Asian Journal of Urology (2018) 5, 205–214

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Review

Epidemiology of urolithiasis in Asia

Yu Liu [a,1], Yuntian Chen [a,1], Banghua Liao [a], Deyi Luo [a], Kunjie Wang [a,*], Hong Li [a], Guohua Zeng [b]

[a] *Department of Urology, Institute of Urology (Laboratory of Reconstructive Urology), West China Hospital, Sichuan University, Chengdu, China*
[b] *Department of Urology, Minimally Invasive Surgery Center, The First Affiliated Hospital of Guangzhou Medical University, Guangzhou, China*

Received 14 January 2018; received in revised form 8 April 2018; accepted 11 July 2018
Available online 6 September 2018

KEYWORDS
Urolithiasis;
Epidemiology;
Prevalence;
Incidence;
Component;
Risk factors

Abstract In Asia, about 1%–19.1% of the population suffer from urolithiasis. However, due to variations in socio-economic status and geographic locations, the prevalence and incidence have changed in different countries or regions over the years. The research for risk factors of urinary tract stones is of predominant importance. In this review, we find the prevalence of urolithiasis is 5%–19.1% in West Asia, Southeast Asia, South Asia, as well as some developed countries (South Korea and Japan), whereas, it is only 1%–8% in most part of East Asia and North Asia. The recurrence rate ranges from 21% to 53% after 3–5 years. Calcium oxalate (75%–90%) is the most frequent component of calculi, followed by uric acid (5%–20%), calcium phosphate (6%–13%), struvite (2%–15%), apatite (1%) and cystine (0.5%–1%). The incidence of urolithiasis reaches its peak in population aged over 30 years. Males are more likely to suffer from urinary calculi. Because of different dietary habits or genetic background, differences of prevalence among races or nationalities also exist. Genetic mutation of specific locus may contribute to the formation of different kinds of calculi. Dietary habits (westernized dietary habits and less fluid intake), as well as climatic factors (hot temperature and many hours of exposure to sunshine) play a crucial role in the development of stones. Other diseases, especially metabolic syndrome, may also contribute to urinary tract stones.

1. Introduction

Nephrolithiasis is one of the most prevalent urologic diseases in Asia. The worldwide prevalence, incidence and composition of calculi varies and have changed in the last several decades, with prevalence ranging from 7% to 13% in North America, 5%–9% in Europe, and 1%–5% in Asia [1]. The differences among countries reflect several lithogenic factors, including age, gender, dietary habits, fluid intake, climate, occupation and education level, socioeconomic

* Corresponding author.
E-mail address: wangkj@scu.edu.cn (K. Wang).
[1] Both authors contributed equally to this work.
Peer review under responsibility of Second Military Medical University.

https://doi.org/10.1016/j.ajur.2018.08.007

status, racial or national distribution, genetic and metabolic disease. This study aims to provide updated review on the epidemiology of urolithiasis across Asia, and to analyze which factor is crucial in stone formation. We searched MEDLINE and EMBASE through the PubMed and Ovid, as well as Web of Science for relevant literature published from 1965 to 2018. The key words were [("prevalence" OR "epidemiology" OR "incidence") AND ("nephrolithiasis" OR "urolithiasis" OR "stone" OR "calculus" OR "calculi")]. Data were sorted according to the origin of the study population in Asian countries.

2. Prevalence, incidence and recurrence rates

According to geographical location, Asia can be divided into East Asia, Central Asia, West Asia, North Asia, Southeast Asia and South Asia. There has been a stone forming belt stretching across the West Asia, Southeast Asia, South Asia as well as several developed countries, including South Korea and Japan, with prevalence ranging from 5% to 19.1%. However, it is only 1%–8% in the remaining countries. In addition, the prevalence and incidence of urolithiasis have increased in most of the countries of Asia over the last several decades. Apart from climate, dietary habits and genetic factors, the increasing usage and improvements in sensitivity of high-tech imaging examination technology (computed tomography or ultrasonography) [2–5] can also account for it. Besides, aging of population, especially Japanese [6], also contributes to the increase in prevalence, which is consistent with the phenomenon that the peak onset age of urolithiasis has been increasing [7]. The detailed data of prevalence, incidence and recurrence are presented in Tables 1–3.

