

## Prevalence of and risk factors for gallstones in Uighur and Han Chinese

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### Abstract

**AIM:** To perform a single-centre survey of the prevalence of and possible risk factors for gallstones in Uighur and Han Chinese.

**METHODS:** Complete medical data for 9455 patients were collected from the medical centre of our hospital, and the overall prevalence of gallstones as well as the prevalence in different ethnic groups was studied. The risk factors for gallstones in different ethnic groups were identified in a univariate analysis, and variables with statistical significance were analysed by unconditional multiple logistic regression, to primarily explore the similarities and differences in gallstone risk factors between different ethnic groups.

**RESULTS:** The prevalence of gallstones was significantly higher in the Uighur population than in the Han

population (22.87% vs 11.64%,  $P < 0.05$ ). Further analysis of risk factors for gallstones based on the different ethnic areas revealed that age was a risk factor for gallstones in both groups; triglycerides, body-mass index (BMI) and high-density lipoprotein were risk factors for gallstones in the Han population, while total cholesterol (TC), gender and fatty liver were risk factors in the Uighur population. The Uighur patients were older than the Han patients, and had higher BMI, TC, low-density lipoprotein, female rate and fatty liver rate, while the incidence of hypertension was lower than that in the Han patients.

**CONCLUSION:** The prevalence of and risk factors for gallstones differ between the Uighur and Han populations.

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**Key words:** Gallstones; Risk factors; Prevalence

**Core tip:** The prevalence of gallstones in the Uighur population is higher than that in the Han population in Xinjiang, but there are few relevant epidemiological data or risk analysis reports. This single-centre case-control study enrolled healthy people to compare and analyse the risk factors for gallstones in Uighur and Han patients. The results suggest that age is a risk factor in both populations. Total cholesterol, gender and fatty liver are risk factors in the Uighur population, but in the Han population, those with elevated triglycerides, reduced high-density lipoprotein and obesity are at greater risk for gallstones.

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## INTRODUCTION

Gallstones are the most common non-fatal disease of the biliary system. Pain caused by gallstones in the right upper quadrant, along with the associated nausea, vomiting, postprandial fullness, and discomfort in the right upper quadrant and other symptoms, can seriously affect quality of life. The prevalence of gallstones in adults in developed countries is 10%-15%<sup>[1]</sup>. In United States, there are 20-25 million newly diagnosed gallstone patients each year, with medical costs for the prevention and treatment of gallstone disease of almost \$62 billion annually<sup>[2]</sup>. There is one relevant report about the nationwide prevalence of gallstones in China. In 1989, type-B ultrasonic screening revealed that the prevalence of gallstones was about 6.29% among 102.6 thousand people, and the detection rate in different regions ranged from 3.0% to 11.0%<sup>[3]</sup>. With improvements in living conditions, changes in diet, the widespread use of type-B ultrasound, the popularity of health care and other factors, the incidence of gallstones is increasing, with an approximately two-fold increase every 10 years<sup>[4]</sup>.

Xinjiang is a region with a high incidence of gallstones. A previous epidemiological survey showed that the incidence of gallstones in Xinjiang was 11.1%-15.5%<sup>[5,6]</sup>, exceeding the national level, which was considered to be associated with ethnicity, region and dietary habits. Liu<sup>[6]</sup> performed a survey towards the 1998-2001 examination results of 14760 healthy people in the Urumqi municipal public institutions, and found that the prevalence of gallstones in ethnic minorities (mainly Uighur, Kazak and Russian) was 13.8%, while in the Han population it was 10.4%. However, no further analysis of the risk factors for gallstones among ethnic groups was performed. There is little information on the gallstone situation in Xinjiang. For this reason, we selected 10130 subjects who agreed to undergo physical examination in the medical centre of the People's Hospital of Xinjiang Uygur Autonomous Region from March to June 2013. Of these subjects, 9455 had all the information required to perform the relative analysis. The objective of this study was to investigate the prevalence of and risk factors for gallstone disease among adults of different ethnic groups, thus providing a scientific basis for the prevention and treatment of gallstones in this region.

