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Original article

Epidemiology of Urolithiasis with Sex and Working Status Stratification Based on the National Representative Cohort in Republic of Korea

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ABSTRACT

Background: This study aimed to estimate the annual prevalence and incidence of urolithiasis stratified by work status based on a large nationwide sample.
Methods: This study used data from the National Health Insurance Service-National Sample Cohort from 2002 to 2015. The prevalence and incidence of urolithiasis were estimated based on work status and gender stratification. The risk of urolithiasis among workers was calculated using age-standardized incidence ratio with stratification of work type.
Results: The prevalence of urolithiasis was significantly higher in workers than in non-workers, especially men, during the follow-up period. The total estimated number of urolithiasis cases was 41,086 and the overall incidence of urolithiasis was 0.3%. The age-standardized incidence ratio of urolithiasis was significantly higher among the total workers (1.14; 95% confidence interval, 1.13–1.16), self-employed workers (1.08; 95% confidence interval, 1.06–1.11), and paid workers (1.19; 95% confidence interval, 1.17–1.21) than among the non-working population.
Conclusions: Workers, especially paid workers and men, were vulnerable to urolithiasis. Further studies are required to investigate the effects of working conditions on urolithiasis.

1. Introduction

Urolithiasis (ULT), also known as nephrolithiasis or kidney stone disease, is a heterogeneous disorder with varying physiochemical backgrounds among patients [1]. It is the most common disease of the urinary tract [2]. Kidney stones are a major source of morbidity, accounting for >2 billion dollars spent on treatment each year [3]. ULT is associated with an increased risk of myocardial infarction [4], depression [5], elevated stress levels [6], chronic kidney disease, hypertension, diabetes [7], and end-stage renal disease [8]. The symptoms of ULT include hematuria, flank pain, renal colic, urinary tract infections, nausea, and vomiting. Thus, ULT has a negative impact on a patient's quality of life.

The known risk factors for ULT are male sex [9], hyperinsulinemia due to obesity [10], renal cystic disease [11], dietary habits [12], and certain working conditions [13]. The risk of ULT development varies among different study groups, and much of this variation is likely due to geographic, racial, and socioeconomic differences [14]. In previous studies, the overall probability of kidney stone development ranged from 1% to 5% in Asia, 5% to 9% in Europe, 13% in North America, and 20% in Saudi Arabia [15]. However, only a few epidemiological studies on ULT have been conducted in Asian populations. Although working conditions are likely to affect the prevalence and incidence of ULT [13], the impact of working status on ULT has yet to be studied across a wide range of ages and in large-scale groups.

In this study, we aimed to assess the prevalence and incidence of ULT using data from the National Health Insurance Service (NHIS) in Republic of Korea from 2002 to 2015. All Koreans are enrolled in the NHIS database. The NHIS database covers a wide range of information, including age, sex, working condition, diagnosis, and prescription. The wide age range, long observation period, large

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sample size, and geographic diversity of the Korean NHIS database make it a reliable resource for estimating the prevalence and incidence of ULT.

2. Methods

2.1. Data and study participants

The NHIS provides mandatory public health insurance for all Korean citizens, covering medical care services consistent with the policies of the National Health Insurance, Medical Aid, and Long-term Care Insurance programs. This system covers the entire population residing within the territory of Korea, and all citizens are required by law to participate. The NHIS covers approximately 98% of all Korean residents. The NHIS-National Sample Cohort (NHIS-NSC) is a population-based cohort established by the NHIS in Republic of Korea from 2002 to 2015, to provide public health researchers and policy makers with representative, useful information about citizens' utilization of health insurance and health-related services. The NHIS-NSC includes qualification data such as age, sex, region, income, insurance type, identification number, and family information, as well as medical service data such as all covered inpatient and outpatient visits, procedures, and medical diagnosis codes using the standardized protocol of the Korean Classification of Diseases and Causes of Death, 4th edition, which corresponds to the International Classification of Diseases, 10th revision (ICD-10).

For the calculation of ULT prevalence from the NHIS-NSC cohort, we selected a total of 848,900 participants after excluding 119,391 persons who were under 15 or over 65 years old in 2002. For the calculation of ULT incidence we selected a total of 823,999 participants after excluding 187,435 persons who were under 15 or over 65 years old in 2004 and 5,146 persons who were diagnosed with ULT in 2002 or 2003 for wash-out of past UTL. The person-year of current study was calculated by determining the end of the observation as the occurrence of the ULT or censoring (death or loss to follow-up). The study flow and schematic diagram of the participant selection process are shown in Fig. 1.

