The prevalence and associated factors of simple hepatic cysts in Shanghai: a population-based cross-sectional study

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To the Editor: Simple hepatic cyst is a common reason for consultation with gastroenterologists and hepatologists. Although most patients have a benign course, some suffer from serious complications, such as intracystic infection, hemorrhage, and even rupture, or symptoms caused by severe oppression of the surrounding tissues and organs. Understanding the prevalence of, and characteristics of, and factors associated with simple hepatic cysts is helpful for better treatment of symptomatic patients. The reported prevalence of the disease varies widely, ranging from 2.5% to 18.0%, and most of them were based on hospital surveys.[1-4] As an asymptomatic disease in most cases, simple hepatic cysts are usually discovered incidentally on abdominal imaging. Therefore, surveys based on hospital populations cannot represent true prevalence. Furthermore, due to the absence of healthy controls, surveys with hospital populations have been unable to identify associated factors for simple hepatic cysts.[1-4]

The present population-based, cross-sectional survey was performed with inhabitants from 18 districts and 242 community health service centers in Shanghai, which is a highly socioeconomically developed city located in eastern China. The inclusion criteria consisted of subjects without serious chronic diseases who lived in the selected community for more than 6 months and who were aged between 16 and 65 years. The exclusion criteria included the following: pregnancy, fracture, severe mental disorder or dementia, reduced mobility, hepatitis B and C, tuberculosis, human immunodeficiency virus infection, or other infectious diseases. Finally, a total of 4120 adults were enrolled in the survey. The study was reviewed and approved by the Shanghai Changzheng Hospital Institutional Ethics Committee (No. 2016SL018) in accordance with the *Declaration of Helsinki*. Written informed consent was obtained from all participants. The included subjects were privately interviewed by well-trained medical staff equipped with a uniform and complete questionnaire. Anthropometric measurement data were obtained, and blood samples were collected at each community health service center. At the same visit, the abdomens were scanned by clinicians experienced in ultrasound who were blinded to the clinical findings.

Among 4120 adults enrolled in the survey, 40 were excluded because of missing or incomplete sonographic data, and 15 with ages elder than 65 years were also excluded. Finally, 4065 subjects were included in the study [Supplementary Figure 1, http://links.lww.com/CM9/A452]. The basic demographic, clinical, and biochemical characteristics of the study population are shown in Supplementary Table 1, http://links.lww.com/CM9/A452. Among the participants, 312 (7.68%) patients with a mean age of 50.52 ± 9.58 years were diagnosed with simple hepatic cysts. Among them, 148 (47.44%) were males and 164 (52.56%) were females. For males, the prevalence was 8.34%, while for females, it was 7.16% [Supplementary Table 2, http://links.lww.com/CM9/A452]. The prevalence increased linearly with age for total, male and female subjects (Cochran-Armitage test for trend, all $P < 0.0001$) [Supplementary Table 2, http://links.lww.com/CM9/A452]. Moreover, 228 (73.08%) patients were diagnosed with single cysts, and 84 (26.92%) were diagnosed with multiple cysts [Supplementary Table 3, http://links.lww.com/CM9/A452]. The most common site was the right anterior segment (30.68%) [Supplementary Table 3, http://links.lww.com/CM9/A452]. We compared the demographic and clinical characteristics between subjects with

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Table 1: Univariate and multivariate logistic analysis of the associated factors for hepatic cysts.

	Univariate analysis			Multivariate analysis		
Variables	**OR**	**95% CI**	***P***	**OR**	**95% CI**	***P***
Age	5.734	4.209–7.812	<0.0001	5.135	3.515–7.504	<0.0001
Hypertension	2.564	1.945–3.381	<0.0001	1.323	0.978–1.790	0.069
Smoking	1.589	1.228–2.056	<0.0001	1.206	0.873–1.667	0.256
Long-term medication	1.708	1.206–2.417	0.003	0.884	0.590–1.324	0.549
BMI	1.450	1.147–1.183	0.002	1.150	0.851–1.555	0.363
Gallstones	1.435	0.970–2.123	0.070	1.159	0.735–1.826	0.525
Sex	0.846	0.671–1.067	0.157	–	–	–
Diabetes mellitus	1.320	0.719–2.423	0.371	–	–	–
Hyperlipidemia	1.337	0.820–2.180	0.244	–	–	–
NAFLD	1.215	0.957–1.544	0.110	–	–	–
Schistosomiasis	1.515	0.454–5.059	0.500	–	–	–
Radioactive exposure	0.987	0.763–1.277	0.922	–	–	–
Chemical exposure	0.902	0.662–1.229	0.514	–	–	–
Health supplements	1.104	0.851–1.432	0.455	–	–	–
Alcoholism	1.239	0.948–1.619	0.117	–	–	–

