Prevalence of Nontraumatic Osteonecrosis of the Femoral Head and its Associated Risk Factors in the Chinese Population: Results from a Nationally Representative Survey

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Abstract

Background: Nontraumatic osteonecrosis of the femoral head (NONFH) is a debilitating disease that represents a significant financial burden for both individuals and healthcare systems. Despite its significance, however, its prevalence in the Chinese general population remains unknown. This study aimed to investigate the prevalence of NONFH and its associated risk factors in the Chinese population.

Methods: A nationally representative survey of 30,030 respondents was undertaken from June 2012 to August 2013. All participants underwent a questionnaire investigation, physical examination of hip, and bilateral hip joint X-ray and/or magnetic resonance imaging examination. Blood samples were taken after overnight fasting to test serum total cholesterol, triglyceride, and high-density lipoprotein (HDL) and low-density lipoprotein (LDL) levels. We then used multivariate logistic regression analysis to investigate the associations between various metabolic, demographic, and lifestyle-related variables and NONFH.

Results: NONFH was diagnosed in 218 subjects (0.725%) and the estimated NONFH cases were 8.12 million among Chinese people aged 15 years and over. The prevalence of NONFH was significantly higher in males than in females (1.02% vs. 0.51%, $\chi^2 = 24.997$, $P < 0.001$). Among NONFH patients, North residents were subjected to higher prevalence of NONFH than that of South residents (0.85% vs. 0.61%, $\chi^2 = 5.847$, $P = 0.016$). Our multivariate regression analysis showed that high blood levels of triglycerides, total cholesterol, LDL-cholesterol, and non-HDL-cholesterol, male, urban residence, family history of osteonecrosis of the femoral head, heavy smoking, alcohol abuse and glucocorticoid intake, overweight, and obesity were all significantly associated with an increased risk of NONFH.

Conclusions: Our findings highlight that NONFH is a significant

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public health challenge in China and underscore the need for policy measures on the national level. Furthermore, NONFH shares a number of risk factors with atherosclerosis.

Key words: Nontraumatic Osteonecrosis of the Femoral Head; Prevalence; Risk Factors

Introduction

Nontraumatic osteonecrosis of the femoral head (NONFH) is a pathological process that occurs at the femoral head as a result of interruption of blood supply following ischemic insult. This progressive, multifactorial, and debilitating condition can result in significant morbidity in patients of any age. Although its clinical manifestations have been well-defined, the etiology and epidemiology of NONFH have yet to be fully elucidated. Although few epidemiological studies to date have reported on the incidence of NONFH in the general population, between 300,000 and 600,000 people in the United States suffer from this condition.[1] Furthermore, studies from the late 1990s showed that 10,000 to 20,000 new cases of NONFH were diagnosed in the United States each year.[2,3] In Japan, an estimated 2500–3300 new cases are reported annually[4] while around 11,400 patients were found to have sought treatment in 2004.[5] Another recent analysis has showed that the annual incidence rate in Japan is 1.91 per 100,000.[6] In Korea, prevalence has increased from 20.53 per 100,000 in 2002 to 37.96 in 2006, and the average number of new cases annually has been estimated at 14,103.[7]

Few previous epidemiological studies have investigated NONFH in a Chinese context, however, we therefore undertook a nationally representative survey, including a questionnaire, blood sample, a hip joint examination, and X-ray or magnetic resonance imaging (MRI) scanning from June 2012 to August 2013 to estimate the prevalence of NONFH and characterize its associated risk factors among the Chinese general population aged 15 years or over.

Methods

Study design

We employed multistage random sampling to obtain a nationally representative sample of people aged 15 years and over in the general population. Sampling took place in five provinces and autonomous regions in Northern China (Heilongjiang, Liaoning, Shaanxi Provinces, and Inner Mongolia and Xinjiang Uyghur Autonomous Region) and four provinces in Southern China (Yunnan, Hunan, Zhejiang, and Hainan provinces) as defined by the Qinling-Huaihe Line (32–34.5°N).

