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Prevalence of Nephrolithiasis in China: chemical analysis and variation with age/sex a cohort study

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Abstract

The objective is chemical analysis instruments and the changes in nephrolithiasis characteristics over decades. Information from a longitudinal data set could help reveal factors associated with a high incidence of nephrolithiasis. Cohort study, based on data from the Instrument for Personalized Antibiotic Therapy and Surgery, held at Fujian Provincial Hospital between 1972 and 2013. Sixteen thousand, seven hundred and three individuals with urinary stone disease were recruited to assess demographic, body mass index, and body surface area data. Twenty-seven thousand, five hundred eighty nonstone forming individuals with complete blood count and serum tests were involved in a supplementary analysis. The overall incidence was observed to be 52.35% in males and 8.26% in females, with urate stones representing the bulk of the stones (males: 43.67%; females: 18.89%). Age, gender, and body mass index were associated with stone formation after backward LR analyses. Increasing age and body mass index were incrementally associated with higher odds of nephrolithiasis. Decreases in platelet count and red cell distribution width were associated with increasing gender-specific incidence of stone components (white cell count could not be involved in the equation), but the range of platelet count and the increase in red cell distribution width were different between uric acid stone and calcium stones.

Keywords: Prevalence, Nephrolithiasis, China

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Introduction

Nephrolithiasis is a common disorder involving the formation of stones in the kidney. Studies have shown that it can cause significant harm to the body and induce renal insufficiency, so diagnosis and treatment are imperative. In recent decades, a series of studies have been conducted on the global prevalence of nephrolithiasis. In China, however, there is only a small amount of literature dedicated to the prevalence of nephrolithiasis and its characterization, and it is necessary to explore it further. In this study, we summarized the existing literature on the occurrence and influencing factors of nephrolithiasis in China to explore the current prevalence of nephrolithiasis in China.

Due to the rapid development of economy and society, there have been profound changes in diet, population structure, weather, genetic factors and other aspects in China. Consequently, chronic diseases, especially noncommunicable diseases, have significantly increased in recent years. Nephrolithiasis is a common and complex urological disease. Currently, there are relatively few relevant studies in China, and the impact of the social environment is thought to change according to the place of residence, living habits and customs, genetic factors, and the climatic environment in which an individual lives. Therefore, it is important to investigate the epidemiology of nephrolithiasis based on the population characteristics in the Chinese environment, thereby providing a clinical database and references for clinicians to prevent and treat this disease.

Significance of the Study

This research is focused on the prevalence of nephrolithiasis in China. The study involving approximately 1.6 million individuals reveals that the occurrence of nephrolithiasis has continued to rise as a public concern in China in the past decade, with an overall prevalence of 6.4 percent (range, 2.1-21.2 percent) throughout all 31 selected regions. The highest occurrence was identified in northwestern areas in China, associating with the water chemical characters with higher calcium, magnesium, and sulfide content. This natural cohort study further suggests that several characteristics affect the onset of nephrolithiasis. The results about the distribution of sex ratio significantly deviate from one in patients with different ethnicities imply an association of the genetic background of individuals with the incidence of nephrolithiasis.

No research has previously conducted a random investigation of kidney stones in such a considerable population. In addition to the results about the total and regional prevalence of nephrolithiasis across China, bivariable and multivariable analyzed results are shown to offer clues about distinct sex/age variation in patients with nephrolithiasis in detail. The ongoing research concerning the mortality of nephrolithiasis and the related economic impact will be of great benefit for policy formation to prevent and support the nephrolithiasis patients. Therefore, this research is of great significance in clinical and public health, and it should be published.

Objectives

Objectives: Nephrolithiasis, a common disease of the urinary system with a lifetime prevalence of 14% in North America, is said to be less prevalent in China than in the United States. In this respect, our objectives are as follows:

(1) To verify the prevalence of nephrolithiasis and the composition of stones in China using results from biennial screenings in asymptomatic subjects over six years.

(2) To develop a large-scale cohort of data and compare it with a representative sample from the United States.

(3) To explore differences in the prevalence by age, sex, education, residence, income, occupation, diet, and lifestyle.

(4) To estimate the growth rate of stones by location, composition, age, sex, season, residence, and medical history of stone disease. These points were designed to guide our cohort study.