All data from the NHIS-NSC were collected with written informed consent from all participants by the NHIS of the Republic of Korea, and the data were anonymized. The Institute Review Board of the Gil Medical Center, Gachon University, approved this study (IRB number: GCIRB2020-070).

2.2. Definition of ULT

ULT was defined as ICD-10 codes N20 (calculus of the kidney and ureter), N21 (calculus of the lower urinary tract), or N22 (calculus of the urinary tract in diseases classified elsewhere) during the follow-up period in the medical records of participants who had visited a hospital facility.

2.3. Classification of working status

Working status was categorized according to the insurance type. The NHIS-NSC had information on five types of insurance: employee subscriber, employee dependent, district subscriber, district dependent, and medical aid. The workers were defined as employee subscribers and district subscribers. Paid workers were defined as those whose insurance type was employee subscriber, and self-employed workers were defined as those whose insurance type was district subscriber.

2.4. Statistical analysis

A chi-square test was conducted to compare differences in characteristics between the groups with and without ULT. We estimated the age-standardized incidence ratio (SIR) and 95% confidence interval (CI) of ULT according to worker type and sex, using all NHIS-NSC participants as the reference group. In this study, the SIR rates were calculated as the weighted average of age-specific incidence density rates. We stratified age in 5-year groups and set the entire study-participating NHIS-NSC population as the reference group. We used the indirect standardization method, which uses age-specific ULT incidence rates and the number of person-years in each age group of the entire study-participating NHIS-NSC population (reference group) to calculate the expected number of ULT cases after adjusting for age. The ratio of the observed to the expected number of cases was the SIR. In the analysis, if the SIR was more than 1 and the lower limit of the 95% CI was also more than 1, the risk of ULT was considered significantly higher in the subgroup of the working population than in the reference group. To estimate the prevalence of ULT, we defined the working status and ULT every year during the follow-up period. Incidence was estimated with a washout period, excluding participants who had been diagnosed with ULT between 2002 and 2003. The incidence of ULT was estimated for all medical facility visits starting after the washout period i.e., from 2004 to 2015. All analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC, USA).

3. Results

A total of 11,961,507 person-years were included in the incidence study, with 41,086 (0.3%) cases of ULT. The incidence of ULT according to the baseline characteristics of the study participants is

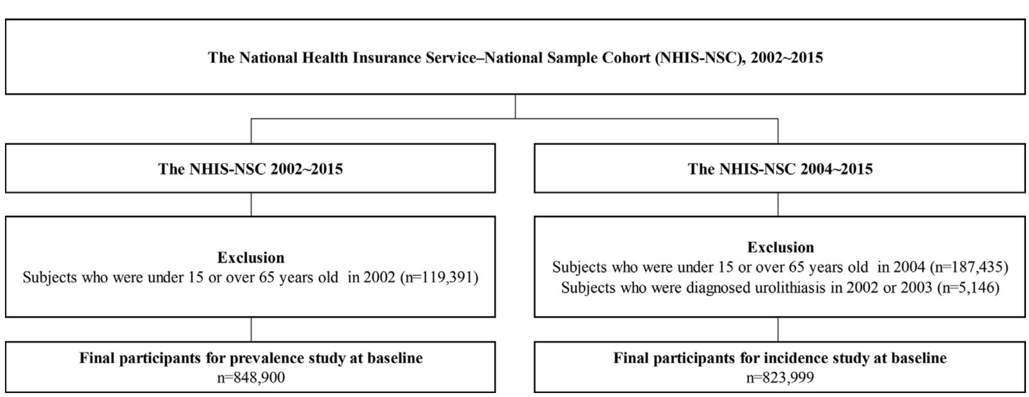

Fig. 1. Schematic diagram of participant recruitment.

Table 1
Overall incidence of urolithiasis from 2004 to 2015 according to baseline characteristics of study participants.