## MATERIALS AND METHODS

### Subjects

A total of 9455 subjects who agreed to undergo physical examination in the medical centre of the People's Hospital of Xinjiang Uygur Autonomous Region from March to June 2013 and had all the required information were selected. Their mean age was  $45.58 \pm 13.11$  years (range 20-80 years). There were 5962 males and 3493 females, among whom 8213 were Han and 1242 were Uighur Chinese.

### Methods

**Type-B ultrasonic examination:** ALOKA SSD-5000 colour Doppler ultrasound scanner was used, and the conventional abdominal B-ultrasonic method was performed, with a probe frequency of 3.5 MHz. All subjects were required to fast before examination. Examination was performed in the supine position, and the liver, gallbladder, pancreas and spleen were examined in turn. A gallstone was diagnosed if the cholecystic cavity exhibited a hyperechoic mass, with a stable shape; the rear of the hyperechoic mass exhibited a clear acoustic shadow; after changing position, the hyperechoic mass moved in the direction of gravity. In patients undergoing cholecystectomy for cholelithiasis, B-mode ultrasound was used to describe the circumstances of the common bile duct and whether a gallstone existed inside the liver or not, and "gallbladder removed for cholelithiasis" was recorded in such circumstances. Fatty liver was diagnosed if patients with the following item A and any of items B-E: A, the echo in the near-field of the hepatic region exhibited diffuse enhancement, while the echo in the far-field decayed; B, the intrahepatic duct structures were unclear; C, the liver exhibited mild to moderate enlargement, with a blunt edge angle; D, colour Doppler image suggested that the intrahepatic colour blood flow signal was reduced or difficult to visualise, while the strikes of intrahepatic blood vessels were normal; and E, the echoes of the hepatic right lobe membrane and diaphragm were unclear or incomplete.

**Physical examination and diagnostic criteria:** Basic data on height, weight, systolic blood pressure, diastolic blood pressure and other parameters were collected from all patients. The diagnostic criteria for hypertension were: systolic blood pressure  $\geq 140$  mmHg and/or diastolic blood pressure  $\geq 90$  mmHg; previously diagnosed hypertension; had taken or was taking antihypertensive drugs.

**Laboratory examination parameters:** Five millilitres of venous blood were collected in the morning after an overnight fast, and the fasting plasma glucose (FPG), triglycerides (TG), total cholesterol (TC), low-density lipoprotein (LDL) and high-density lipoprotein (HDL) were tested using an automatic biochemical analyser (ARCHITECT c16000). The dyslipidaemia standard was taken from the Prevention Guide Standard of Chinese Adult Dyslipidemia in 2007: normal lipid ranges were: TC  $< 5.18$  mmol/L, TG  $< 1.70$  mmol/L, LDL  $< 3.37$  mmol/L and HDL  $\geq 1.04$  mmol/L. The diagnostic criteria for diabetes were: FPG  $\geq 7.0$  mmol/L; previously diagnosed diabetes; had undergone or was undergoing hypoglycaemic therapy.

### Statistical analysis

The collected data were input into EXCEL by two people independently, who also examined and corrected the

**Table 1 Variable assignments**

Name	Negative assignment	Positive assignment
Gender	Male = 0	Female = 1
Age	≤ 50 = 0	> 50 = 1
Ethnic group	Han = 0	Uighur = 1
Hypertension	Normal or less than normal = 0	Hypertension = 1
Diabetes	Normal or less than normal = 0	FPG ≥ 7.0 mmol/L = 1
Fatty liver	(-) = 0	(+) = 1
TG	TG ≤ 1.70 mmol/L = 0	TG > 1.70 mmol/L = 1
TC	≤ 5.18 mmol/L = 0	> 5.18 mmol/L = 1
HDL-C	≥ 1.04 mmol/L = 0	< 1.04 mmol/L = 1

TG: Triglycerides; TC: Total cholesterol; HDL-C: High density lipoprotein cholesterol.

data to maintain accuracy. SPSS 16.0 statistical software was used for the data analysis. Continuous variables are expressed as mean ± SD, and intergroup comparisons were performed using the *t*-test. Categorical variables were analysed using the  $\chi^2$  test. The risk factors that might affect gallstone formation were first identified in a single-factor analysis of variance; significant variables were assessed via multivariate logistic regression. The independent variables were selected using the stepwise Wald forward method (the probability of inclusion of independent variables in the model was 0.05, and the exclusion probability was 0.1). The significant level of  $\alpha$  was set at 0.05. The assignments of specific variables are shown in Table 1.