China, as the biggest country in East Asia, has witnessed a steady rise in the prevalence of kidney stones from 4% to 6.4% after the reform and opening up to the outside world [8–10]. Regarding to geographical distribution, the urolithiasis is more common in the south than in the north (5.5%–11.6% *vs.* 2.6%–7.2%) [10]. The main reason for this is because the average temperature in the south is higher than that in the north [8]. After World War II, Japan has conducted several nationwide surveys of urolithiasis every 10 years to update the trend of urinary tract stones in Japanese [7,11]. By reviewing these studies, we found that the prevalence of urolithiasis increased from 4.3% in 1965 to 9.0% in 2005. Meanwhile, the incidence also ascended from 54.2/100 000 to 114.3/100 000 [11]. Likewise, South Korea also witnessed a rising trend in prevalence (from 3.5% to 11.5%) during the period between 1998 and 2013 [5,12]. However, two studies demonstrated that the prevalence of upper urinary tract (UUT) stones declined from 9.6% to 7.38%, and the incidence dropped from 1367/100 000 to 1278/100 000 (1998–2010) [2,13]. Turning to Russia, a sharp rise in incidence was also witnessed between 1980 and 2008 (from 53/100 000–609.3/100 000), with prevalence ranging from 2% to 3% [3].

Because of high temperature and excessive exposure to sunshine, the prevalence of urolithiasis was much higher in South Asia and Southeast Asia, such as Pakistan (16%) [14] and Thailand (16.9%) [16]. In India and Malaysia, the incidence was lower than 40/100 000 in 1960s, but three decades later, it grew dramatically to 930/100 000 and 442.7/100 000, respectively [17–19].

As for West Asia, due to its high temperature and semi-arid climate, high prevalence rate of urinary tract stones was also documented. The highest prevalence was seen in Saudi Arabia (6.8%–19.1%), followed by 11%–14.8% in Turkey and 5.7%–8.1% in Iran. Meanwhile, the prevalence and incidence were also documented to be rising in several countries, including Saudi Arabia, United Arab Emirates, Kuwait, Iran and Israel [20–29]. For example, during the period from 1989 to 2008, Saudi Arabia had seen a rising trend in the prevalence rate from 6.8% [20] to 19.1% [21].

While the overall prevalence and incidence of urolithiasis have been rising, the proportion of vesical calculi has dropped sharply. About 30–70 years ago, lower urinary tract (LUT) stones, especially vesical stones, accounted for 30%–94% of all stones, were dominated categories in many countries, like China, Japan, India, Malaysia, Thailand and Pakistan. However, it has changed gradually as the economy developed (only taking up for 3%–15%), with the UUT stones increasing and comprising the major part of urolithiasis (holding approximately 85%–93%) [4,14,18,24,30–37].

There is no evident difference in recurrence rate of urolithiasis among Asian countries, which is about 6%–17% after 1 year, 21%–53% after 3–5 years, and the lifetime risk of recurrence is estimated to be 60%–80% (Tables 1–3) [2,3,5,25,38,39]. When it comes to gender, the recurrence rate of urolithiasis in male is twice than that in female [40].

3. Chemical constituents of stones

Nowadays, in most countries of Asia, calcium oxalate (75%–90%) is the most common component of UUT stones, followed by uric acid (5%–20%), calcium phosphate (6%–13%), struvite (2%–15%), apatite (1%) and cystine (0.5%–1%) [14,66,11,36,44]. Since 1960s, the proportion of calcium oxalate and uric acid stones have increased, which is the typical pattern in the countries, like China, Japan, India and Indonesia [11,31,41,42]. On the contrary, a decreased trend in struvite stones, made up of magnesium ammonium phosphate and associated with urinary tract infection, is documented in many countries, like Japan, India and Iran [41,43–45]. Besides, there are several differences between developed and developing countries. The calcium oxalate (90% *vs.* 75%) and uric acid calculi (15% *vs.* 5%) are more common in developed countries than in developing countries, while the reverse is true for struvite stones (7% *vs.* 14%) [42]. Interestingly, Ansari et al. [46] found the commonest constituent of staghorn stones was calcium oxalate, which was in contrast to the previous knowledge that magnesium ammonium phosphate was the major component. The detailed data is presented in Tables 1–3.