Age and BMI are grouped using medians as cut-off values. BMI: Body mass index; –: not available. NAFLD: Non-alcoholic fatty liver disease; OR: Odds ratio; CI: Confidence interval.

hepatic cysts and subjects without hepatic cysts. As shown in Supplementary Table 4, http://links.lww.com/CM9/A452, the mean age of patients with hepatic cysts was significantly greater than that of subjects without hepatic cysts (50.52 *vs.* 41.41 years, $P < 0.0001$). The mean body mass index (BMI) of hepatic cyst patients was also significantly higher than that of subjects without hepatic cysts (24.41 *vs.* 23.89, $P = 0.003$). Surprisingly, the levels of sex hormones, including follicle-stimulating hormone (FSH) and luteinizing hormone (LH), were significantly higher in patients with hepatic cysts than in subjects without hepatic cysts. Because FSH and LH levels vary greatly between males and females, as well as between females of reproductive age and menopausal females, we further analyzed the values of FSH and LH for patients with hepatic cysts and subjects without hepatic cysts in four sub-groups: males younger than 45 years, males older than 45 years, females younger than 45 years, and females older than 45 years. As shown in Supplementary Table 5, http://links.lww.com/CM9/A452, the significantly higher values of FSH and LH in patients with simple hepatic cysts than in subjects without hepatic cysts were observed exclusively in females younger than 45 years who were of reproductive age.

To determine the associated factors for hepatic cysts, a univariate logistic regression analysis was performed on several variables, including demographic characteristics (age and sex), comorbidities (obesity as assessed by BMI, hypertension, diabetes mellitus, gallstones, hyperlipidemia, non-alcoholic fatty liver disease, and schistosomiasis), lifestyle factors (smoking status and alcohol use), toxic exposure (radioactive exposure and chemical exposure), and medication history (long-term medication history and health supplement administration). As shown in Table 1, age, hypertension, smoking, long-term medication, and BMI were variables with significant differences when comparing patients with and without hepatic cysts. In multivariate analysis, only age (odds ratio = 5.135; 95% confidence interval: 3.515–7.504; $P < 0.0001$) was an independent associated factor. We then divided subjects into four sub-groups according to age and sex. In male subjects younger than 45 years, increasing age and complications of gallstones were two independent associated factors [Supplementary Table 6, http://links.lww.com/CM9/A452], while in male subjects older than 45 years, increasing age was not a significant associated factor [Supplementary Table 7, http://links.lww.com/CM9/A452]. In female patients younger than 45 years, receiver operating characteristic curve analyses were first performed to determine the optimal cut-off values of FSH and LH for stratifying subjects with or without hepatic cysts [Supplementary Figure 2, http://links.lww.com/CM9/A452]. Multivariate logistic analysis identified increasing age and FSH values as two independent associated factors [Supplementary Table 8, http://links.lww.com/CM9/A452], while in female subjects older than 45 years, we also failed to find any factor significantly associated with hepatic cysts [Supplementary Table 9, http://links.lww.com/CM9/A452].

In conclusion, new insight has been obtained in terms of prevalence of, and factors associated with, simple hepatic cysts. We confirmed that age is an important factor associated with simple hepatic cysts and provided clues about the undisclosed roles played by reproductive hormones and gallstones in hepatic cysts. These observations provide novel directions for future research on simple hepatic cysts, which may help to better manage the severity of this disease.

Conflicts of interest

None.

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