	Total participants, person-years	Urolithiasis, cases (%)	*p*
Total participants	11,961,507	41,086 (0.3)	
Sex			<0.0001
Men	6,062,920	25,836 (0.4)	
Women	5,898,587	15,250 (0.3)	
Age			<0.0001
15–25	4,116,767	7,073 (0.2)	
26–35	2,514,352	9,194 (0.4)	
36–45	2,458,601	11,059 (0.5)	
46–55	1,684,176	8,370 (0.5)	
56–65	1,187,611	5,390 (0.5)	
Worker			<0.0001
Yes	5,152,265	23,148 (0.5)	
No	6,809,242	17,938 (0.3)	
Type of employment			<0.0001
Self-employed worker	1,959,217	9,027 (0.5)	
Paid worker	3,193,048	14,121 (0.4)	

shown in Table 1. Among the male participants (6,062,920 person-years), there were 25,836 cases (0.4%) of ULT. Among the female participants (5,898,587 person-years), there were 15,250 cases (0.3%) of ULT. Among the age groups, the incidence of ULT was higher in the elderly. Participants aged 15–25 years had the lowest incidence rate of 0.2%, and participants aged 26–35 years had an incidence rate of 0.4%. The rest of the age groups had an incidence rate of 0.5%. Among the total participants, 5,152,265 (43%) were workers and 6,809,242 (57%) were non-workers. The incidence was 0.5% in workers and 0.3% in non-workers. The workers were either self-employed or paid workers. The incidence of ULT among self-employed workers was 0.5%, and that among paid workers was 0.4%. The incidence rates according to baseline characteristics and working status are depicted in Supplementary Table 1.

Table 2 shows the SIR and 95% CI of the ULT among workers. The SIR (95% CI) of the ULT in workers was 1.14 (1.13-1.16). Among workers, men had a higher percentage of ULT cases. The incidence rate was 0.5% in men and 0.3% in women. The SIR (95% CI) was also higher in men (1.06, [1.04–1.07]) than in women (1.01, [0.98–1.04]). In the self-employed worker group, the incidence rate was 0.5%, with an SIR of 1.08. In this group the incidence rate in men (0.5%) was higher than that in women (0.3%). However, the SIR was higher in women (1.01) than in men (0.98). In the group of paid workers, the largest gap in incidence rate between the sexes was observed: 0.5% in men and 0.2% in women. The SIR in this group was similar to the other groups: 1.12 in men and 1.02 in women, respectively.

Table 2
Age-standardized incidence ratio (SIR)* and 95% confidence interval (CI) of urolithiasis among workers.

	Urolithiasis			
	Person-years	Cases (%)	SIR (95% CI)	*p*
Total workers	5,152,265	23,148 (0.5)	1.14 (1.13–1.16)	<0.0001
Men	3,454,246	18,505 (0.5)	1.06 (1.04–1.07)	<0.0001
Women	1,698,019	4,643 (0.3)	1.01 (0.98–1.04)	0.3942
Self-employed workers	1,959,217	9,027 (0.5)	1.08 (1.06–1.11)	<0.0001
Men	1,381,231	7,181 (0.5)	0.98 (0.96–1.01)	0.1347
Women	577,986	1,846 (0.3)	1.01 (0.96–1.05)	0.7573
Paid workers	3,193,048	14,121 (0.4)	1.19 (1.17–1.21)	<0.0001
Men	2,073,015	11,324 (0.5)	1.12 (1.09–1.14)	<0.0001
Women	1,120,033	2,797 (0.2)	1.02 (0.98–1.05)	0.3972

* The SIR was estimated by the indirect standardized method, with the entire study-participating NHIS-NSC population as the reference group.

The prevalence of ULT is depicted in Fig. 2. The prevalence increased steadily among men and the gap between workers and non-workers became larger in men than in women (Fig. 2b and c). The incidence of ULT among the total population was almost 0.35% (approximately 0.45% among workers and almost 0.28% among non-workers) during the follow-up period thus indicating opposite trends among these two populations (Fig. 3). The incidence of ULT among men was similar to that of the total population (Fig. 3b). The incidence of ULT was higher in the workers than in the other groups. The difference in the incidence of ULT according to working status was not significant in the last years of the follow-up period.

4. Discussion

We conducted the current study to investigate the prevalence and incidence of ULT in the Korean population according to sex and working conditions. The estimated overall incidence of ULT in 2002 was 0.3% among 1.2 million participants, which is lower than the overall incidence (0.4%) estimated in a previous study using the 2009 Korean Health Insurance and Review and Assessment Service-National Patient Sample data [16]. Moreover, from 2002 to 2015, the annual prevalence and incidence did not increase over time. Men (0.4%) and workers (0.5%) had a higher incidence than women (0.3%) and non-workers (0.3%). The age-SIR was significantly higher among total workers (1.14; 95% CI, 1.13–1.16), self-employed workers (1.08; 95% CI, 1.06–1.11), and paid workers (1.19; 95% CI, 1.17–1.21) than in the reference group.