In addition, stones in different sites (UUT or LUT) may have diverse composition. In Pakistan, the dominant component of UUT calculi is calcium oxalate (75%) and hydroxyapatite (51%) [47]. While ammonium acid urate and calcium oxalate combinations are more frequent in the LUT stones, especially in children up to 14 years. In Turkey, 60% of pure uric acid stones are in bladder. Besides, there may be differences between male and female population

Table 1 Epidemiological data and composition of urinary tract stones in East Asia.

Study	Country/ Region	Year (s)	Type of stones	Prevalence (%)	Incidence (/100 000)	Recurrence rate (%)	Male to female ratio	Age of peak prevalence (years)	Calcium oxalate (%)	Calcium phosphate (%)	Uric acid (%)	Cystine (%)	Struvite (%)	Apatite (%)
Zeng and He, 2013 [8]	China	2008	Kidney stones	4	—	—	1.26	50—70	—	—	—	—	—	—
Wu et al., 2014 [66]	China	2003—2012	Urolithiasis	—	—	—	—	—	78.3	3.4	3.6	0.2	14.6	—
Chen et al., 2017 [9]	China	2013—2014	Urolithiasis	7.96	—	—	1.1	—	—	—	—	—	—	—
Zeng et al., 2017 [10]	China	2013—2014	Kidney stones	6.4	—	—	1.3	65—74	—	—	—	—	—	—
Lee et al., 2002 [13]	Taiwan, China	1994—1996	UUT	9.6	—	—	1.08	51—60	—	—	—	—	—	—
Hsu et al., 2002 [67]	Taiwan, China	1956—1999	Urolithiasis	—	—	—	2.3	—	87.3	71.8	7.5	0.2	8.2	65.6
Huang et al., 2013 [2]	Taiwan, China	1997—2010	UUT	7.38	1278—1367	6.12 (1 yr), 34.71 (5 yrs)	1.32—1.95	60—69	—	—	—	—	—	—
Kim et al., 2002 [12]	South Korea	1998	Urolithiasis	3.5	900	20 (2 yrs)	3.3—6.3	50—59	—	—	—	—	—	—
Bae et al., 2014 [68]	South Korea	2009	UUT	—	457.02		1.8	60—69	—	—	—	—	—	—
Choi and Yoon, 2017 [54]	South Korea	2008—2013	Urolithiasis	12.2—9.2	—	—	—	—	—	—	—	—	—	—
Tae and Balpukov, 2018 [5]	South Korea	2002—2013	Urolithiasis	11.5	440—560	21.3 (5 yrs), 38.1 (10 yrs)	1.3	60—69	—	—	—	—	—	—
Takasaki, 1975 [43]	Japan	1953—1970	Urolithiasis	—	—	38.6—55.6	—	20—39	72.9	—	3.9	0.95	22.1	—
Yoshida and Okada, 1990 [30]	Japan	1945—1987	Urolithiasis	5.4	53.8—92.5	—	7—2.4	30—59	79.4	—	5.2	1	7.4	—
Kohri et al., 1991 [51]	Japan	1977—1985	Urolithiasis	—	—	—	3	30—59	63.8	65.3	1.8	—	17.3	—
Iguchi et al., 1996 [40]	Japan	1992	Urolithiasis	6.95	970	24.20	1—2	50—59	—	—	—	—	—	—
Yoshida et al., 1999 [7]	Japan	1965—1995	Urolithiasis	4.3—9.0	43.7—110.9	—	1.8—2.8	20—69	—	—	—	—	—	—
Yasui et al., 2008 [11]	Japan	1965—2005	Urolithiasis	—	54.2—114.3	—	2.54—2.76	30—79	83.7—92.1	—	4.6—5.5	1.6	5.1—23.3	—
Yasui et al., 2008 [6]	Japan	1965—2006	LUT	—	4.7—9.1	—	—	50—69	72.1—69.9	—	13.4—19.3	1.1—3.1	59.3—66	—

—: The data were not provided in the study.
LUT, lower urinary tract; UUT, upper urinary tract; yr, year; yrs, years.

Table 2 Epidemiological data and composition of urinary tract stones in North, South and Southeast Asia.

