failure and cancers. Although the etiology of NAFLD is still unknown, previous studies have suggested that this disease is associated with glucose intolerance, lipidemia, metabolic syndrome (MS), cardiovascular diseases, and insulin resistance (8). Because ethnic background affects the development and pathogenesis of NAFLD (6), the risk factors for the development of NAFLD specifically in the Northern Chinese are of considerable interest.

The goal of this study is to determine the prevalence of NAFLD and identify the risk factors that are associated with this disease in Northern China.

Methods

Study population

We conducted a population-based cross-sectional study using survey data from the city of Dehui collected in 2007. The average levels of economic and living standards in the Jilin province are represented in the city of Dehui. A total of 6063 adults (> 18 years old) were surveyed for age, gender, occupation, education, income, medical history, genetic disease history, smoking, exercise (< 30 min, 30 min to 2 hours, and > 2 hours), sleep (< 4 hours, 7-8 hours, > 10 hours, and other), diet, medication, and detailed information on alcohol consumption. Among these subjects, 3850 were randomly selected for physical examination, tested for fasting blood glucose levels, fasting blood lipid profiles, liver function tests, hepatitis B and C infection, and underwent liver ultrasound examination as well as. All of the selected subjects were required to fast 12-14 hours and not to smoke 30 min before the collection of blood. Individuals with a history of or current viral hepatitis infection, chronic gastrointestinal diseases in the past 6 months, and/or a nutritional deficiency were excluded from the study.

Written informed consent was obtained from each participant. The Institutional Review Board of the

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Protection of Human Subjects at the First Hospital of Jilin University approved the experimental protocols.

Collection and analysis of blood samples

All blood samples were collected according to acceptable laboratory procedures. Blood samples were centrifuged and the collected plasmas were frozen and tested in the Clinical Laboratory of the First Hospital of Jilin University. Fasting plasma glucose and lipids were analyzed by an enzymatic technique on an auto-analyzer (WLCYON-300 auto-analyzer, Becker, France).

NAFLD criteria

Fatty liver was diagnosed according to the criteria of ultrasound examination for the fatty liver of Chinese subjects, as established by the Chinese Liver Disease Association (1). Individuals with NAFLD were identified by the following factors : 1) consumed less than 40 g/week of alcohol ; 2) were without viral and/or gastrointestinal diseases ; 3) had clinical symptoms such as fatigue, pain or discomfort in the upper-right abdomen, and enlarged liver and spleen ; 4) abnormal levels of alanine aminotransferase (ALT), gamma glutamyl transpeptidase (GGT), and triglycerides (TG) ; 5) a positive ultrasound result ; or 6) pathological characteristics of a fatty liver (1).

Metabolic syndrome (MS) criteria

Individuals with MS were diagnosed according to the criteria of the International Diabetes Foundation (2005). These subjects were identified by being centrally obese (defined as a waist circumference ≥ 90 cm for males and ≥ 80 cm for females, according to WHO west pacific obesity standard), and had any two of the following four signs of MS : 1) high blood pressure (BP) : systolic BP ≥ 130 mmHg or diastolic BP ≥ 85 mmHg, or history of hypertension ; 2) high plasma TG : ≥ 150 mg/dL (1.70 mmol/L) ; 3) low HDL cholesterol : ≤ 40 mg/dL (1.04 mmol/L) in males and ≤ 50 mg/dL (1.30 mmol/L) in females ; 4) high fasting plasma glucose (FPG) : ≥ 100 mg/dL (5.6 mmol/L), history of type 2 diabetes, or treatment for high blood glucose levels.

BMI Criteria

Body mass index (BMI) is defined as the individual's body weight divided by the square of his or her height. According to Asian adult BMI standard (2000), normal is defined as a BMI of 18.5-22.9 kg/m^2, overweight is a BMI≥ 23 kg/m^2, obese I is a BMI ≥ 23 kg/m^2, obese II is a BMI ≥ 25 kg/ m^2, and obese III is a BMI ≥ 30 kg/m^2.

Dyslipidemia diagnosis criteria

TG ≥ 1.70 mmol/L, TC ≥ 6.0 mmol/L, LDL ≥ 4.30 mmol/L, HDL-C < 1.04 mmol/L for male and < 1.30 mmol/L for females.