In the subsequent stages of sampling cities and rural counties, they were selected from the nine provinces and autonomous regions. We then randomly selected sub-districts, from which neighborhood-level sampling areas were identified. Only those residents who had lived at their current address for ≥5 years were eligible to participate.

Each respondent was requested to complete a questionnaire, and undergo blood sampling, physical examination, and an X-ray in addition to MRI where it was considered appropriate. Data collection was standardized to minimize potential sources of bias. All interviewers attended a training program to familiarize them with the study's aims and methods. Clinical staff members also received training to ensure consistency in diagnostic procedures.

Of a total of 31,036 respondents selected for participation in the study, 535 were excluded due to incomplete demographic data and 421 due to missing X-ray or MRI results. A further 50 were removed following a diagnosis of traumatic osteonecrosis of the femoral head (ONFH). This resulted in a sample of 30,030 participants who were included in our analysis.

The study protocol was approved by the Ethics Committee of the Affiliated Zhongshan Hospital of Dalian University, Dalian, Liaoning, China. The written informed consent was signed by each participant prior to data collection.

Questionnaire

We collected information on participants' place of residence (urban or rural), gender, age, height, weight, clinical history of ONFH and etiology (including hip trauma, dysbarisms, blood system diseases, Gaucher's disease, radiation exposure, hyperuricemia, and other diseases), family history of NONFH, and history of tobacco, alcohol, and steroid use (including type of steroid, duration of use and dose).

A smoking index[8] was derived by multiplying the self-reported number of standard packs of 20 cigarettes smoked per day multiplied by years of smoking. Heavy smokers were defined as having ≥20 pack-years. Heavy drinkers[9] were defined as those reporting an average consumption of ≥40 g pure alcohol per day for men and ≥20 g pure alcohol per day for women during the previous 12 months. Systematic steroid users[10] were defined as those with an intake of ≥2 g of prednisone or its equivalent within a period of 3 months. Body mass index (BMI) was calculated by dividing weight in kilograms by height in meters squared.

Blood sampling

Blood specimens were collected using a vacuum tube after at least 10 h of overnight fasting to measure participants' serum total cholesterol, triglyceride, high-density lipoprotein (HDL), and low-density lipoprotein (LDL) levels.

Diagnosis of nontraumatic osteonecrosis of the femoral head

All participants underwent a physical examination including assessments of gait, hip deformity, tenderness in the groin

area, pain in the region of the greater trochanter, and range of motion of the hip joint and leg length, in addition to the flexion, abduction, and external rotation (FABER) test, internal rotation test, and Trendelenburg test.

An X-ray was then performed on both hip joints. MRI was used for those participants at a higher risk of ONFH and reported hip pain but whose X-ray results suggested a negative diagnosis (n = 553). A team of six orthopedic surgeons and radiologists interpreted the results of these tests to determine a diagnosis of NONFH.

Outcome measures and diagnostic criteria

Criteria used to diagnose NONFH were based on those proposed by the Research Committee on Idiopathic Osteonecrosis of the Femoral Head in Japan[11] and the findings of an expert committee based in China.[12] The major diagnostic criteria comprised (1) Cystic and sclerotic changes in femoral head without joint space narrowing or acetabular abnormality, (2) collapse of the femoral head and/or presence of the crescent sign without joint space narrowing or acetabular abnormality on radiographic images, and (3) a circumscribed subchondral "band-like" lesion with low signal intensity on T1-weighted images and/or a "double-line" sign is seen on T2-weighted images. The two minor criteria were (1) Pain (groin area, greater trochanteric area, ipsilateral buttock, and knee) and/or movement limitation of the hip and (2) positive finding on physical examination of the hip (e.g., FABER test, internal rotation test, and Trendelenburg test). A positive diagnosis of NONFH was given when participants fulfilled one of the three major criteria with or without one of the two minor criteria. The Association Research Circulation Osseous (ARCO) classification system was used to determine the stage of NONFH progression.[13]