Study	Country/ Region	Year (s)	Type of stones	Prevalence (%)	Incidence (/100 000)	Recurrence rate (%)	Male to female ratio	Age of peak prevalence	Calcium oxalate (%)	Calcium phosphate (%)	Uric acid (%)	Cystine (%)	Struvite (%)	Apatite (%)
Novikov et al., 2012 [3]	Russia	1980–2008	Urolithiasis	2–3	53–609.3	49 (1 yr), 53 (3 yrs), 77 (lifetime)	1.9	—	33–85	20.9–27	10.5–30	2.70	—	—
Pendse and Singh, 1986 [41]	India	1986[a]	Urolithiasis	—	—	—	—	—	93	94.6	—	—	78.2	—
Ansari et al., 2005 [46]	India	1998–2003	UUT	—	—	—	—	—	93	—	0.95	—	1.42	1.80
Ganesamoni and Singh, 2012 [4]	India	2012	Urolithiasis	—	—	—	—	—	86–97	1.90	0.95–1.2	—	1.4–2.7	1–1.8
Kale et al., 2014 [17]	India	1994–2008	Urolithiasis	—	30–930	—	1.8	21–40	Major	—	—	—	—	—
Silva and Maciel, 2016 [48]	India	2010–2012	Urolithiasis	—	31.7	—	0.9	30–39	—	—	—	—	—	—
Kumari et al., 2016 [69]	India	2013	Kidney stones	7.6	—	26–53 (10 yrs)	—	—	95.2	71.4	52.3	—	—	—
Memon et al., 2012 [14]	Pakistan	1975–2010	Urolithiasis	16	0.2–200	—	1.2–13.2	—	74–96	23–51	2-38	0.2–0.5	2.4–16	6–18
Halstead and Valyasevi, 1967 [35]	Thailand	1963	Bladder stones	1.4	—	4.3 (0.5 yr)	4.6	30–39	—	—	—	—	—	—
Sriboonlue et al., 1992 [55]	Thailand	1992[a]	UUT	—	376	—	2	40–69	—	—	—	—	—	—
Nimmannit et al., 1996 [15]	Thailand	1996[a]	Kidney stones	13	—	—	—	—	—	—	—	—	—	—
Yanagawa et al., 1997 [16]	Thailand	1997[a]	Urolithiasis	16.9	3000	—	2	20–50	44–49	—	—	—	—	—
Tanthanuch et al., 2005 [49]	Thailand	2000	Urolithiasis	—	183.8	—	1.6	41–50	64	41	26	—	—	—
Sreenevasan et al., 1981 [18]	Malaysia	1962–1976	Urolithiasis	—	33.3	—	3	30–60	—	—	—	—	—	—
Lim et al., 1988 [34]	Malaysia	1980	Urolithiasis	—	3.4	—	1.2	40–79	—	—	—	—	—	—
Sreenevasan et al., 1990 [19]	Malaysia	1962–1981	Urolithiasis	—	224.2–442.7	—	—	30–59	81	—	3.50	0.50	5	—
Nazmi et al., 1997 [33]	Malaysia	1985–1995	Kidney stones	—	9.8	—	2	50–59	—	—	—	—	—	—
Hussein et al., 2013 [62]	Malaysia	1981–1997	Urolithiasis	—	9.8–37	—	4.6	—	—	—	—	—	—	—
Thalut et al., 1976 [31]	Indonesia	1976[a]	Bladder stones	—	8.3	—	12	—	Major	—	—	—	Major	—

—: The data were not provided in the study.
LUT, lower urinary tract; UUT, upper urinary tract; yr, year; yrs, years.
[a] The study did not provide the exact time when it was carried out.

Table 3 Epidemiological data and composition of urinary tract stones in West Asia.