Statistical analysis

All data were entered into a database and the difference of categorical variables between groups was analyzed by the Chi-squared test. The association of NAFLD with potential risk factors was analyzed by logistic regression, odds ratio (OR), and 95% confidence interval (CI). The potential confounders that we considered were age, race, education, marital status, occupation, and gender. Statistical analyses were performed using the Statistical Package for Social Science program, version 13.0 (SPSS Inc. Chicago, IL, USA). A two-tailed p-value of < 0.05 was considered statistically significant.

Results

To determine the prevalence of NAFLD in Northern China, a total of 6043 subjects were surveyed. Of these subjects, 3850 were randomly selected to undergo a physical examination and ultrasound scanning. There was a similar distribution in the gender, age, and occupation between the total population surveyed and the selected population that was physically examined, which reflected the distribution of these categories in the population of Northern China (Table 1).

Of the selected 3850 subjects, 3815 (99%) completed physical examination, laboratory tests, and ultrasound scanning. Among these subjects, 831 were diagnosed with fatty liver disease, 284 were diagnosed with an alcohol-related fatty liver, and 30 were hepatitis B or C positive. A total of 626 subjects had NAFLD, and the prevalence was 15.9%. Of note, several characteristics of the subjects with NAFLD were comparable with those of the non-NAFLD control group and total population studied. We found that marital status, occupation, level of education, income, and weekly exercise were not associated with the development of NAFLD in this population. However, the percentage of subjects with NAFLD among females and those older than 60 years was significantly higher than that of the average prevalence (Table 2, $p < 0.01$). In contrast, the percentage of NAFLD in subjects younger than 30 years of age was significantly lower than that of the average rate in this population. Further analysis revealed that females at 50 years of age were more likely to have NAFLD (Table 3). The data show that, while there was no difference between males and females in younger age groups, the frequency of NAFLD cases in 50-year-old females was significantly higher than that of 50-year-old males ($p < 0.001$).

Previous studies have suggested that hypertension, MS and associated glucose intolerance, and dyslipdemia are associated with NAFLD. We further analyzed the potential association of these factors with NAFLD in this population. We found that the percentages of subjects with NAFLD were greater among subjects with elevated FPG and diabetes, MS, central obesity, abnormal BMI, hypertension, serum cholesterol, higher LDL and lower HDL levels, and triglyceride levels versus the control

Table 1. — **Demographic characteristics of selected subjects**

Demographic characteristics		Total subjects (n = 6043)		Selected subjects (n = 3850)	
		n	%	n	%
Gender	Male	3804	51	1552	44.3
	Female	2959	49	1949	55.7
Age (years)	18-30	999	16.5	468	13.4
	31-40	1527	25.3	847	24.2
	41-50	1528	25.3	924	26.4
	51-60	1398	23.1	868	24.8
	> 60	591	9.8	394	11.3
Occupation	Farmer	3416	56.5	1715	49.0
	Worker	693	11.5	495	14.1
	Government worker	358	5.9	233	6.7
	Teacher	114	1.9	77	2.2
	Manager in state-owned enterprise	149	2.5	108	3.1
	Self-employed	493	8.2	254	7.3
	Other	820	13.6	617	17.6