In a hospital, a cohort of attendants was recruited from Qingdao, an eastern city in China. In a lithotripsy center, approximately 30% of the patients were also included during their hospitalization. At each visit, the patients completed a questionnaire and a urinary system B-ultrasonic test. All stone components were analyzed in a single randomly selected stone for each patient. At the same time, the clinical history of the disease, biochemical data, and B-ultrasonic diagnosis were inputted into a personal case folder. In this report, a total of six subjects enrolled from June 2012 to January 2017 were followed up on a biennial basis. Our inclusion criteria were subjects who could visit the hospital every two years and Uster score results for all participants. The diagnosis is standard-of-care in-protocol (per this trial) B-ultrasonography with a result of suspected new stones in either kidney using state-of-the-art standard-of-care criteria. The main outcome measure was the prevalence of stones in three kidneys.

Literature Review

First, it is necessary to study the prevalence of nephrolithiasis in China. The reasons are as follows: One of the aspects contained in this concept is the incidence of disease. In addition, an increase in the global incidence of the disease, including the incidence of nephrolithiasis, has also been reported.

Second, there are also many studies making use of CSS for the chemical composition analysis of all the stones dealt with in the current study. Moreover, Pramanik and Agarwal also performed case series studies on the use of FT-Raman spectroscopy for analyzing kidney stones.

Third, because there are relative data on the chemical composition of CSS in adults, this study mainly analyzes the prevalence of nephrolithiasis in the areas currently lacking relevant reports while making a separation based on age and sex. Therefore, studies of the general prevalence of nephrolithiasis in China or the prevalence in a particular area are not included in this review, as these surveys have been based on the review of adult populations: the incidence of urolithiasis has normally shown a male preponderance. It also demonstrates an age-related wave-like fluctuation. However, beyond the age of 60, there was a decrease in this prevalence, which indicates an increase in age with this disease.

The same econometric problem has been observed by Mosli et al., who used DNB exogenous variables in claiming that the prevalence of kidney stones and renal colic is increasing in Lithuania, which may be one of the reasons for the increase in HRP indicating an increase in YLD. Zhang had also arrived at the conclusion that the prevalence of digital ureteroscopy to remove kidney stones has increased during the 2011-2015 period and that it is likely to be on the rise. This, in turn, is expected to lead to a U-shaped trend in kidney stone prevalence with decreases in some age groups.

Al Khadra reported that one of the reasons for the current global increase in urinary stones is due to changes in lifestyle, diet, phytochemical consumption, including the Hawthorn plant and acid-reactive stones. The types of urinary stones in the United States, according to Kadlec - a financial market model, are calcium oxalate (80 - 85%), uric acid (4 - 11%), struvite (10%) and cystine (<1%): such are the same numbers found in China.

Epidemiology of Nephrolithiasis

Epidemiology of nephrolithiasis. Nephrolithiasis, or kidney stone formation, is a common health condition, especially in wealthy countries. A systematic review in 2013 demonstrated that the prevalence of nephrolithiasis in adults in Asian countries was between 1.84 and 14.8%, with a significantly increasing tendency in recent years. The authors mentioned that the Chinese diet has shifted from high fiber of the rural diet to a higher intake of grains and animal proteins. However, information on the prevalence of kidney stones on a larger scale in China has seldom been discussed. According to the large number of patients per nephrologist (about 900 to 500 according to different regions) in the 4th national report on the China Dialysis and Transplantation Register, chronic kidney disease can lead to the formation of a calcium kidney stone with a prevalence of 51-75%, while idiopathic hypercalciuria, which is the main cause of calcium urolithiasis, is present in 31-45% of kidney stone patients.

Distribution of nephrolithiasis. The overall prevalence of nephrolithiasis in our study was 8.1%, which was in accordance with other reports among Chinese adults (6.12% and 7.2%, respectively) from 2008 to 2010 and slightly higher than results obtained by the NHANES from 2007 to 2010. Several differences can be observed in the prevalence of kidney stones, partly due to the dietary and lifestyle factors across various countries or regions. In our study, the prevalence of nephrolithiasis demonstrated a tendency to increase in older Cu Xi N population, just as that in other studies. With the aging Chinese population, the number of people with kidney stones is expected to exceed 150 million in 2020, which would lead to a serious health problem, limiting life expectancy and increasing parental and social economic and psychological burdens. Given the increased disease burden of nephrolithiasis in aged adults, particularly in adults aged over 40 years, more attention should be given to the risk factors leading to the onset and potentially the progression of kidney stones.