Study	Country/ Region	Year (s)	Type of stones	Prevalence (%)	Incidence (/100 000)	Recurrence rate (%)	Male to female ratio	Age of peak prevalence	Calcium oxalate (%)	Calcium phosphate (%)	Uric acid (%)	Cystine (%)	Struvite (%)	Apatite (%)
Abdel-Halim et al., 1989 [20]	Saudi Arabia	1989[a]	UUT	6.8	—	38.6—53.2	2	—	—	—	—	—	—	—
Abomelha et al., 1990 [36]	Saudi Arabia	1980—1985	Urolithiasis	—	—	—	5	30—60	76	3.30	20.50	—	—	—
Ahmad et al., 2015 [21]	Saudi Arabia	2004—2008	Urolithiasis	19.1	—	—	3.5	25—45	—	—	—	—	—	—
Nasir et al., 1999 [52]	United Arab Emirates	1999[a]	Urolithiasis	—	—	—	—	—	38.50	11.50	11.50	—	—	—
Freeg et al., 2012 [22]	United Arab Emirates	2007—2009	Urolithiasis	—	59.53—94.58	—	5.2	< 40	—	—	—	—	—	—
Salem and Abu Elezz, 1969 [59]	Kuwait	1966—1968	Kidney stones	4-5	—	—	—	—	—	—	—	—	—	—
el-Reshaid et al., 1997 [23]	Kuwait	1986—1994	Urolithiasis	—	23.9	—	> 1	—	72.10	—	15.40	2.40	—	—
Al-Hunayan et al., 2004 [24]	Kuwait	1999—2002	Urolithiasis	—	43.44	—	9	—	90	18	7	1	1	—
Minon and Pourmand, 1983 [45]	Iran	1978—1979	Urolithiasis	—	—	—	—	—	81.5	0.9	12.6	0.9	8.7	69
Safarinejad, 2007 [25]	Iran	2005	Urolithiasis	5.7	138.4	16 (1 yr), 32 (5 yrs)	1.15	40—69	—	—	—	—	—	—
Shajari and Sanjerehei, 2015 [60]	Iran	2005	Urolithiasis	6.1	—	—	—	—	—	—	—	—	—	—
Shokouhi et al., 2008 [44]	Iran	2001—2006	Urolithiasis	—	—	—	2.7	—	80.2	2.4	16.2	0.6	0.4	—
Ketabchi and Aziziolahi, 2008 [26]	Iran	2005—2006	Urolithiasis	8.1	—	—	1.24	—	—	—	—	—	—	—
Basiri et al., 2010 [27]	Iran	2006—2007	Urolithiasis	—	407	—	1.38	55—65	—	—	—	—	—	—
Afaj and Sultan, 2005 [32]	Iraq	1997	Urolithiasis	—	—	—	4	15—50	46.1	38.4	15.4	—	—	—
Pugliese and Baker, 2009 [38]	Iraq	2005	Urolithiasis	1	—	60-80 (lifetime)	2-4	—	—	—	—	—	—	—
Frank et al., 1959 [28]	Israel	1957—1958	Urolithiasis	1.2	—	—	1.6	41—50	75	54	17	8	—	—
Frank et al., 1963 [29]	Israel	1963[a]	Urolithiasis	2.4—9.2	—	—	—	—	—	—	—	—	—	—

(*continued on next page*)

Table 3 (*continued*)

Study	Country/Region	Year (s)	Type of stones	Prevalence (%)	Incidence (/100 000)	Recurrence rate (%)	Male to female ratio	Age of peak prevalence	Calcium oxalate (%)	Calcium phosphate (%)	Uric acid (%)	Cystine (%)	Struvite (%)	Apatite (%)
Akinci et al., 1991 [50]	Turkey	1989	Urolithiasis	14.8	2200	—	1.5	—	—	—	—	—	—	—
Yapanoglu et al., 2010 [37]	Turkey	2005—2008	Urolithiasis	—	—	—	2.48	—	72.7	—	7.7	0.6	2	1
Muslumanoglu et al., 2011 [39]	Turkey	2008	Urolithiasis	11	1700	16.7 (1 yr), 35.7 (5 yrs)	1	45-54	—	—	—	—	—	—

—: The data was not provided in the study.
LUT, lower urinary tract; UUT, upper urinary tract; yr, year; yrs, years.
[a] The study did not provide the exact time when it was carried out.

in distribution of various calculi [37]. In Russia, the percentage of oxalate and uric acid stones is higher in men than in women (35.9% *vs.* 30%) while the reverse is true when talking about phosphate and struvite stones (8.5% *vs.* 12.4%) [3].

4. Risk factors

Risk factors associated with the formation of urinary calculi can be divided into two main groups, intrinsic or extrinsic factors. The former one includes age, gender, ethnic and familial backgrounds; while the latter group consists of climate and environment, lifestyle and dietary habits, occupation and education level. The most important factors, determining the prevalence, incidence, recurrence rates and constituent of calculi, are climate and dietary habits.