## RESULTS

### Prevalence of gallstones

Among the 9455 cases, the prevalence of gallstones was 13.11% (1240/9455) in the general population, 11.64% (956/8213) in the Han population, and 22.87% (284/1242) in the Uighur population. The prevalence of gallstones in the Uighur population was significantly higher than that in the Han population ( $\chi^2 = 119.32, P = 0.00$ ). A stratified comparative analysis of gender and age between the two ethnic groups revealed that, when stratified by age, the gallstone prevalence in the Uighur population was higher than that in the Han population ( $\chi^2 = 33.95, P = 0.00; \chi^2 = 74.68, P = 0.00$ ); likewise, when stratified by gender, the gallstone prevalence in the Uighur population was higher than that in the Han population ( $\chi^2 = 44.83, P = 0.00; \chi^2 = 84.51, P = 0.00$ ). The detailed results are shown in Table 2.

### Analysis of general characteristics of gallstones in the two ethnic groups

The general information about the gallstone group (GST) and the non-gallstone group (control) is shown in Table 3. Compared with the control group, patients in the GST group: (1) were older, with a higher body-mass index (BMI); (2) exhibited obvious lipid dysbolism: increased TG, and lower HDL; and (3) were more likely to have hypertension, diabetes and fatty liver. Further analysis

**Table 2 Gallstone prevalence rates in different ethnic groups**

		Prevalence rate	$\chi^2$	P value	
Han	Male (≤ 50)	8.24% (280/3396)	117.02	0.00	
	(> 50)	18.44% (328/1779)			
	Female (≤ 50)	5.45% (120/22320)	306.52	0.00	
		(> 50)			28.29% (228/806)
	Total (≤ 50)	7.11% (400/5628)	357.22	0.00	
		(> 50)			21.51% (556/2585)
	Total male	11.75% (608/5175)	0.16	0.69	
	Total female	11.45% (348/3038)			
	Uighur	Male (≤ 50)	13.96% (68/487)	31.98	0.00
		(> 50)	30.67% (92/300)		
Female (≤ 50)		11.58% (36/311)	121.82	0.00	
		(> 50)			61.11% (88/144)
Sum (≤ 50)		13.03% (104/798)	122.42	0.00	
(> 50)		40.54% (180/444)			
Total male	20.33% (160/787)	7.83	0.01		
Total female	27.25% (124/455)				

regarding ethnic stratification revealed that in the Uighur group: (1) in addition to the dysbolism of TG and HDL, TC was also increased; and (2) the rate of diabetes in the GST group was similar to that in the control group. Further comparative analysis of intergroup characteristics between the Uighur group and the Han group suggested that, compared with the Han patients, the Uighur patients were older, with a higher BMI, and a higher rate of fatty liver association; the concentrations of TC and LDL in the lipid metabolism were significantly higher than those in Han patients. The rates of female patients and fatty liver were also higher. The incidence of hypertension was lower than that in Han patients. There was no difference in TG or HDL between the Uighur group and the Han group (Table 4).

### Logistic regression analysis of risk factors for gallstones in the Uighur and Han populations

The presence of gallstones or not was set as the dependent variable, age and BMI were set as the continuous variables, while the other variables such as ethnic group, gender, TG, TC, LDL, HDL, hypertension, diabetes and fatty liver were set as the categorical variables. The significant variables obtained in Tables 1-3 were set as the independent variables and put into the logistic regression model. This revealed that, in the general population, nationality, TG, BMI and age were the risk factors for gallstones. The odds ratios (ORs) were 2.09, 1.36, 1.07 and 1.06, respectively. In other words, under the premise that the other factors were constant, the gallstone prevalence in the Uighur population was 2.09-fold higher than that in the Han population. The prevalence of gallstones in hypertriglyceridaemia patients was 1.36-fold higher than that in the normal group. In terms of BMI, each additional 1 kg/m<sup>2</sup> increased the risk of developing gallstones by 1.07-fold. Each additional year of age increased the risk of developing gallstones by 1.06-fold (Table 5).