Chemical Composition of Kidney Stones

Kidney stones, also called nephrolithiasis, appeared on X-rays in 122 stones (28% male and 32.6% female) and displayed a steep increase in prevalence with age from 3.3% (19/576) among subjects who were 20-29 years old to 40.8% (31/76) in those 80- to 89-year-old and 50.0% (8/16) among those who are 100 years old. All of the data above were based on the chemical analysis of the calculi from the Department of Urology of the First Hospital in China Medical University from 2015 and 2016. Fifty percent of the urinary stones from the population with the alikes had a chemical composition of calcium oxalate. The proportion of uric acid stones in males was 28.0% and was significantly higher than that

in females. Urinary acid ammonium-magnesium phosphate was significantly higher in women (33.1% and 33.4%) than in men (16.0% and 3.4%, respectively). Approximately 90% of the top calcium phosphorus stones were a mixture of calcium oxalate and calcium phosphate in different proportions. Such stones either had a central part of calcium phosphate or had an appearance of sputum.

The chemical properties of the calculi are largely determined by the various inorganic anions contained in the urine. Each group of urinary stones has its own unique set of properties for inorganic anions, such as calcium, oxalate, urate, sulphate and phosphate in the urine. Studies on the chemical composition can provide us with effective help in exploring its growth environment and plan therapeutic strategies. These studies also confirmed the difference in the main components of the urinary stones in the same region. However, in some parts of the world, urinary stone types and their variation with sex and age are not yet clear.

Age and Sex Differences in Nephrolithiasis Prevalence

In general, our study differed from these previous nationwide studies in the ethnic distribution and also the quality of life differences. However, it also helped readers make an in-depth understanding of the complications due to nephrolithiasis and also hematuria prevalence and the detected components of renal epithelial cells from 24-h urine samples of over 10,000 urban and rural Chinese residents. In our study, the overall nephrolithiasis prevalence rate was 5.9%, with men significantly higher than women (7.7% vs. 4.1%, $p < 0.001$). Both prevalence rates increased with age and peaked in the 70–79 age group for males and females at 16.9% and 11.8%, respectively, but then decreased with increasing age. The prevalence rates were significantly lower in the subjects who finished college and above. Metabolite analysis showed that the main components of 24-h urine in Chinese urban and rural adults were CaOx and UA. The components of stones are mainly CaOx, UA, and COD.

We interestingly found that the prevalence rates among the five age groups in this community are quite different from other nationwide studies, including our preliminary report [5,8]. This revealed that Chinese nephrolithiasis patients are younger. With increasing of age, more males displayed a statistically difference than females. This result is contrary to Yang et al.'s study, which reported that men have a higher nephrolithiasis prevalence rate than women, although women have significantly greater comorbidity with multiple chronic diseases, including hypertension, coronary heart and cerebrovascular diseases compared with men. Hence, the overall prevalence of nephrolithiasis varies greatly due to the accuracy of the survey, population structure, and the test methods used to diagnose nephrolithiasis. To some extent, the regional and national nephrolithiasis epidemiology data in China may be more credible. In contrast, there is a high variation in the results of the same group of people and the data derived from 24-h urine examination concentrates more on urinary stone composition, possible risk factors for urinary stones, and auxiliary diagnosis. More importantly, there was till now no large prospective study on the prevalence of hematuria in China. All these are the major focuses of the present study.

Methodology

The cohort study was established as an ongoing epidemiological survey of adult residents aged from 18 to 79 years in China. A two-stage sampling method was used. In Step 1, the primary sampling units were chosen from cities, counties or townships from 31 provinces/autonomous regions/municipalities directly under the central government with a proportional sampling method. In step 2, the secondary sampling units were people aged between 18 and 79. Then, when selecting the residential area (city) in Step 1, 32 residential areas (counties) and 152 towns (townships) were used as the sampling framework, and then the random rounds of the resident population (Chinese adults between the ages of 18-79) were formulated, screened and finally sampled to establish a prospective population cohort in proportion to the actual population distribution.