Statistical analysis

We first performed a descriptive analysis to describe the demographic and metabolic characteristics of the overall sample and estimate the crude and adjusted prevalence of NONFH. Means were given with 95% confidence intervals (*CI*s) for continuous variables and percentages (with 95% *CI*s) were given for categorical variables. Statistics was then calculated according to participants' gender, age (15–24 years, 25–34 years, 35–44 years, 45–54 years, 55–64 years, 65–74 years, and ≥75 years), place of residence (urban or rural), and region of China (North or South). The overall prevalence of NONFH in the Chinese general population aged 15 years and older was then estimated using 2010 census data.

We then investigated the crude associations between BMI and metabolic risk factors and NONFH. Participants were classified according to BMI as underweight, normal, overweight, or obese using WHO standard guidelines.[14] We then classified participants' non-HDL-cholesterol (HDL-C) and LDL-cholesterol (LDL-C) levels as desirable, above desirable, borderline, high or very high group, and the triglyceride levels as normal, borderline, high, or very high according to 2014 United States guidelines.[15] We analyzed the association between NONFH and metabolic, demographic, and lifestyle-related factors using multivariate logistic regression and reported adjusted odds ratios with 95% *CI*s. While age and BMI (<18.5 kg/m², 18.5–24.9 kg/m², 25.0–29.9 kg/m², or ≥30.0 kg/m²) were included as categorical variables, gender, family history of NONFH, residence (urban or rural), smoking status (smoker or nonsmoker), alcohol use (heavy drinker or nonheavy drinker), and glucocorticoid intake were operationalized as binary variables. Blood levels of triglyceride (change per 50 mmol/L), total cholesterol (change per 30 mmol/L), LDL-cholesterol (change per 30 mmol/L), and non-HDL-C (change per 30 mmol/L) were also included as categorical variables. Two-tailed P values were given and values of <0.05 were considered statistically significant. All statistical analyses were conducted using R version 3.1.1 (R Foundation for Statistical Computing, Vienna, Austria).

Results

Prevalence of nontraumatic osteonecrosis of the femoral head

The overall prevalence of NONFH among our nationally representative sample, whose characteristics are shown in Table 1, was found to be 0.725%. The prevalence of NONFH was significantly higher among males than females (1.02% vs. 0.51%, $\chi^2 = 24.997$, $P < 0.001$). Within various age groups, prevalence of NONFH consistently was higher in male (15–24 years: 0.27%, 25–34 years: 1.27%, 35–44 years: 1.64%, 45–54 years: 0.68%, 55–64 years: 1.08%, 65–74 years: 1.11%, and ≥75 years: 0.94%) than females (15–24 years: 0.15%, 25–34 years: 0.27%, 35–44 years: 0.49%, 45–54 years: 0.33%, 55–64 years: 0.59%, 65–74 years: 0.86%, and ≥75 years: 0.85%) [Figure 1a]. In addition, significant difference was found in age groups of 25–34, 35–44, and 55–64 years old (χ^2 value was 9.033, 15.348, and 4.643, respectively, and P value was 0.003, <0.0001, and 0.031, respectively). Among NONFH patients, urban (female: 0.59%, male: 1.14%, $\chi^2 = 13.272$, $P = 0.0003$) and North (female: 0.62%, male: 1.19%, $\chi^2 = 12.807$, $P = 0.0003$) residence were subjected to higher prevalence of NONFH than those of rural (female: 0.41%, male: 0.90%, $\chi^2 = 12.820$, $P = 0.0003$) (0.80% vs. 0.64%, $\chi^2 = 2.534$, $P = 0.111$) [Figure 1b] and South (female: 0.40%; male: 0.87%, $\chi^2 = 12.661$, $P = 0.0003$) (0.85% vs. 0.61%, $\chi^2 = 5.847$, $P = 0.016$) [Figure 1c].