The significant independent variables in the single factor analysis in Tables 1-3 were also put into a logistic regression model, and the results suggested that gender,

**Table 3 Analysis of general data in gallstone group and controls based on different ethnic groups**

		Age	BMI	Fatty liver	Debates	Hypertension	TG	TC	LDL	HDL
Sum (9455)	GST (1240)	54.65 ± 12.98	26.41 ± 3.64	46.13%	7.74%	33.55%	2.02 ± 1.35	4.89 ± 0.90	2.79 ± 0.76	1.28 ± 0.31
	Control group (8215)	44.21 ± 12.57	24.77 ± 3.62	34.16%	3.70%	24.25%	1.79 ± 1.52	4.84 ± 1.02	2.81 ± 1.57	1.34 ± 0.41
	$\chi^2$ or <i>t</i>	27.14	14.87	67.25	43.43	49.09	5.05	1.70	0.53	4.50
	<i>P</i>	0.00	0.00	0.00	0.00	0.00	0.00	0.09	0.59	0.00
Han (8213)	GST (956)	55.07 ± 13.65	26.00 ± 3.53	44.35%	8.37%	35.15%	2.03 ± 1.21	4.84 ± 0.86	2.72 ± 0.75	1.29 ± 0.33
	Control group (7257)	44.21 ± 12.69	24.60 ± 3.42	33.82%	3.47%	24.75%	1.80 ± 1.53	4.84 ± 1.00	2.80 ± 1.64	1.34 ± 0.42
	$\chi^2$ or <i>t</i>	23.31	11.84	41.19	52.20	47.52	4.53	0.03	1.49	3.99
	<i>P</i>	0.00	0.00	0.00	0.00	0.00	0.00	0.97	0.14	0.00
Uighur (1242)	GST (284)	53.23 ± 10.29	27.80 ± 3.68	47.89%	5.63%	28.17%	2.00 ± 1.76	5.05 ± 1.00	3.01 ± 0.77	1.26 ± 0.24
	Control group (958)	44.18 ± 11.67	26.09 ± 4.62	36.74%	5.43%	20.46%	1.77 ± 1.42	4.86 ± 1.09	2.89 ± 0.88	1.29 ± 0.37
	$\chi^2$ or <i>t</i>	12.60	6.49	11.41	0.02	7.53	2.29	2.70	1.30	2.40
	<i>P</i>	0.00	0.00	0.00	0.89	0.01	0.02	0.01	0.20	0.03

BMI: Body-mass index; TG: Triglycerides; TC: Total cholesterol; LDL: Low-density lipoprotein; HDL: High-density lipoprotein; GST: Gallstone.

**Table 4 Analysis of general data in Han and Uyгур patients with gallstones**

Item	Uighur (n = 284)	Han (n = 956)	$\chi^2$ or <i>t</i>	<i>P</i> value
Age	55.07 ± 13.65	53.23 ± 10.29	7.47	0.00
BMI	27.80 ± 3.68	26.00 ± 3.53	2.44	0.02
TG	2.00 ± 1.76	2.03 ± 1.21	0.30	0.76
TC	5.05 ± 1.00	4.84 ± 0.86	3.49	0.00
LDL	3.01 ± 0.77	2.72 ± 0.75	5.75	0.00
HDL	1.26 ± 0.24	1.29 ± 0.33	1.34	0.18
Fatty liver	52.11%	44.35%	5.31	0.02
Diabetes	5.63%	8.37%	2.92	0.13
Hypertension	28.17%	35.15%	4.78	0.03
Female/male	43.66%	36.40%	4.90	0.03

BMI: Body-mass index; TG: Triglycerides; TC: Total cholesterol; LDL: Low-density lipoprotein; HDL: High-density lipoprotein.

fatty liver, TC and age were risk factors in the Uighur group, while HDL, TG, BMI and age were risk factors in the Han group (Table 6).