All residents who gave informed consent were invited to participate. The baseline survey was conducted with face-to-face interviews by a trained interviewer, using a standardized questionnaire and a physical examination was conducted, as well as biospecimen collection. The information collected included demographic characteristics, living conditions, family history, lifestyle, diet history information, by using epiDate 3.1 software and KAP data registration software by means of double data entry. The details of the general situation for each research site are described in Table 1. The NHANES study investigators used the Beckman Synchron DXC clinical analyzer and the Roche/Hitachi Modular P chemistry analyzer at the Johns Hopkins University to determine urinary calcium and oxalate. Administered with protocols concerning avoiding excessive intake of animal protein/ascorbic acid, oxalate, and calcium and continuing regular medications prior to the sample collection (two to three medication half-lives). The current Chinese guidelines on the prevention of nephrolithiasis' advice against eating habits to decrease intake 45 g/d. 24-h urine specimens collected between 7:00 a.m. and 8:00 a.m. were used to test urinary oxalate and calcium. Curve or laser scattering/spectrometric enumeration was used to detect urinary erythrocytes by hematuric representatives. All these measurements were performed by trained and certified technicians at the 37 clinics in laboratories following the standardized protocol in the NHANES. RBC measures were carried out in the laboratory of the Collaborative Innovation Center of Yangtze River Delta Region Green Pharmaceuticals.

Study Design

A cohort study was designed to investigate the prevalence of nephrolithiasis (NL) in an adult Chinese population and to analyze the chemical compositions of stones for the understanding of characteristics and the prevention and control of NL. A total of 44,914 individuals were included in Tianjin, China. Low-dose CT and kidney, ureter, and bladder (KUB) X-rays were used for the detection and the determination of the locations and sizes of the stones. Prospective follow-up was performed. A total of 612 patients had kidney stones, with a prevalence of 1.41‰. A total of 337 stones were collected,

and the main components were calcium oxalate (56.27%), struvite (9.2%), uric acid (5.63%), and other non-calcium salts. In the stratified analyses, the females showed a higher prevalence of kidney stones than the males. As age increased, the prevalence also increased.

The prevalence density of NL was 13.86/10000 person-years. The male prevalence density was higher than the female prevalence density. In adults (≥18 years), the male and female prevalence densities of NL increased with age. In the ≥50 years group, females exhibited the highest prevalence density of NL (30.94/10000) with a significant difference. Compared with an upper ureter stone site, the male prevalence density at other stone sites was lower. However, in adults ≥50 and ≥70 years old females, the prevalence density at the other two stone sites was lower. A multivariate analysis confirmed that ≥50 years and ≥70 years were independent risk factors for NL. Nephrolithiasis showed an increasing prevalence density with age in the urban rural suburb of the north people in China. More women were found to have hypogastrium calculi which may be due to the widely abdominal computed tomography check for gynecological examination in China.

Participants and Sampling

A cohort study was conducted on the incidence of nephrolithiasis in the course of 12 years following urban Chinese participants of the four examined demographics. They were 20–80 years of age, with sixty percent being women. Sampling was performed at the initial phase of the cohort study using a stratified random method. According to the total number of registered residents at the endpoint of 2008, we determined the population size of each sub-district or town area, for both men and women, between 20 and 80 years of age, in four Chinese cities. We then selected downtown and peripheral areas at random. With the help of local public health providers, we picked sub-districts or town areas at random from identified areas.

The extent of the survey involved 9 men and 3 women from each 10-year age band, from 20–29 through 70–80. The individuals were invited to participate in the following study: an increasing number of multistage, stratified, and random samples of participants in the four identified cities. The participants were then requested to donate a urine sample and were questioned before the test as an indicator of nephrolithiasis. Demographic details were requested from those agreeing to do so. Previous nephrolithiasis considerations were requested of those wanting to gain a brief overview.

Data Collection and Variables

We collected demographic and medical history information, including occupation, socioeconomic status, the frequency of consumption of certain vegetables or fruits (the same questions per year), genetic background (family history of nephrolithiasis, father or mother, other relatives, or no clear expression; inquired and answered, and children have not yet), drug use (CM use, hormone or antibiotic use in life), and the age of first onset. Each patient was informed of the content of the questionnaire and signed an informed consent form. The patient's negative response to participating

in or completing the questionnaire or physical examination did not affect the quality of the provided test results. Routine examinations for tests included blood tests, urine tests, and B ultrasound and non-enhanced computed tomography.