Based on Chinese population data from 2010,[16] we estimated that there are around 8.12 million cases of NONFH among the Chinese general population aged 15 years and over. We found that 36.70% of the cases in our study sample were newly diagnosed, of which 86.25% had early-to-middle stage NONFH (18.75% in ARCO stage I, 51.25% in ARCO stage II, 16.25% in ARCO stage III, and 13.75% in ARCO stage IV). The mean age of newly-diagnosed NONFH patients was significantly lower than that of patients previously diagnosed with the condition (47.19 years vs. 55.48 years, $P < 0.001$).

Table 1: General characteristics of Chinese participants enrolled in this survey

Variables	Number of participants (*n*)	Percentage (%, 95% *CI*)			Mean (95% *CI*)				
		Heavy smoking	Alcohol abuse	Glucocorticoid intake	BMI (kg/m^2)	Cholesterol (mmol/L)	Non-HDL-C* (mmol/L)	LDL-C (mmol/L)	Triglyceride (mmol/L)
Gender									
Women	17,334	0.35 (0.26–0.43)	3.61 (3.33–3.89)	2.75 (2.51–3.00)	23.51 (23.44–23.57)	200.54 (199.93–201.15)	142.48 (141.87–143.08)	87.72 (87.32–88.11)	116.98 (116.25–117.71)
Men	12,696	12.91 (12.36–13.53)	12.36 (11.782–12.96)	2.66 (2.38–2.94)	22.03 (21.97–22.09)	192.85 (192.14–193.55)	135.54 (134.84–136.24)	84.21 (83.76–84.66)	113.65 (112.81–114.48)
Age									
15–24 years	2519	8.06 (7.00–9.12)	8.89 (7.78–10.00)	2.10 (1.54–2.66)	20.83 (20.71–20.94)	187.80 (186.28–189.32)	130.25 (128.73–131.76)	79.82 (78.82–80.82)	108.56 (106.96–110.16)
25–34 years	3381	8.58 (7.63–9.52)	8.61 (7.66–9.55)	3.19 (2.60–3.79)	21.87 (21.76–21.97)	188.59 (187.15–190.03)	130.18 (128.77–131.59)	82.27 (81.38–83.16)	112.20 (110.60–113.80)
35–44 years	4948	7.24 (6.51–7.96)	7.24 (6.51–7.96)	3.21 (2.72–3.70)	22.54 (22.44–22.64)	190.06 (188.93–191.19)	132.37 (131.25–133.49)	83.07 (82.36–83.78)	112.87 (111.48–114.27)
45–54 years	6161	4.56 (4.04–5.08)	6.35 (5.74–6.96)	2.78 (2.37–3.19)	23.04 (22.94–23.14)	198.20 (197.20–199.19)	140.02 (139.02–141.01)	86.47 (85.83–87.12)	114.87 (113.63–116.10)
55–64 years	7186	4.52 (4.04–5.00)	6.51 (5.94–7.08)	2.89 (2.51–3.28)	23.46 (23.37–23.56)	202.86 (201.93–203.79)	145.29 (144.36–146.21)	89.03 (88.41–89.64)	119.38 (118.23–120.53)
65–74 years	3945	3.60 (3.02–4.18)	7.98 (7.14–8.83)	2.23 (1.77–2.69)	23.75 (23.62–23.89)	205.86 (204.59–207.13)	148.52 (147.26–149.77)	90.71 (89.87–91.55)	120.36 (118.73–121.98)
≥75 years	1890	5.56 (4.52–6.59)	8.04 (6.82–9.27)	1.48 (0.94–2.03)	23.81 (23.60–24.01)	202.39 (200.59–204.19)	145.34 (143.55–147.12)	89.42 (88.24–90.60)	115.82 (114.03–117.60)
Place of residence									
Rural	14,215	5.38 (5.01–5.75)	7.76 (7.32–8.20)	2.37 (2.12–2.62)	22.53 (22.47–22.59)	207.26 (206.64–207.88)	148.42 (147.79–149.05)	89.52 (89.07–89.96)	116.33 (115.49–117.17)
Urban	15,815	5.94 (5.57–6.31)	6.93 (6.53–7.33)	3.02 (2.76–3.29)	23.20 (23.14–23.26)	188.32 (187.67–189.97)	131.56 (130.92–132.20)	83.28 (82.89–83.68)	114.89 (114.16–115.61)
North	14,838	6.37 (5.98–6.76)	7.01 (6.60–7.42)	2.97 (2.69–3.24)	23.01 (22.95–23.07)	204.29 (203.65–204.92)	145.57 (144.93–146.21)	88.73 (88.30–89.16)	116.59 (115.81–117.38)
South	15,192	5.00 (4.65–5.34)	7.63 (7.21–8.05)	2.47 (2.22–2.72)	22.76 (22.70–22.82)	190.46 (189.80–191.11)	133.65 (133.01–134.30)	83.79 (83.38–84.21)	114.66 (113.80–115.34)