The incidence and prevalence of ULT were higher in men than in women. The reason was presumed to be the higher obesity and drinking rates in men than in women, resulting in more oxalic acid production in men in general. According to a 2018 study by the Ministry of Health and Welfare, the obesity rates in men and women were 44.7% and 28.3%, respectively. The level of obesity control was 80.7% in men and 91.2% in women. The drinking rate also differed according to sex. According to the same study, the monthly drinking rate was 70.5% in men and 51.2% in women. The monthly overdrinking rate (drinking more than five glasses on one occasion in women and more than seven glasses on one occasion in men, at least once a month in the recent year) was 50.8% in men and 26.9% in women.

Occupational risk factors for ULT have been well established in previous studies. In a study of Swedish battery factory workers, cumulative exposure to cadmium was found to increase the risk of kidney stone formation [17]. A similar result was obtained in a prospective 7-year study that showed that chronic exposure to cadmium increased the prevalence of calcified upper urinary tract stone disease [18]. In a study on silkscreen printers, exposure to ethylene glycol ethers was associated with a 2.4-fold increased risk of urinary stones compared to office workers [19]. Exposure to oxalic acid is also associated with urinary stone formation [20]. Occupational exposure to trimethyltin, a by-product of plastic stabilizers, was significantly associated with a high prevalence of nephrolithiasis [21].

Besides chemical exposure, chronic exposure to high temperatures and dehydration are also known to be major risk factors for ULT [22,23]. These associations were also observed in various study groups: male workers in the steel industry [13], residents of five U.S. metropolitan areas [24], sugarcane cutters in El Salvador [25], and full-time workers in the Thai Cohort Study [26].

A case report showed that kidney stone and bladder dysfunction in a chauffeur may have been associated with the strict regulation of toilet breaks by the employer [27]. Although no large-sample

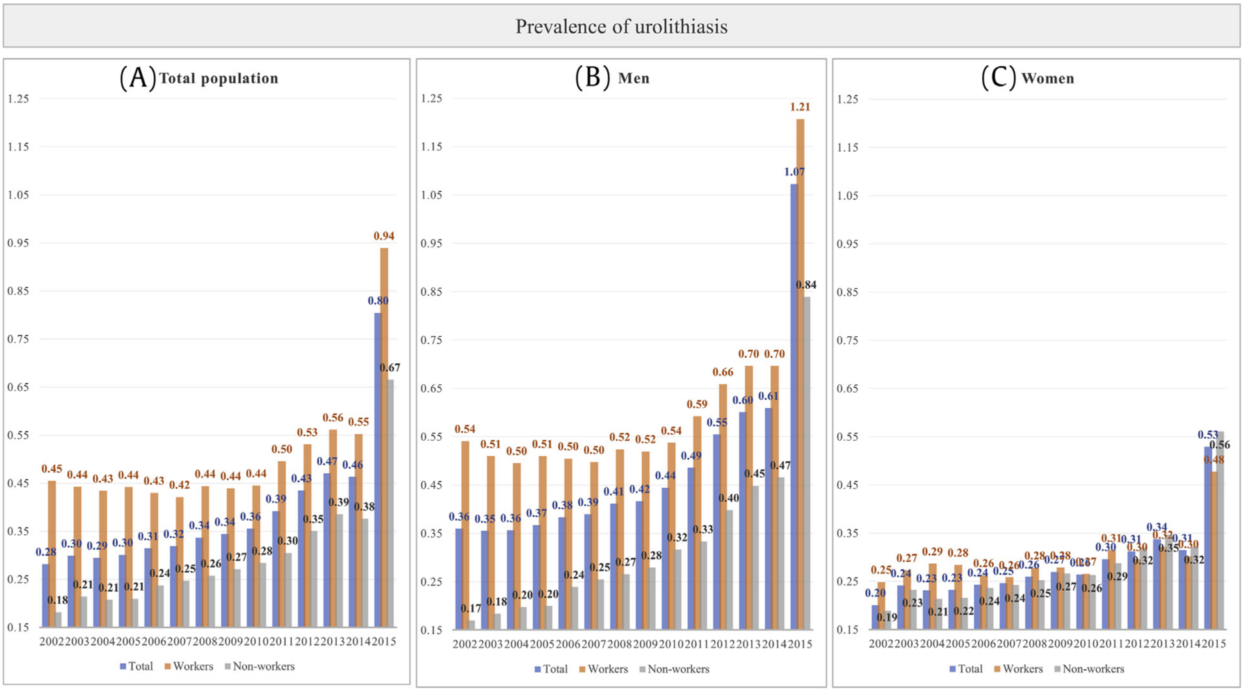

Fig. 2. Prevalence of urolithiasis according to working status with sex stratification from 2002 to 2015.

epidemiological study is currently available on this topic, this may explain our finding that paid workers had a higher SIR of ULT than self-employed workers.