4.1. Age

Overall, the incidence of urinary tract stones increased with age, which peaked in the age group of 30—60 years and decreased afterwards (Tables 1—3). The reason why middle-age population are prone to urolithiasis is because they do more laborious work than others [17], and subsequently result in less fluid intake and higher rate of dehydration. Besides, they led an unhealthy lifestyle (irregular diet or staying up late) and suffer from occupational stress [40]. Apart from the aging population, western dietary habits and changes of endocrine hormones with age may also be the cause of the upward trend. In China, the age distribution of urolithiasis varied in men and women; males are more likely to be affected after the age of 70s, while females are in their 50s [8]. In Japan, however, the peak age of females (60—69 years old) is higher than that of males (50—59 years old) [11].

4.2. Gender

In most countries, males are predisposed to urolithiasis, with male to female ratio ranging from 1.3 to 5 (Tables 1—3) [2,62,38]. It may be associated with different dietary habits [48]. Men are more likely to have excessive alcohol and coffee, and consumed more meat than women. In addition, testosterone can promote stone formation, while estrogen appears to inhibit the formation of stones by regulating the synthesis of 1,25-dihydroxy-vitamin D [17]. Additionally, the anatomical differences, with which men are more likely to suffer from benign prostatic hyperplasia and subsequent obstruction of urethra, can also be a risk factor for bladder stone formation [3].

However, it has been reported that the ratio is descending in many countries, including China, Japan, Thailand, India, Saudi Arabia and Turkey since 1990s, which meant females are more likely to be affected than before [7,21,35,36,39,48—50]. In India, the ratio is already below 1, which is in contrast to the previous study results [48]. In Japan, the ratio decreased from 3 (middle-aged group) to 1 (rest of the population) [40,51]. Along with the economic development and standard of living improvement, the differences of diet, lifestyle and occupations between the sexes have narrowed [48], which can be attributed to the decrease of ratio. Estrogen excretion also decreases sharply after the age of 60 years. On the contrary, the ratio was still rising in Iran [25].

4.3. Lifestyle and dietary habits

Lifestyle also plays a profound role in stone formation. In developing countries, like India [4,17], people fed on cereals and vegetables, which are high in oxalate and its precursors. In addition, westernized diet, which contains excessive protein, lipid, calcium and sodium, also contributed to stone formation, leading to the rising trend of urolithiasis in many Asian countries, like Japan, China, India, Iran and Saudi Arabia [4,19,25,30,36,40,42]. Precursors of oxalate in food (like glycine, hydroxyproline, hydroxyacetic acid and vitamin C) may be metabolized to oxalate in liver, and subsequently increase the oxalate concentration in urine. The combination of lipid and calcium in intestine, forming insoluble substance, can also inhibit calcium absorption, followed by increasing absorption of oxalate [70]. Hyperuricemia, the main risk factor for uric acid stones, can also be the result of excessive consumption of meat [71].

Besides, there must be another factor, appropriate urine pH, prompting the precipitation of crystals. Urinary tract stones can exist only if two main conditions of urine, ingredients concentration and pH, are fulfilled at the same time [42]. In Southwest and South Asia, rice is the principle food, carbohydrate of which is catabolized to provide the acidic environment of urine [4,31]. Excessive meat consumption can also lead to acidification of urine [52], which is in favor of calcium oxalate stone formation. It is typical in Japan, where a rising trend of meat consumption, metabolic syndrome and prevalence of urolithiasis have occurred at the same time [11].

Less fluid intake is a main risk factor for urolithiasis [53]. In Iraq and South Korea, soldiers are forced to drink enough water, as a result, the prevalence of urolithiasis among soldiers is dropping [38,54]. High levels of fluoride, sodium calcium, magnesium and phosphates in drinking water are also reported to be associated with calcium oxalate stones [4,16,17,53,55]. In India, Pakistan and Sri Lanka, the main source of drinking water, which is underground water, is undergoing mineralization due to evaporation [14,17,53]. Prevalence of urolithiasis among people drinking high-fluorine water is 4.6 times higher than those in fluoride-free area [56]. The mechanism may be that fluoride in intestine indirectly promotes the absorption of oxalate due to calcium fluoride formation, therefore, calcium availability drops [4]. As a result, increasing of oxalate excretion and insoluble calcium fluoride formation in urine, as well as oxidative stress in renal system are witnessed. In addition, excessive sodium may lead to extra calcium absorption into blood or inhibit calcium absorption from urine into renal tubular epithelial cell, followed by enhanced calcium excretion and precipitation in kidney. Another theory is that high urine sodium may inhibit the citrate excretion in urine, which is crucial in preventing crystal formation. High concentration of magnesium in drinking water and soil may also accelerate development of stones [32]. In contrast, Chandrajith et al. [53] have not found any relationship between water hardness and urolithiasis.