*Non-HDL-C = Total cholesterol minus HDL-C. 95% *CI*: The rate of 95% confidence intervals; LDL-C: Low-density lipoprotein-cholesterol; Non-HDL-C: Non-high-density lipoprotein-cholesterol; BMI: Body mass index.

Moreover, 19 cases of NONFH were diagnosed by MRI (15 in ACRO stage I and 4 in ARCO stage II).

Risk factors for nontraumatic osteonecrosis of the femoral head

Among participants diagnosed with NONFH, 20.96% of males and 4.42% of females were heavy smokers ($\chi^2 = 13.725$, $P < 0.0001$), 32.93% of males and 7.96% of females reported being heavy drinkers ($\chi^2 = 22.436$, $P < 0.0001$), 26.35% of males and 55.75% of females reported corticosteroid use ($\chi^2 = 23.451$, $P < 0.0001$), and 19.76% of males and 31.86% of females reported none of these risk factors ($\chi^2 = 4.680$, $P = 0.031$) [Figure 2]. While a further seven patients were overweight or obese, sixteen were diagnosed with dyslipidemia and five with dysbarism.

Our results also showed that BMI and levels of non-HDL-C and triglyceride were significantly higher among both males and females diagnosed with NONFH than in males and females without the condition [Table 2].

As shown in Table 3, elevated blood levels of triglycerides and LDL-C and non-HDL-C, male, urban residence, family history of ONFH, heavy smoking, heavy drinking, glucocorticoid intake, overweight and obesity were all positively associated with an increased risk of NONFH in our multivariate model.

Discussion

A positive diagnosis of NONFH was established on the basis of both physical examination and imaging using stringent diagnostic criteria and quality-control procedures. Our results showed a high prevalence of NONFH among the Chinese general population and we estimated that around 8.12 million Chinese people aged 15 years and over are affected by the condition.

Our survey found that 36.70% of NONFH cases in our sample were newly diagnosed after X-ray or MRI examination – some of which were asymptomatic. The majority (86.25%) of patients, however, were in the early or middle stages of disease progression. Given that previous work has shown that early diagnosis and intervention for patients with NONFH can effectively delay disease progression or prevent patients from requiring total hip arthroplasty,[17-21] our findings highlight the importance of active screening for NONFH to detect the disease in its early stages.

While the results of our multivariate analysis show that male, family history of NONFH, and region of residence can influence disease risk, they suggest that changes in lifestyle-related factors such as smoking, alcohol use, corticosteroid intake, overweight, obesity, and dyslipidemia could be contributing to an increase in the burden of NONFH among the Chinese population. Furthermore, the higher prevalence of NONFH among males of all ages could be attributed to higher levels of smoking and alcohol use. Greater fluctuations in temperature, in addition to cultural and lifestyle factors, may also contribute to higher rates of NONFH in Northern China.