Table 2. — **Detailed demographic characteristics of study subjects**

Demographic Characteristics		NAFLD (n = 626)		Control (n = 2875)		*p**
		n	%	n	%	
Gender	Male	243	38.8	1309	45.5*	0.021
	Female	383	61.2	1566	54.5*	0.044
Age (years)	18-30	43	6.9	425	14.8	< 0.001
	31-40	119	19.0	728	25.3	
	41-50	177	28.3	747	26.0	
	51-60	193	30.8	675	23.5	
	> 60	94	15.0	300	10.4	0.002
Race	Han	622	99.4	2862	99.5	
	Other	4	0.6	13	0.5	
Marriage	Un-married	10	1.6	129	4.5	
	Married	616	98.4	2746	95.5	
Education	Less than Elementary school	22	3.5	104	3.6	
	Elementary school	203	32.4	855	29.7	
	Middle school	246	39.3	1171	40.7	
	High school or Technical school	108	17.3	489	17.0	
	Junior college	36	5.8	170	5.9	
	4-year college	11	1.8	86	3.0	< 0.001
Occupation	Famer	272	43.5	1443	50.2	
	Worker	109	17.4	386	13.4	0.017
	Government worker	51	8.1	182	6.3	0.01
	Teacher	12	1.9	65	2.3	
	Manager in state-owned enterprise	24	3.8	84	2.9	0.01
	Self-employed	40	6.4	214	7.4	
	Other	116	18.5	501	17.4	
Monthly Income (Yuan)	< 200	98	15.7	422	14.7	
	200-399	62	9.9	251	8.7	
	400-599	150	24.0	781	27.2	
	600-799	167	26.7	812	28.2	
	800-1999	142	22.7	595	20.7	
	2000-2999	6	1.0	11	0.4	0.01
	3000-4000	1	0.2	3	0.1	0.01
Exercise	< 30 min	18	2.9	77	2.7	
	30 min to 2 hours	68	10.9	276	9.6	
	> 2 hours	540	86.3	2522	87.7	

NAFLD, non-alcoholic fatty liver disease. *p-values were calculated by χ^2 tests, as compared to the average percentage of NAFLD in the population ; other measures were not significant (data not shown).

Table 3. — **Gender and age-related distribution of NAFLD**

Age group (years)	Male (n = 243)		Female (n = 383)		χ^2	p
	NAFLD (n)	NAFLD (%)	NAFLD (n)	NAFLD (%)		
18-30	30	10.2	13	5.9	3.125	0.1051
31-40	54	13.1	65	12.7	1.1749	0.3145
41-50	70	15.1	107	18.2	0.1954	0.6719
51-60	58	11.4	135	26.6	15.2094	< 0.001
> 60	31	12.9	63	30.2	12.6564	< 0.001

NAFLD, non-alcoholic fatty-liver disease.

Table 4. — **Factors associated with NAFLD**

Factor	NAFLD (n = 605)		Non-NAFLD (n = 2978)		χ^2	p
	n	%*	n	%*		
High FPG or Diabetes	180	29.8	781	27.7	1.083	0.2981
Abnormal BMI	466	74.4	1133	39.4	254.035	< 0.001
Hypertension	360	57.6	842	19.3	182.182	< 0.001
Waist circumference	491	78.6	719	25.1	647.150	< 0.001
Metabolic Syndrome	216	50.12	229	12.0	333.771	< 0.001
Hypercholesterolemia	65	10.7	84	3.0	73.209	< .0001
Hypertriglyceridemia	333	55.4	515	18.3	359.053	< .0001
Hypolipoproteinemia	169	37.6	618	31.2	6.667	0.01
Dyslipidemia	322	74.5	805	41.8	151.812	< .0001

FPG, fasting blood glucose ; BMI : body mass index. Data shown are the number and percentage of cases in each group.
* The denominator of the percentage fraction may vary due of missing data.

group (Table 4, $p < 0.04$ to $p < 0.001$). In addition, analysis of individual factors revealed that gender, BMI, fasting glucose level, hypertension, waist circumference, dyslipidemia, and MS were all significantly associated with an increased risk of NAFLD in this population (Table 5). Lastly, the prevalence of NAFLD was positively associated with the number of MS-related risk factors in this population (Table 6). Therefore, MS-related risk factors may synergistically increase the development of NAFLD.

Table 5. — **The association between the number of MS-related risk factors and NAFLD**

MS-related Diseases	Total	NAFLD	
		n	Prevalence (%)
0	1064	26	2.4
1	1016	78	7.7
2	723	152	21.0
3	539	220	40.8
4	221	117	52.9
5	20	12	60.0

NAFLD : Non-alcoholic fatty liver disease ; MS, metabolic syndrome.

Discussion

The goal of this study was to examine the prevalence and risk factors of NAFLD in Northern China. We first examined the demographic characteristics of 6043 subjects and then evaluated the characteristics of the 3815 randomly selected subjects. The distribution of gender, age, and occupation was similar, suggesting that the selected 3815 subjects were representative of the whole study population.