The "healthy worker effect" is an important issue in occupational health-related epidemiologic studies. The presence of a healthy worker effect could lead to an underestimation of mortality and morbidity rates owing to the early exit of unhealthy persons from work. The current study found a higher prevalence and incidence of ULT among workers than among non-workers. This result may be explained by the lower healthy worker effect of ULT or an underestimation of our findings. Further studies are required to clarify this issue.

Our study had several limitations. Because NHIS data are based on individual medical records, there may be some differences in diagnostic criteria among different physicians. Information on asymptomatic ULT cases may have been missing from the database because the patients did not visit the hospital. Another limitation was that our analysis did not include diagnostic information, such as the location and composition of the stones. However, according to previous studies [28,29], the Korean NHIS database has little

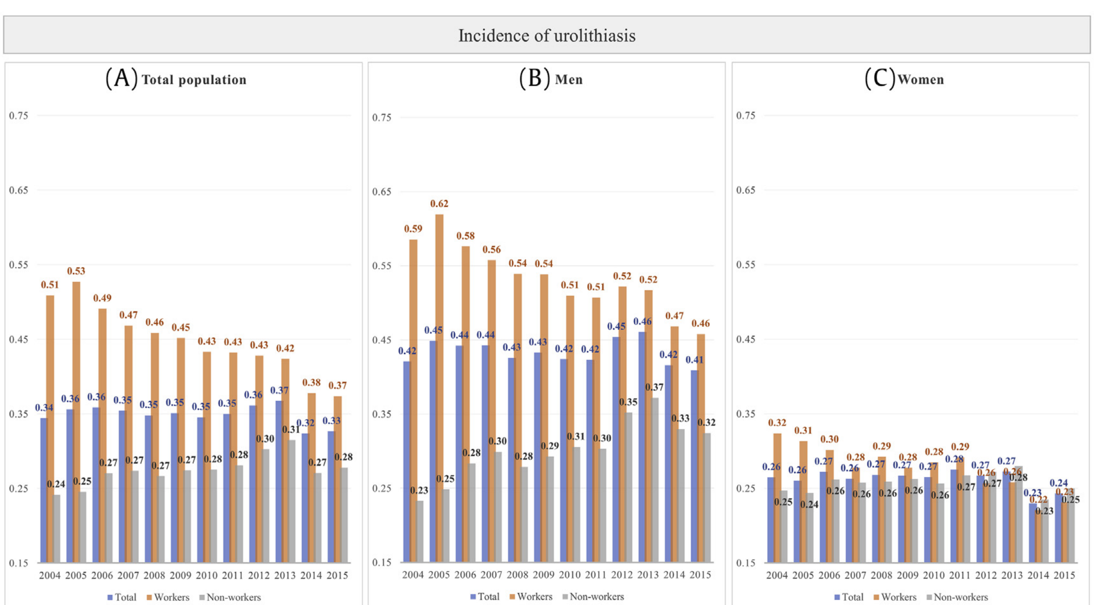

Fig. 3. Incidence of urolithiasis according to working status with sex stratification from 2004 to 2015.

misclassification error in the diagnosis of severe or fatal diseases. Although ULT has severe symptoms, it is not fatal. In addition, our study was limited by a lack of information on working conditions that can be risk factors for ULT, such as shift work, long working hours, insufficient rest breaks, absence of voiding during working hours, and prolonged sedentary work [30]. Further detailed analysis is needed to reveal the association between the occupational environment and the risk of ULT development. These data must be interpreted with caution because baseline job was defined as an occupation during follow-up periods, changing of job was not demonstrated. Further analysis such as the generalized estimating equations regarding short-term effect of recent occupation on ULT cases would be worthwhile.

5. Conclusion

This study showed the trends in the incidence and prevalence of ULT from the NHIS in Republic of Korea, which provides nationally representative data with a large sample of participants, according to sex, age, employment status, and job type. Workers, especially paid workers and men, are vulnerable to ULT. Further studies are required to investigate the effect of working conditions on ULT.

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Conflicts of interest

The authors declare that there are no conflicts of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.shaw.2022.07.002.

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