## DISCUSSION

Seventy-five percent of gallstone cases are asymptomatic, whereas in the other 25% the symptoms seriously affect quality of life due to biliary pain, acute cholecystitis and acute cholangitis caused by gallstones. The prevalence of gallstones differs by region and ethnicity, at 5.9%-21.9% in Western countries, 5.9%-21.9% in Asian countries<sup>[7]</sup>, about 70% in north American Indians<sup>[8]</sup>, and less than 5% in Africans<sup>[7]</sup>. In China, the prevalence of gallstones is out of date and inaccurate<sup>[5]</sup>. Epidemiological surveys showed that the prevalence of gallstones varied from 4.2% to 12.1% in different regions of China<sup>[9-12]</sup>. The differences in prevalence may be due to the inclusion of different standards (including cholecystectomy for gallstones or not) and regional factors. Overall, the domestic gallstone prevalence was reported to be close to that of Japan and Taiwan<sup>[13,14]</sup>. Xinjiang is located in northwest of China. The economy in Xinjiang is underdeveloped,

**Table 5 Non-conditional logistic regression analysis for gallstones**

Variable	$\beta$	SE	<i>P</i> value	OR	95%CI
Ethnicity	0.74	0.08	0.00	2.09	1.77-2.46
TG	0.31	0.07	0.00	1.36	1.19-1.55
BMI	0.07	0.00	0.00	1.07	1.06-1.09
Age	0.06	0.00	0.00	1.06	1.06-1.07

BMI: Body-mass index; TG: Triglycerides.

but the prevalence of gallstone disease, which is believed to be more common in middle-to-high income classes, is higher (11.1%-15.5%) in Xinjiang than in other regions of China. Meanwhile, the prevalence of gallstones is significantly higher in Uighur people than in the Han population<sup>[5,6,15]</sup>, which are the main two ethnic groups living in Xinjiang. Our results also revealed that the prevalence of gallstones in the Uighur population is significantly higher than that in the Han population, not only in different age groups but also in different gender groups.

First, these differences may be attributed to the different dietary habits and living habits of these two groups. The food habits of the Uighur people are more westernized: high fat, high sugar, high proteins such as honey, cheese, raisins, dried apricots, milky tea, walnuts and other products, and low consumption of vegetables, fish and seafood. Second, the different gallstone types contributed to the difference in prevalence. According to the clinical data, cholesterol stones were the main type of gallstones and most were found inside the gallbladder in the Uighur group, while pigment stones were the most common type in the Han group and were often found inside the intrahepatic bile duct<sup>[16]</sup>. Third, different pathogenic conditions may be involved: metabolic factors are the main cause of cholesterol stones, while bile pigment stones are mainly associated with bacterial and parasitic infections of the biliary tract, bile duct stricture, cholestasis and other factors<sup>[15,14,17,18]</sup>. Lastly, ethnicity itself could be a contributing factor. This should be confirmed by genetic studies or epidemiological investigations of a larger



**Table 6** Non-conditional logistic regression analysis in different ethnic groups

	Variable	$\beta$	SE	P value	OR	95%CI
Uighur	Gender	0.80	0.15	0.00	2.21	1.64-2.99
	Fatty liver	0.48	0.15	0.00	1.62	1.21-2.17
	TC	0.31	0.15	0.04	1.37	1.02-1.83
	Age	0.07	0.01	0.00	1.07	1.06-1.09
Han	HDL	0.29	0.09	0.00	1.34	1.12-1.59
	TG	0.28	0.08	0.00	1.33	1.15-1.54
	BMI	0.08	0.01	0.00	1.09	1.06-1.11
	Age	0.06	0.00	0.00	1.06	1.06-1.07

BMI: Body-mass index; TG: Triglycerides; TC: Total cholesterol; HDL: High-density lipoprotein.

sample.