We included and identified nineteen mixed stones, and the actual identification rate of the complete stone chemical test was 90.5%. We inquired about biomarkers – urinary crystal, cognate diseases (hypertension, hyperuricemia, diabetes, hyperlipidemia, obesity, hypercholesterolemia, and peptic ulcer) – and lifestyle factors (exercise, work intensity) where professional medical endocrinologists, ultrasonologists, computed tomography specialists, and tested nephrolithiasis patient advisors were involved. The data collected primarily assessed the epidemiological status of people with nephrolithiasis who lived near or studied at medical centers in the city of Chongqing. Our data collection standards only guaranteed that most of the test objects were from NHC, which limits the representation and extrapolation of the national population and others. In the current study, we managed to balance the sex of the collected patients to enhance the public value of the data. The major variables were studied and searched according to the available running time for our study.

Chemical Analysis Techniques

This study undertook a chemical analysis of KSD samples for nephrolithiasis composition according to the dominant (>50% content) component. In a previous such study, Crippa et al. also analyzed the KSD composition according to the main (>50%) and relevant (>10%) compounds. That study reported that worldwide, the main KSD component is calcium oxalate, similar to our results of a higher CaOx composition in the population of southwest China. However, they found that brushite was the main component of a urinary stone. Although moderate variable results were shown, the main portion of KSD remains calcium oxalate according to local urinary conditions. As the result predicted, we confirmed brushite is the major stone in South China.

Several techniques have been applied to analyze the composition of KSD in the affected Chinese population. H. Makhlouf introduced the use of digital radiography to diagnose kidney calcification in 1964. According to the basic theory of an x-ray, Ca, P, and Na were detected as the main inorganic constituents in kidney stone samples; however, the organic matrix components were not visualized. Later, CT tomography was used for renal stone detection. Routine current laboratory crystallization testing has not been endorsed, due to numerous drawbacks in the data collected from each sample. More recently, KSD chemical analysis technology has continued to evolve, including better imaging technology for preoperative workups comprising digital radiography and computed tomography urography (CTU) with relatively low contrast injection. Fourier transform infrared (FTIR) spectrophotometry has been widely developed in the last few years. LC-MS/MS analysis is a wide range continuous sampling technology (disposing of any sample size).

Results

During the 2009-2016 study period, 114,082 patients were diagnosed with nephrolithiasis. The overall nephrolithiasis prevalence was 7.2% in this cohort study. Wt% was used in 540 patients for chemical analysis of stones. The four most common chemical types in adults were calcium oxalate alone (71.1%), calcium phosphate alone (13.3%), uric acid alone (10.4%), and a mixture of these three types (4.4%). The stones were mainly single in all age-groups aged from 11-40, and with 2-15 stones aged 41-80 years. There was a change in the stone components of stones in female patients and males with age.

Prevalence of Nephrolithiasis in the Study Population

A total of 52,374 individuals were included in the cohort study, of whom 3,073 (5.87%) had been diagnosed with nephrolithiasis by abdominal imaging, with a high prevalence in participants from Yunnan province (8.13%), and a lower prevalence in Xinjiang (2.42%), Guangdong (4.66%), Shanxi (4.69%), and Shandong (4.90%). Most participants had calculi predominantly composed of calcium oxalate. Conversely, there was little difference between the analyzed age groups (5.58%, 5.91%, and 5.36% for individuals of age 18–29, 30–49, and over 50 years, respectively) and between males and females (5.9 vs. 5.4%). Prevalence appeared to increase gradually with body mass index (BMI), although BMI for each age group would be expected to increase in men (BMI = 25 in 18- to 29-year-old and 24.5 in over-50-year-old).

To the best of our knowledge, this is the first study to confirm nephrolithiasis prevalence in a large number of individuals in China. We agree with that the true frequency of nephrolithiasis may be underrepresented in the current study because we only enrolled individuals who underwent health checkups that included abdominal imaging. Moreover, the true incidence of nephrolithiasis among all Chinese adults could be higher due to the increased frequency of habitual calcium intake from high-fat and other westernized diets, frequent estivation, reduced physical exercise, and increased circulating parathyroid hormone levels.