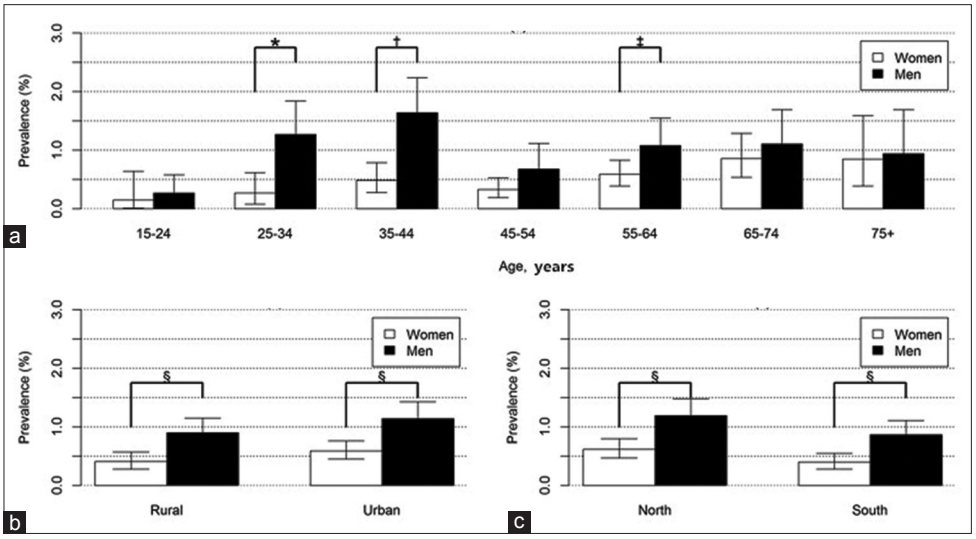

Figure 1: Age-specific prevalence of nontraumatic osteonecrosis of the femoral head in Chinese participants 15 years and over (a). Prevalence of nontraumatic osteonecrosis of the femoral head among Chinese adults 15 years and over, according to urban and rural residence (b) and North and South region (c). Error bars indicate 95% confidence interval. *$P < 0.01$, †$P < 0.0001$, ‡$P < 0.05$, §$P < 0.001$.

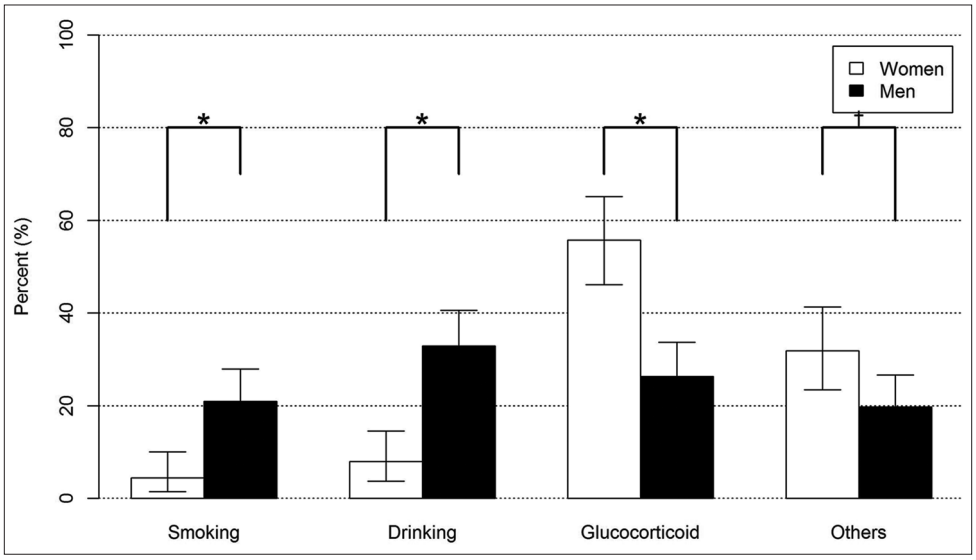

Figure 2: The percent of different causes of nontraumatic osteonecrosis of the femoral head between women and men. Error bars indicate 95% confidence interval. *$P < 0.0001$, †$P < 0.05$.