In addition to the ethnicity, the other risk factors are not all the same between the Uighur and Han groups. Age was a risk factor in both groups. The relationship between age and gallstones has been demonstrated among different ethnic groups<sup>[14,19]</sup>. As age increased, the risk of gallstones in the Uighur and Han groups increased, with ORs of 1.07 and 1.06, respectively. Furthermore, when using 50 years old as a cut-off, the risk of gallstones in the over-50s was 3.02-3.11-fold higher than that in those under 50 years old, which was consistent with studies by Shaffer<sup>[20]</sup> and Liu *et al.*<sup>[21]</sup>. Shaffer reported that the prevalence of gallstones in the over 40s was 4-10 times higher than that in those under 40 years old. Liu *et al.*'s findings confirmed that age was a risk factor for gallstones: the older the age, the greater the risk of developing gallstones. Possible reasons could be that: (1) as age increased, the incidence of metabolic syndrome increased, and metabolic syndrome is closely related to the occurrence of gallstones<sup>[11]</sup>; (2) a long-term sedentary lifestyle, as well as older people's long-term exposure to risk factors, might lead to a higher prevalence of gallstones<sup>[22,23]</sup>; and (3) gallstones are a chronic disease, and thus their prevalence would increase with increasing age<sup>[24]</sup>.

The relationship between gender and gallstones remains controversial<sup>[8,14,25,26]</sup>. Gender was a risk factor in the Uighur group but not the Han group. The difference in gallstone types between the two groups was one possible cause of this phenomenon. Gender was more closely associated with cholesterol stones. A number of Western studies (in which cholesterol stones were the main stone type) confirmed that women were more susceptible to gallstones due to oestrogen as an obvious risk factor<sup>[27]</sup>, with the ratio of male to female cases being 1:2 to 1:3<sup>[20,21,28,29]</sup>. Studies from Taiwan<sup>[26]</sup> and Sichuang<sup>[11]</sup> also confirmed this conclusion. However, most studies among Asian patients (bile stones as the main stone type) have failed to identify a gender-related difference<sup>[9,24]</sup>.

The effects of gender on the occurrence of gallstones also interacted with age. Among those  $\leq 50$  years old, the prevalence of gallstones in men was higher than that in women, while in those  $> 50$  years old, gallstones were more common in women than in men<sup>[21]</sup>. Our findings in the Uighur and Han population  $> 50$  years old were more

consistent with the findings of this study, but among the population  $\leq 50$  years old, the prevalence in females was equal to or a little less than that in males. Within any age range, the prevalence of gallstones was higher in Uighur women than in Han women. Some studies found that the impact of gender on gallstones was limited by age<sup>[9,30]</sup>, while other studies demonstrated that postmenopausal women exhibited a higher prevalence of gallstones. Before the menopause, the prevalence of gallstones in women was higher than that in men<sup>[18,21]</sup>, suggesting that the menopause is a risk factor for gallstones<sup>[18]</sup>. Our study confirmed that the impact of gender on gallstones depends on ethnicity and age. Menopause might be a cause of gallstones in women  $> 50$  years old and oestrogen levels may influence the occurrence of gallstones in women  $\leq 50$  years old. Uighur women may suffer from a higher gallstone prevalence than Han women due to multiple pregnancies, their younger child-bearing age and earlier age at menarche.