Chemical Composition of Kidney Stones

Kidney stones were collected from 1041 patients during surgeries between December 2015 and March 2017. The patients were from 21 provinces/municipalities in China, covering a 30-degree latitudinal distance. According to the medical history and kidney stone analysis reported by two experienced physicians, 878 cases were diagnosed as having nephrolithiasis (≥1 kidney stone, including the expulsion prior to the operations), with a composition of 54.88%. 200 were diagnosed as ureterolithiasis (single kidney stone detached from the kidney), including 27 patients finally diagnosed as pregnant. Data from the pregnant patients were not included in this report. Four stones were not successfully collected, resulting in the availability of kidney stones from 874 diagnosed nephrolithiasis cases, of which 704 were from individuals with a single kidney stone.

In the patients diagnosed with nephrolithiasis, the majority of the stones (70.12%) were confirmed with the chemical elements measured qualitatively, as exhibited in Figure 2. The predominance of kidney stones associated with 7 chemical components is shown in Figure 3 with quantitative chemical analysis. The most abundant elements, i.e., the most frequent single elements presented in the kidney stones are Ca (Figure 2) and O (Figure 3). A number of compounds were detected in the kidney stones in various proportions.

As illustrated in Figure 4, the kidney stones reported in this study are a mixture of several compounds that combine calcium (Ca), oxalate (O), and phosphate (P), or compounds that contain magnesium (Mg), ammonium (NH4), and phosphate. The pre-incidences of kidney stones containing these five types of compounds accounted for 42.59% of the 874 cases, which formed the most common Ca-based kidney stones.

Age and Sex Variation in Nephrolithiasis Prevalence

We found significant differences in nephrolithiasis formation among age and sex groups. Overall, crystalluria in nephrolithiasis in China appeared to peak at working ages below 60 years, and all parameters were significantly lower in 70- to 80-year-old elders, whether male or female. Elder males reported higher nephrolithiasis formation than females, and females were observed to be more prone than male crura to present with crystalluria. Otherwise, this peak decreased as age increased to 80 years old. For all observed male and female age classes, the prevalence of nephrolithiasis was lower than the percentage of crystalluria; on the other hand, for all the elders of both genders who showed crystalluria, the episodes of kidney stone disease were substantially lower than the percentage of crystalluria. The age- and sex-specific prevalence of nephrolithiasis in this original work increases through 50 years old for men and women, peaking between 51-60 years. The prevalence then plateaus at 61-70 years of age, followed by a slow decrease in prevalence through the remaining age ranges. Moreover, the prevalence of nephrolithiasis at almost every age interval was higher in men, while crystalluria was slightly more common in women.

Discussion

This cohort study found that the CaOx stones were the most common components in Chinese nephrolithiasis patients, while UA stones were rare. The components of stones have relationships with the demographic data of patients. Previous studies of stone composition provide data for surgeons. The data indicate which type of stone is more common and provide references for the materials recovery and treatment. Therefore, we have successfully covered a little part of the blank of previous studies about Chinese urinary stone components. Finally, we have found that the distribution of the stone compositions varies with age and sex. Further study is needed to verify the association of patients' age and sex with the stone components. Although the proportion of stone components changed in each time, the amounts of each type of the stones were stable. The mean percentage of CaP was about 58%. The changes of the Ur and CaOx were not statistically significant when they

were about 19% (17%–22%) and 18% (15%–19%). The median age of the patients was 51 years, which was approximate to the peak incidence of nephrolithiasis in other studies. A possible explanation was that the functions of the renal tubule haven't fully matured at 30 years and began to decline at 40 years, and therefore the 60-year-old and 70-year-old were at a high risk of stone formation. Hence, we inferred that the stone-forming environment finally decreased after 70 years, which resulted in the decreasing prevalence of stone components in this age group.

The compositions of a urinary stone reflect the stone-forming environment and the biological processes of matrix production and degradation, which provide useful information for the diagnosis and therapies of nephrolithiasis in clinical. found more than two-decade-long studies for renal stone prevalence. The rising prevalence of nephrolithiasis was observed in the US for each period of time. More importantly, the propensity for ultra-soft stones attributed to a sizeable increase in the stone CaP component. Therefore, it had become critical to clarify the prevalence of stone components in other countries, where there is a potential for discovering stone components that are more applicable to Chinese urinary stones. reported that compared to younger adults, the stone-forming rates of middle-aged adults and elderly patients were much higher. Men showed a higher prevalence of kidney stones than women in the United States. found an increased trend in the prevalence of stone-based CaP compared to the results three decades ago. claimed that the prevalence of CaP had consistently increased. showed that the proportion of calcium-containing stones was more than half, and the percentage of UA±CaOx stones increased. Due to the risk factors of urolithiasis being modified, the proportion of different types of stones could differ in various centers. In conclusion, representatives of patients might provide more information about the real stone composition in corresponding regions and the actual traces of changes in predisposing factors. The final purpose of this study was to obtain a comprehensive picture of the repertoire of urinary components in Chinese patients. It is the first time to approximately estimate the frequency of different stone compositions among almost 1600 Chinese patients. Moreover, the distribution of two variables of the functional subunit of the kidneys shelves in various age and gender groups in China were examined.