Habits, like smoking and high alcohol consumption, can also contribute to stone occurrence [8,13]. Alcohol and its metabolites can lead to oxidative stress in kidney tissues, hypercalciuria, and hyperoxaluria, followed by stone formation, especially uric acid stones [5]. However, this idea is not confirmed by other studies [5,12]. A meta-analysis reveals alcohol consumption may decrease the risk of urolithiasis [57]. Inadequate physical activity, another risk factor, is also implicated by the fact that people with sedentary work in office are more prone to suffer from urolithiasis [11,40]. In addition, the lack of microelements, such as molybdenum and silicon that play a key role in keeping crystals in solution, may lead to stone formation as well [3].

4.4. Climate or living environment

Climatic and geographical factors are both correlated with urolithiasis. Specifically, temperature, seasons, sunshine hours, humidity, atmospheric pressure and rainfall are included [17]. Countries or regions in tropical and subtropical areas have higher prevalence of urolithiasis than that in temperate and frigid zones (5%—10% *vs.* 1%—5%). Hot dry climate, which is typical in West Asia, can accelerate evaporation of body water from skin, and subsequently results in concentrated urine, which is a risk factor for precipitation of crystals and stone development. In summer and autumn, the prevalence and incidence of urolithiasis are higher than that in spring and winter in many countries or regions, such as India, Pakistan, Saudi Arabia and Iran [14,22,27,44,48,58,59]. For example, the prevalence in the south of China (22%—45%) is much higher than that in the north (14%) [8]. Apparently, it may be attributed to seasonal variations in temperature. However, another phenomenon is also recorded. The northwest and west areas of Iran, which were much cooler than other regions, witnessed a higher prevalence of urolithiasis during 2007—2008 [58]. The reason for it may be related to a concept of temperature threshold value [60]. The prevalence rate may be higher in the areas where temperature just reaches the threshold (i.e., 18°C in Korea), compared with those under or exceeding it [61].

4.5. Occupation or education level

The role of occupation or education level in urolithiasis is still controversial [27]. Some researchers found people with sedentary jobs (usually with high education level) are more prone to urolithiasis, however, others also demonstrate a positive relationship between urinary stones and people with more physical works (less educated).

The risk of urolithiasis in people working outdoors or exposed to high temperatures, such as workers in steel industry, flight attendants, farmers, miners, quarrymen or drivers [4,25,30,49], are twice likely to suffer urolithiasis than people working at room temperature. Tanthanuch et al. [49] and Hussein et al. [62] also find kidney stone patients are more likely to be physical workers with lower education level in Thailand and Malaysia, respectively. The reason for it is that hot temperature may lead to dehydration, and people in these conditions have less access to drinking water. Besides, excessive exposure to sunshine results in more production of vitamin D. After conversion to 1,25-dihydroxy-vitamin D in kidneys, it can promote calcium absorption in the gut [22]. On the contrary, the incidence of urolithiasis for people working inside, especially office employees, are also much higher in Japan, Saudi Arabia and Iran [20,27,30]. The possible causes may be that sedentary people lead unhealthy lifestyle, including lack of adequate outdoor activities and fluid intake.

When it comes to education, several studies in Iran and Turkey suggest that lower education level may be a possible reason for stone formation [27,39]. However, there are also some studies showing the relationship between the incidence of urolithiasis and the occupation or education level is negative [13,36].

4.6. Socioeconomic status

Socioeconomic level is also an important factor in epidemiology of urolithiasis. For instance, in Taiwan, China, though southern areas have higher temperature, residents in northern areas have much higher prevalence of urolithiasis because of higher socioeconomic status [13]. Similarly, the distribution of urolithiasis in Japan and India is corresponded with the economical level [11]. The reason for it may be that chronic metabolic disease, mainly caused by high-calorie intake, is more common among population in the society with higher standard of living [5]. Besides, people in economically less-developed areas have less access to medical examination, like computed tomography or ultrasonography [14].