Obesity is closely associated with the incidence of gallstones, which may occur in up to 25% of the severely obese<sup>[31]</sup>. The relationship between obesity and gallstones is not associated with age<sup>[32,33]</sup>, but might be associated with gender. Different levels of obesity exhibit different degrees of risk for gallstones. The risks of gallstones in overweight, moderate obesity and severe obesity were 1.46, 1.83 and 3.10 times higher than in normal weight or underweight, respectively, and the risk in women was 2.73, 5.75 and 7.71 times higher, respectively<sup>[34]</sup>. The impact of obesity is higher in women than in men, and the risk in women with a BMI  $\geq 32$  kg/m<sup>2</sup> was 6.0 times that in normal/underweight women<sup>[25]</sup>. Our study also found that obesity was a risk factor for gallstones and had the most impact on female patients in both ethnic groups. Setting BMI  $\geq 25$  kg/m<sup>2</sup> as the cut-off to distinguish the obese group and the normal group, the risk of gallstones in the obese males and females was 1.43 and 4.07 times higher, respectively, in the Uighur population and 1.63 and 2.56 times higher in the Han population (results not shown). However, when BMI was set as a continuous variable and put into the logistic regression, it was not an independent risk factor in the Uighur group. Reasons for this may be as follows: (1) the Uighur population had a higher obesity rate. Liu *et al.*<sup>[35]</sup> and Zhou *et al.*<sup>[36]</sup> conducted an epidemiological survey of overweight and obese adult Han, Uighur and Kazak people in Xinjiang. The results revealed that the prevalence of obesity was higher in men than in women, and higher in the Uighur population than in the Han population; and (2) the confounding effect of obesity on different genders and the effect of gender itself on gallstones precluded the inclusion of obesity in the regression model. The possible mechanism of obesity in the formation of gallstones might be associated with the activities of the rate-limiting enzyme of cholesterol synthesis (liver enzymes, HMG-CoA), which increase the synthesis of hepatic cholesterol, and promote cholesterol supersaturation and secretion into the bile duct, while inhibiting peristalsis of the bile duct, thus contributing to

gallstone formation<sup>[37]</sup>.

Lipid dysbolism is the chemical basis of gallstone occurrence. A number of clinical cases and comparative control studies confirmed that gallstones are normally accompanied by lipid dysbolism, and the prevalence of gallstones in patients with hyperlipidemia increased. Our study also confirmed that, compared with non-gallstone patients, gallstone patients had higher levels of triglycerides ( $2.02 \pm 1.35$  vs  $1.80 \pm 1.53$ ) and lower levels of HDL ( $1.28 \pm 0.31$  vs  $1.34 \pm 0.41$ ), which were consistent with Shebl *et al.*<sup>[38]</sup>, Petitti *et al.*<sup>[39]</sup>, Ahlberg<sup>[40]</sup>, Banim *et al.*<sup>[41]</sup> and other studies. The trend for gallstones due to dyslipidaemia might be due to the high level of triglycerides that would lead to cholesterol supersaturation and reduced biliary power, thus contributing to gallstone formation<sup>[42]</sup>. The high level of triglycerides could also reduce the activities of phospholipid transfer protein and haptoglobin, thus affecting the lipoprotein reverse metabolic process through which LDL could be transformed into HDL<sup>[42]</sup>. In addition, high triglycerides are often associated with obesity and insulin resistance<sup>[43]</sup>, which could also promote the formation of gallstones. HDL is mainly responsible for regulating the reverse transportation of cholesterol, and it could reduce the occurrence of gallstones from the mechanism of action<sup>[10]</sup>. During circulation, reduced HDL concentrations could inhibit the reverse transportation of cholesterol, thus increasing the secretion of hepatic cholesterol, while reducing the secretion of bile salts and phospholipids<sup>[23]</sup>. Our results confirmed that a reduction in HDL might promote gallstone formation. This is consistent with a number of studies<sup>[1,28,38,42]</sup>, although other studies reported that there was no correlation between HDL and gallstones<sup>[44]</sup>. Besides the lipid dysbolism mentioned above, hypercholesterolaemia is also one of the main types in Uighur patients. Dietary habits may be the key reason for this lipid dysbolism. The serum cholesterol metabolism can be divided into the exogenous metabolism and the endogenous metabolism. The exogenous metabolism mainly involves food intake, and animal experiments have confirmed this<sup>[45]</sup>. Indeed, a high cholesterol diet is often used in animal models to induce gallstones. Following a high-cholesterol diet, the concentration of plasma cholecystokinin could be significantly reduced, resulting in dysfunction of gallbladder motility and thus promoting gallstone formation. The endogenous metabolism mainly involves the hepatic metabolism. When cholesterol levels within the blood increase, it can be transported and secreted into the bile through the liver cell membrane, increasing the concentration of bile cholesterol and resulting in an imbalance of bile cholesterol/bile acid. The cholesterol would thus crystallize and form a gallstone.