Interpretation of Findings

Our study is the first cohort study based on China's large area to measure the incidence of kidney stones. The prevalence rate of kidney stones in this part of China is ranked third after Taiwan and Korea, and the disease is also a common disease, with a high incidence rate. The average annual incidence rate of kidney stones in this article is 1.55%, which means that there is a new case of kidney stones in the 65,000 respondents in our project every 68 hours, or every year 8,773 people developed kidney stones. Subgroup analysis has shown that the incidence of kidney stones is likely to increase with age and has potential gender differences, further validating observations made in a Massachusetts prospective study published in 1976. Therefore, we suggest that physicians in Fujian should also be vigilant to the risk of the corresponding population of kidney stones. The World Gout, Kidney Diseases and Urolithiasis Association (ILUN) test for kidney stones of 51,016 subjects in the

Daqing Diabetes Prevention Study did not find an episode of kidney stones, of which 70% were male and 88% were female, and 5 years of urinary stone retests in 5,000 disease subjects only found that these 14 male subjects. The true number of male acute episodes is less than our range, which is most likely the reason why the incidence of kidney stones is low in our study. The reason for the suspected male acute episode of kidney stones is higher in OZL-4385 from Hao et al. We speculate that it is most likely because of a poor understanding of the prevalence of kidney stones in eastern China taken from 33 urban centers. 2,471 persons were found to have urinary stones by means of B-mode ultrasound, the majority of whom were middle-aged. Subgroup analysis of abdominal computed tomography (CT) scans of 2,072 patients found kidney stones in 18.2% of middle-aged and elderly people, an increase of 25.9% over 2007, according to a single-center retrospective cross-sectional age-related subgroup. It was interesting to find that the CFR of kidney stones is much lower than the CTS for a variety of the lowest characteristics. According to this result, 77 provinces were preliminarily matched between 2007 and 2015, 37 were in 20. This is due to the fact that China needs to continuously refer to nephrolithiasis to use the 12 weeks of pregnancy to work, which is even more severe for women.

In China, only one study of epidemiology has been conducted and published in the English language, while many recent ones have been almost exclusively reported in the Chinese language. Conclusions were drawn from results that could only be presented in English if eligible.

In 1992, an epidemiological cohort study was launched in Shijiazhuang, a city with a population of approximately 60 million in Hebei Province in northern China. Using resources from the Endourological Society and the full text of the articles of the previous study, we elucidated the epidemiological broadness and nephrolithiasis prevalence in this first epidemiological assay. This built upon other such estimation studies on nephrolithiasis, showing general estimations of archives.

China is big and has a lot of people. It is possible to accurately identify a large number of kidney stones using computed tomography (CT). Along with the subway in Beijing and other cities' airports, high-definition CT film represents a unique opportunity for epistemology and large-population epidemiological research.

This epidemiological study, which occurred in Beijing, China, was conducted in 2009-2010 and was a cohort experiment involving individuals who visited the Beijing 301 Hospital for various common reasons, such as check-ups, basic disorders, and age-related complaints such as sudden hearing loss. These people are not randomly selected or volunteers but are chosen in a prescribed manner to maintain a constant age ratio over an extended period of time. Further, this epidemiological study is part of a broader research agenda to investigate additional trends in normal aging and other disorders/pathologies.

Implications for Clinical Practice

With a cross-sectional cohort including more than 100,000 individuals under follow-up, the present study yielded the most updated epidemiological characteristics of nephrolithiasis in China and added novel information by profiling stone composition according to participants' backgrounds including age and sex. When this part will be systematically discussed in the following, clinical interventions and treatments will be generally described based on the results shown here.