Although the pathophysiology of NONFH has yet to be fully elucidated, previous studies hypothesize that NONFH is induced by vascular impairment, altered bone cell physiology, oxidative stress, and insufficient blood supply among other factors.[1,2,22,23] Meanwhile, alcohol intake[24-26] and steroid use[10,27-30] have been identified as the major risk factors for NONFH. While this is consistent with our findings, glucocorticoid intake was found to have a stronger association with NONFH than alcohol use. Numerous studies[31,32] have also concluded that hyperlipidemia in the femoral head induced by steroid and alcohol use are associated with NONFH. Both of these factors precipitate an increase in fat volume in bone marrow and blood lipid levels, thereby increasing deposition of fat and interrupting blood flow to the femoral head. In addition to these two major risk factors, our results and those of previous studies suggest that cigarette smoking may also be conducive to NONFH.[33-35] This may be due to changes in nitric oxide bioavailability, resulting in increased oxidative stress and endothelial dysfunction.

We also identified obesity as a risk factor for NONFH, and our results show that risk of NONFH is positively associated with BMI. In general, overweight and obesity are often associated with hyperlipidemia. This in turn is associated with elevated fasting and postprandial plasma insulin concentrations that can promote adipose synthesis and inhibit the decomposition of adipose tissue. Given that hypercholesterolemia has also been associated with idiopathic avascular necrosis,[36] this

Table 2: Contingency table of ONFH prevalence stratified by BMI, non-HDL-C, LDL-C, and triglyceride levels in men and women

Items	Men		Women	
	Non-ONFH	NONFH	Non-ONFH	NONFH
BMI				
Under weight	1596	6	1492	2
Normal	9133	93	10,612	43
Over weight	1436	24	3611	28
Obese	402	6	1530	16
χ^2	13.121		19.632	
P	0.0043		0.0002	
Non-HDL-C				
Desirable	5832	21	6655	12
Above desirable	3512	32	5098	15
Borderline	2201	34	3622	26
High	729	27	1315	19
Very high	286	15	544	17
χ^2	127.384		113.362	
P	<0.0001		<0.0001	
LDL-C				
Desirable	9467	100	12,022	64
Above desirable	2591	26	4286	19
Borderline	432	3	798	6
High	55	0	113	0
Very high	22	0	26	0
χ^2	1.346		2.07	
P	0.854		0.723	
Triglyceride				
Normal	10,260	78	13,664	48
Borderline	2155	31	3338	19
High	128	20	204	22
Very high	24	0	39	0
χ^2	240.628		383.746	
P	<0.0001		<0.0001	

Figures are numbers of participants unless stated otherwise. The Chi-square test was used. $P<0.05$ is significant. NONFH: Nontraumatic osteonecrosis of the femoral head; LDL-C: Low-density lipoprotein-cholesterol; Non-HDL-C: Non-high-density lipoprotein-cholesterol; ONFH: Osteonecrosis of the femoral head; BMI: Body mass index.

Table 3: Multivariate-adjusted *OR*s for ONFH in Chinese participants

Variables	ONFH, *OR* (95% *CI*)	*Z*	*P*
Triglyceride, per increase of 50 mmol/L	1.11 (1.02–1.20)	2.528	0.0112
Cholesterol, per increase of 30 mmol/L	1.29 (1.07–1.57)	2.602	0.0093
LDL-C, per increase of 30 mmol/L	0.52 (0.42–0.64)	−6.191	<0.0001
Non-HDL-C*, per increase of 30 mmol/L	1.51 (1.20–1.91)	3.458	0.0005
Male	2.26 (1.61–3.17)	4.708	<0.0001
Urban residency	1.46 (1.07–1.98)	2.405	0.0161
Family history of NONFH	5.33 (2.51–11.31)	4.352	<0.0001
Heavy cigarette smoking	2.10 (1.38–3.21)	3.446	0.0006
Alcohol abuse	2.98 (2.08–4.27)	5.968	<0.0001
Glucocorticoid intake	35.46 (26.16–48.06)	23.000	<0.001
BMI groups			
Overweight†	1.97 (1.36–2.86)	3.568	0.0004
Obesity‡	2.32 (1.39–3.86)	3.233	0.0012