Numerous studies have confirmed that fatty liver is closely associated with gallstones. The incidence of gallstones was significantly higher in fatty liver patients than in the normal population, especially in those with non-alcoholic steatohepatitis<sup>[46,47]</sup>. An epidemiological survey of 14760 cases showed that in the Urumqi region of

Xinjiang<sup>[48]</sup>, 17.33% of fatty liver patients had gallstones, compared with 9.21% of the non-fatty liver group. Our results showed a similar pattern (16.93% vs 10.99%), and the difference was much more obvious in the Uighur population (14.73% vs 9.97% in the Han population, 29.65% vs 18.33% in the Uighur population, respectively) and in women (26.52% vs 10.20% in women, 14.39% vs 11.66% in men, respectively). These data are not presented in the Results section. The detection rate of fatty liver was higher in women<sup>[49,50]</sup>. The common risk factors for fatty liver and gallstones are age, obesity, metabolic syndrome, insulin resistance and hyperlipidaemia<sup>[28,51]</sup>. The main pathological process of fatty liver involves the infiltration and accumulation of a large number of fat cells inside the liver cells, resulting in liver ischaemia, degeneration, necrosis and cirrhosis. Liver function is thus damaged, leading to a reduction in the synthesis of bile acids and phospholipids in the liver, and in turn, a deficiency of cholinergic and non-saturated fatty acids. At the same time, the fatty liver combined with dyslipidaemia would promote the supersaturation of cholesterol in the bile, and these three factors would work together to accelerate the formation of gallstones<sup>[47,52,53]</sup>.

This single-centre study confirmed that, among the overall population, the prevalence of gallstones was 13.11%, with the Uygur population having a higher prevalence than the Han. The risk factors differed between the Uighur and Han populations. After eliminating the only common factor (age), the risk factors in the Han population included BMI, TG and HDL, while those in the Uighur population included TC, gender and fatty liver. A further comparative analysis of general characteristics of the Han and Uighur populations revealed that the Uighur patients were older than the Han, with higher levels of BMI, more women and fatty liver, a higher LDL rate and a higher TC rate, while the incidence of hypertension was lower than in the Han population.

## COMMENTS

### Background

Xinjiang is a multi-ethnic area and is one of the high-risk areas for gallstones in China. However, there have been few studies about the prevalence of gallstone disease, especially in the Uighur group.

### Research frontiers

The authors designed a cross-sectional study with a large sample of Han and Uighur subjects to evaluate the prevalence of and risk factors for gallstones, and to compare and analyze shared and exclusive risk factors between the two ethnic groups. They concluded that the prevalence of gallstones was higher in the Uighur population than in the Han population; that gender, total cholesterol, fatty liver and age are the risk factors for Uighur patients; and that triglycerides, high density lipoprotein cholesterol, obesity and age are the risk factors for Han patients.

### Innovations and breakthroughs

This study confirmed that age and hyperlipidaemia are positive risk factors for gallstone disease, but that the types of hyperlipidaemia differ between the Uighur (hypercholesterolemia) and Han patients (elevated triglycerides and reduced high-density lipoprotein). Gender is a risk factor for Uighur but not Han patients, and the effects of gender on gallstones interacted with age, and could combine to affect the occurrence of gallstones. Obesity is a risk factor for gallstones and has a greater impact in women in both ethnic groups. The study

complemented the background prevalence of gallstone disease in Xinjiang, China, especially in the Uighur population.

### Applications

The results of this paper could guide clinicians to target high-risk groups for related inspection and early treatment. Furthermore, preventive strategies could be identified and planned according to these results.

### Peer review

This paper provides information about the prevalence of and risk factors for gallstone disease in Xinjiang. The results of this study provide a basis for further research to explore the genetic molecular mechanisms of gallstones in the two ethnic groups. The presentation of results is logical and the discussion is comprehensive.

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