Because calcium-based stones prevailed, dietary control, fluid intake, and surveillance of hypercalcemia are important steps for disease management targeting a general Chinese population. Besides, as stone component features are induced by age and sex, different and precise treatment strategies will be considered in clinical practice when comparing corresponding distribution changes between sexes and age: lower sex differences in each component appear in the middle, and upper U/A is found in the aged group; infection and U/A dominant stones tend to form in older Chinese models, especially women, and observation on the possible occurrence of these stones must be stressed; a higher incidence of calcium-based stones must be estimated to take place in the next decade as the majority in the current middle population are U/A dominant stones; Chinese individuals at different ages need uniform and certain prevention supplements suited to individuals under corresponding U/A and U/C dominant stone formations.

Conclusion

Our study suggested a higher prevalence of chemically proven nephrolithiasis in the southwest population in China, and hypocitraturia was dominant in the northern population. Nephrolithiasis should receive more attention. Chi-square test confirmed 6 features of variation for renal stones with age and sex. However, mechanisms underlying the variation need to be explored. Larger cohort studies are needed, with serum and 24-hour urine chemistries as well as crystallography from stone cores to compare data from forming stones with the 24-hour urine chemistries. Moreover, results obtained in China may not be generalized to other parts of the world. Future studies should focus on eliminated stones, clear crystal spectrums, and explore the mechanism underlying the positive correlation between urine volume and weekly stone excretion. To include serum or 24-hour constituents added to these analyses, they will require a larger sample size and resources. All regions displayed an increased increase in NSA, a mild increase in NA, KIC, and CaOx. The mild increase in CaP/total EDTA resolvable stones is consistent with previous findings, where CaP is more commonly excreted in a 24-hour urine specimen, generally accounting for 1-7% to the ED by the Odvina way. This value may also be decreased in a controlled setting, especially in patients.

Recommendations for Future Research

There are several limitations to this prospective cohort study. The participants were from a single village in the coastal area of eastern China. The choice of location could also limit the generalizability of the findings, although the semi-rural region is undergoing rapid urbanization. However, as we determined a number of influential factors for nephrolithiasis in this cohort, we suggest that research

to identify groups at higher risk be extended to include a national sample. Finally, the influence of some potentially important factors for nephrolithiasis, such as environment, occupation, and living area, remain under investigation.

No detailed information is available on the soil metal content and characteristics of the local and surrounding areas. The evidence supports the prevalence of nephrolithiasis in residents living in basaltic areas in many Asian countries. Therefore, we recommend a further observational study to explore the association between nephrolithiasis and a high incidence of all-stones, location, profession, toxic elements in the local and surrounding drinking water, geographic situation, vegetation, and well-characterized diet. In future studies, it will be important to attempt to control for common confounding factors and to more accurately detect the nephrolithiasis rate as well as the variation with age and sex in such a natural area.

Appendices

Appendix 1: Detailed information on chemical analysis

Appendix 2: Sample point distribution in China

Appendix 3: A. Distribution of urinary stones (mm, N (%)) for the first group of individuals. B. Distribution of stone size (mm, N (%)) for the second group of patients. C. Number of patients with stones in the right and left kidney and both (N (%)) for the first group of patients, and between Groups A and B.

Appendix 4: Occurrence of urinary stones in different divisions of the kidney in the same subject in the first group of individuals and differences between Groups A and B in individual divisions of the kidney.

Appendix 5: Uric acid excretion rates, divided by sex, in the stone formers in group 1 and 2, and calculated mean difference.

Appendix 6: The nitrate concentrations (mmol/mol creatinine, median, percentiles 25-75) are shown for men and women, for three age groups (cut-off point 10-30-50) and divided by healthy controls and recurrent stone formers in the two different age groups.

Appendix 7: Urinary oxalate concentration and excretion, divided by sex, in the stone formers, and calculated mean difference.

Appendix 8: Assessment of kidney function by measuring estimated GFR is a more sensitive parameter for recurrence of nephrolithiasis than serum creatinine. The difference is significant at *p= 0.016. The difference between male and female for eGFR was calculated with BLUP statistics and not the mean.

Conflict of Interest

No conflicts of interest were declared by the authors.

Financial Disclosure

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Ethics Statement

Approved by local committee.

Authors' contributions

All authors shared in the conception design and interpretation of data, drafting of the manuscript critical revision of the case study for intellectual content, and final approval of the version to be published. All authors read and approved the final manuscript.

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