All covariables listed were included in the model simultaneously. $P<0.05$ is statistically significant. *Non-HDL-C = Total cholesterol minus HDL-C; †Overweight was defined as a BMI between 25.0 and 29.9; ‡Obesity was defined as a BMI of 30.0 or more. 95% *CI*: The rate of 95% confidence intervals; NONFH: Nontraumatic osteonecrosis of the femoral head; LDL-C: Low-density lipoprotein-cholesterol; Non-HDL-C: Nonhigh-density lipoprotein-cholesterol; *OR*: Odds ratio; ONFH: Osteonecrosis of the femoral head; BMI: Body mass index. *OR*s were calculated with the use of multinomial log it models.

is consistent with our finding that elevated triglyceride and LDL and non-HDL-C levels in the blood are associated with an increased risk of NONFH. Non-HDL-C is considered a more reliable indicator for assessing cholesterol-related risk and is often the first to be used when evaluating patients with NONFH. Our novel findings support the hypothesis that the factors involved in the pathogenesis of atherosclerotic cardiovascular disease (ASCVD) could also contribute to the progression of NONFH. A 3-year follow-up study[37] found that patients were at an increased risk of developing coronary heart disease after being diagnosed with NONFH, and that this patients could be attributable to risk factors such as smoking, obesity, and dyslipidemia. Further work is needed to fully elucidate the mechanisms for this association.

Because these risk factors for NONFH, which occurs as a result of ischemic insult and disruption of blood supply to the femoral head, have also been identified as risk factors for ASCVD,[38] this suggests that both conditions may share the same etiology and occur as a result of dyslipidemia. A previous study[39] has suggested that statins may offer some protection against osteonecrosis when steroid treatment is indicated. We may, therefore, speculate that strategies for preventing ASCVD may also be applicable to NONFH. Future studies are warranted to validate this hypothesis.

NONFH is a multifactorial disease that is associated with both genetic susceptibility and exposure to certain risk factors, and previous work has already shown that specific genetic polymorphisms are associated with NONFH.[40,41] Our results identified family history of NONFH as a risk factor for the conditions, which may hint to the influence of genetic factors on the pathogenesis of NONFH. Further work on specific genetic polymorphisms may prove beneficial in terms of characterizing genetic risk profiles for NONFH.

One of the major strengths of the present study was the use of a large nationally representative sample of the Chinese general population rather than a clinical sample, which may have led to oversampling of more severe cases of NONFH. At the same time, the use of clinical measurements in addition to self-reported data allowed us to investigate whether overweight, obesity, and dyslipidemia represented risk factors for NONFH in the Chinese population and to identify previously undiagnosed cases.

In summary, our results show that NONFH is highly prevalent in China. More concerning is the finding that a considerable proportion of asymptomatic cases remains undiagnosed. Early diagnosis and treatment are essential for delaying disease progression and minimizing the need for costly and invasive procedures in younger NONFH patients, who may require multiple hip replacement surgeries during their lifetime. Given that the direct cost to patients for undergoing primary total hip arthroplasty per hip without revision is between $8000 and $10,000 in China, this suggests that the overall cost of treating all outstanding cases on the national level could total at least $64 billion – representing a substantial financial burden on the Chinese healthcare system. Our results indicate that NONFH has the potential to be a national public health challenge and underscores urgent need for national strategies aimed at the prevention, detection, and treatment of NONFH among the Chinese general population.

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Conflicts of interest

There are no conflicts of interest.

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