We found that the prevalence of NAFLD was 15.9% in this population, which was similar to that in southern China (7), suggesting that both the Northern and Southern Chinese had a similar prevalence of NAFLD. Notably, the prevalence of NAFLD increased with age. The prevalence of NAFLD in subjects younger than 30 years or older than 60 years was significantly lower than that of the average rate of this disease and other subject age groups. The lower prevalence of NAFLD in the young age group may be due to a lower level of stress and increased social activity, a healthier life style, and more physical exercise in younger people. Interestingly, the prevalence of NAFLD in females (18.9%) was higher than that in males (14.3%), which was different from another domestic study (9). The higher prevalence of NAFLD in females may be due to the high rate of female obesity in Northern China. Many women in this region have fewer life burdens and participate in less physical activity than men in China. Some male patients with fatty liver while drinking alcohol become alcoholic fatty liver disease. Subjects with certain occupations, such as workers in companies (22%) and in the government (22.2%), and managers in state-owned enterprises (22.2%) had a higher prevalence of NAFLD than others, which may reflect the typical culture of food consumption in these jobs in China. The percentage of subjects with advanced education (college or higher) had a significantly lower percentage of NAFLD (11.3%). Furthermore, people with a relatively greater monthly income had a higher rate of NAFLD.

Table 6. — **Correlation analysis of individual factors related to NAFLD**

Variable	Beta	SE	Wald	*p*	OR	95.0% CI (OR)	
						Lower	Upper
Gender	0.837	0.209	15.981	< 0.001	0.433	0.287	0.653
Occupation	0.056	0.033	2.844	0.092	1.058	0.991	1.129
Marriage	0.107	0.599	0.032	0.858	0.898	0.278	2.905
Age	0.004	0.009	0.245	0.621	0.996	0.978	1.013
BMI	1.057	0.108	95.152	< 0.001	2.879	2.328	3.561
Abnormal fasting glucose	0.168	0.056	8.993	0.003*	0.845	0.757	0.943
Hypertension	0.862	0.224	14.792	< 0.001	2.368	1.526	3.673
Waist circumference	0.162	0.013	168.077	< 0.001	1.176	1.147	1.205
Dyslipidemia	1.471	0.221	44.293	< 0.001	4.354	2.823	6.714
MS	3.152	0.729	18.675	< 0.001	0.043	0.010	0.179

NAFLD, non-alcoholic fatty liver disease.

Several factors, including gender, obesity, dyslipidemia, MS, and hypertension, were significantly associated with an increased risk of NAFLD, and these findings were similar to findings from another study (10). Obesity was the strongest NAFLD risk factor. Between 9% and 26% of obese people have fatty liver disease (11) and the results of this study show that 36% of subjects with central obesity, as determined by waist circumference, had NAFLD, especially in obese female subjects (48.9% in females vs. 22.1% in men). In subjects with NAFLD, 81.1% had central obesity and the prevalence of NAFLD increased with increasing levels of BMI, similarly to previous reports (11,12).

Dyslipidemia and hypertension are two independent risk factors of fatty liver disease (13). In this population, the prevalence of NAFLD in subjects with dyslipidemia was 33.4% and in subjects with hypertension was 28.7%, percentages that were slightly higher than those of other domestic studies (14). Notably, people living in Northern China generally eat a high-calorie diet, have high carbohydrate and salt intake, and participate in less physical activity, which may contribute to the high prevalence of dyslipidemia and hypertension, ultimately leading to NAFLD.

NAFLD is regarded as a manifestation of MS or insulin resistance. Previous studies have demonstrated that the degree of insulin resistance was highly correlated to the severity of NAFLD (15,16). Moreover, subjects with MS are more likely to develop NAFLD (17) and it has been suggested that MS should be included in the diagnosis criteria of NAFLD (18-20). In addition, we found that impaired fasting glucose and diabetes were also associated with NAFLD. These findings extended previous findings that the incidence of cardiovascular events was increased in subjects with type II diabetes or NAFLD (21). More importantly, multiple factor analysis revealed that the prevalence of NAFLD increased from 2.4% to 60.4% as the number of risk factors increased from 0 to 5. These data indicate that these risk factors synergistically increase the risk for the development of NAFLD in the Chinese.

NAFLD is a complicated liver disease influenced by genetic, environmental, and metabolic factors. We are interested in further investigating how genetic factors are associated with the development of NAFLD and forming new strategies to educate the general population about the prevention of MS and NAFLD.

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