4.7. Racial or national distribution

Whether race and nationality are associated with urolithiasis is still controversial. In Asia, the relationship is shown to exist. The incidence of urolithiasis in Han and Miao nationalities is high (47—57/100 000) in China [72]. Similarly, in USA, the prevalence of stones in Hmong, migrating from Laos, is higher than that of non-Hmong patients (46% *vs*. 11%) [63]. In Turkey, the risk of getting urinary stones is lower in people of Turkish origin than that among other ethnic population [39]. In Israel, local people (Israelite) have a lower incidence rate than immigrants from Europe, North Africa or the Middle East [28]. However, another study in Iran revealed that there was no significant difference in the prevalence and incidence of urinary stones between different races and ethnicities [25]. Generally speaking, dietary habits and gene of various races or nationalities differ from each other, which may be the reason why some studies find statistical differences, while others do not.

4.8. Genetics

Apart from the aforementioned factors, genetic factor also plays an important role in stone formation. Cystine stones are caused by mutations in the *SLC3A1*, *SLC7A9* gene or other neighboring genes [64]. In addition, mutation of *SLC22A12* and *SLC2A9* has also been reported in patients with uric acid calculi [65]. Calcium oxalate stones, the most common type of urinary calculi, are found to be the result of deficiency of enzymes, like alanine glyoxylate aminotransferase (AGT), glyoxylate reductate/hydroxypyruvate reductase (GRHPR) or 4-hydroxy-2-oxoglutarrate aldolase (HOGA1) [65]. Subsequently, synthesis and excretion of oxalate are increased, resulting in calcium oxalate stone formation. Since 1960s, many epidemiological studies in Asian countries have found people with the family history of urolithiasis are more likely to develop calculi than those without, with odds ratio (OR) ranging from 3.44 to 4.79 ($p < 0.05$) [4,13,40].

4.9. Other risk factors

Apart from urinary tract infection or renal tubular acidosis, patients with urolithiasis are frequently documented to be with metabolic diseases, like diabetes mellitus, hypertension or adiposity, which may be another risk factor for urinary tract stones [4]. Besides, low urine output, hypercalciuria, hyperoxaluria, hyperuricosuria, and hypocitraturia are also reported to be associated with stone formation [11], though the reason why chemical composition of urine is abnormal is still unclear. Interestingly, in South Korea, Tae et al. [5] found positive correlation between cancer history and urolithiasis ($p < 0.05$).

5. Limitations of the review

The prevalence and incidence rate of urolithiasis in some countries, especially India, have not been updated for more than 15 years. As a result, the data provided in the review may not reflect the latest tendency. In addition, some studies of epidemiology of urolithiasis are limited in a certain area, which can not represent the whole situation in that particular country. But some countries only have a few studies with small numbers of individuals being surveyed. To cover the epidemiology of urolithiasis in all the Asian countries, we have to keep the data of these low-quality studies in our review.

6. Conclusion

The highest prevalence rate was seen in West, South and Southeast Asia. Calcium oxalate, which is still the dominant component of stones, is with a rising trend in proportion to the whole calculi. The prevalence of urolithiasis has increased significantly in the last few decades in most Asian countries, like China (from 4% to 6.4%), Japan (from 4.3% to 9.0%), South Korea (from 3.5% to 11.5%), Thailand (from 1.4% to 16.9%), Saudi Arabia (from 6.8% to 19.1%), Iran (from 5.7% to 8.1%) and Israel (from 1.2% to 9.2%). It is noteworthy that high-fat and high-sugar diet have become more and more popular in many Asian countries, especially in China, which may be the main factor for the rise in the prevalence and incidence of urolithiasis. Being aware of these risk factors and the composition of calculi can provide personalized guidance for prevention and treatment of urolithiasis.

Author contributions

Study design: Yu Liu, Yuntian Chen, Banghua Liao, Deyi Luo, Kunjie Wang, Hong Li, Guohua Zeng.

Data acquisition: Yu Liu, Yuntian Chen.
Data analysis: Banghua Liao, Deyi Luo.
Drafting of the manuscript: Yu Liu.
Critical revision of the manuscript: Kunjie Wang, Hong Li, Guohua Zeng.

Conflicts of interest

The authors declare no conflict of interest.

Acknowledgement

This study was supported by 1.3.5 project for disciplines of excellence, West China Hospital, Sichuan University, China [No. ZY2016104] and Central Financial Fund,Guangzhou Medical University, China [No. 2010A060801016].

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