Epidemiological Trends of Urinary Tract Infections, Urolithiasis and Benign Prostatic Hyperplasia in 204 Countries and Territories From 1990 to 2019

Cong Zhu

Wuhan University Zhongnan Hospital

Dan-Qi Wang

Wuhan University Zhongnan Hospital

Hao Zi

Wuhan University Zhongnan Hospital

Qiao Huang

Wuhan University Zhongnan Hospital

Jia-Min Gu

Wuhan University Zhongnan Hospital

Lu-Yao Li

Wuhan University Zhongnan Hospital

Xin-Pei Guo

Wuhan University Zhongnan Hospital

Fei Li

Wuhan University Zhongnan Hospital

Cheng Fang

Wuhan University Zhongnan Hospital

Xiao-Dong Li

Henan University

Xian-Tao Zeng (✉ zengxiantao1128@163.com)

Wuhan University Zhongnan Hospital <https://orcid.org/0000-0003-1262-725X>

Research

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Abstract

Background

To investigate the disease burden of urinary tract infections (UTI), urolithiasis, and benign prostatic hyperplasia (BPH) in 204 countries and territories from 1990 to 2019.

Methods

Data were extracted from the Global Burden of Disease 2019, including incident cases, deaths, disability-adjusted life-years (DALYs) and corresponding age-standardized rate (ASR) from 1990 to 2019. Estimated annual percentage changes (EAPC) were calculated to evaluate the trends of ASR. The associations between disease burden and social development degrees were analyzed by socio-demographic index (SDI).

Results

Compared with 1990, the incident cases of UTI, urolithiasis, and BPH increased by 60.40%, 48.57%, and 105.70% in 2019, respectively. The age-standardized incidence rate (ASIR) of UTI increased (EAPC = 0.08), while urolithiasis (EAPC = -0.83) and BPH (EAPC = -0.03) decreased from 1990 to 2019. In 2019, the age-standardized mortality rate (ASMR) of UTI and urolithiasis was 3.13/100,000 and 0.17/100,000, respectively. BPH had the largest increase (110.56%) in DALYs in past three decades, followed by UTI (68.89%) and urolithiasis (16.95%). The burden of UTI mainly concentrated in South Asia and Tropical Latin America while the burden of urolithiasis and BPH was recorded in Asia and Eastern Europe. Moreover, the ASIR and SDI of urolithiasis in high SDI regions from 1990 to 2019 were negatively correlated, while the opposite trend was in low SDI regions. In 2019, the ASIR of UTI in female was 3.59 times that of male, while the ASIR of urolithiasis in male was 1.96 times higher than female. The incidence was highest in 30-34, 55-59, and 65-69 age group among UTI, urolithiasis, and BPH, respectively.

Conclusions

Over the past three decades, the disease burden remains increased in UTI, while decreased in urolithiasis and BPH. The allocation of medical resources should be more based on the epidemiological characteristics and geographical distribution of diseases.

Background

Urinary tract infections (UTI), urolithiasis and benign prostatic hyperplasia (BPH) are three of the most common non-malignant conditions in urology. Compared with the shortened survival caused by cancer, these urologic benign diseases affect individuals by impairing the quality of life to a great extent. In the United States, there were approximately 10.5 million ambulatory visits and 2–3 million emergency department for UTI in 2007 and \$3.5 billion were costed per year in 2015(1). A system review and meta-analysis contained 31 studies reported that the lifetime prevalence of BPH was 26.2% (95% CI: 22.8–29.6%)(2). The prevalence of urolithiasis varies in different regions, the prevalence of urolithiasis was 7% in Australia in 2000, 5.06% in Spain in 2007, 8.8% in America in 2010 and 6.5% in China in 2015(3–5). The burden of urolithiasis is increasing drastically over the last half century and the annual estimated financial burden was \$5.3 billion in 2014(6, 7). Over the past decades, the spectrum of diseases has changed as the ageing population, socio-economic development and advances in disease prevention and control. However, there is still a lack of comprehensive and updated epidemiological data on UTI, urolithiasis and BPH.

The Global Burden of Disease Study 2019 (GBD 2019) was a critical resource for informed policymaking, which provided a tool to quantify health loss from hundreds of diseases, injuries, and risk factors. The regularly updated epidemiological data from GBD database could help policymaker to understand the health trends over a period of time at the global, regional, and national levels. In this study, we used the data from GBD 2019 to reveal the epidemiological trends of UTI, urolithiasis and BPH over the past 30 years by global, regional, national, socio-demographic index (SDI), sex, and age.

Materials And Methods

Data sources

This study used data from the GBD 2019, which comprehensively analyzed the incidence, mortality, disability adjusted life-years (DALYs) and age standardized rates (ASR) of 369 diseases and injuries of different sexes and ages in 204 countries and territories around the world. The incidence, death, and DALYs as well as the corresponding ASR and 95% uncertainty interval (UI) of UTI, urolithiasis and BPH were obtained from the Global Health Data Exchange GBD Results Tool (<http://ghdx.healthdata.org/>). The SDI is a composite indicator of development status strongly correlated with health outcomes. SDI ranged from 0 to 1, where 0 represents the minimum level of development, and 1 represents the maximum level of development. The 204 countries and territories were categorized according to SDI quintile into 5 groups: low-SDI, low-middle-SDI, middle-SDI, high-middle-SDI, and high-SDI regions. The age was classified into fifteen subgroups: 0-14, 15-19, 20-24, 25-29, 30-34, 35-39, 40-44, 45-49, 50-54, 55-59, 60-64, 65-69, 70-74, 75-79, and over 80.

The incidence of these three urologic benign diseases were estimated from the data of hospital discharges and claims, with a systematic literature review additionally used for urolithiasis. Then, the DisModMR 2.1 model, a Bayesian metaregression tool, was used to produce estimates by age, sex, year, and country. Disability weight (DW) is the severity of health loss, or the severity of non-fatal disability, and is an important parameter reflecting the burden of disease. DW ranges from 0 to 1, health is 0, death is 1, and the more severe the disability, the closer it is to 1. Years lived with disability (YLD) is equal to number of cases multiplied by duration till remission or death multiplied by DW. The mortality of UTI and urolithiasis was estimated from the vital registration data and verbal autopsy data. The standard CODEm model with location-level covariates was used to model deaths, then the results were adjusted using CodCorrect to reach final years of life lost (YLLs). DALYs are obtained by adding YLD and YLL. BPH is a chronic, non-fatal disease, thus GBD 2019 assumed

that there was no excess mortality related to BPH. The DALYs of BPH are equal to YLD. Detailed data sources and model methods were reported in GBD 2019(8).

Definition of the three urologic benign diseases

In GBD 2019, UTI is defined as a kidney infection that can lead to systemic symptoms such as fever and weakness and can cause discomfort and difficulty with daily activities. urolithiasis is an acute and usually symptomatic episode of urolithiasis, defined as stone formation located anywhere along the genitourinary tract. BPH is defined as a benign proliferation of prostatic tissue, often leading to symptoms such as urinary retention, bladder outlet obstruction, or urinary tract infection. The associated International Classification of Diseases (ICD) codes include N10, N10.0, N10.9, N11, N11.0, N11.1, N11.8, N11.9, N12, N12.0, N12.9, N13.6, N15, N15.1, N15.8, N15.9, N16, N16.0-N16.5, N16.8, N30, N30.0-N30.3, N30.8-N30.9, N34, N34.0-N34.3, and N39.0 for UTI; N20, N20.0, N20.1, N20.2, N20.9, N21, N21.1, N21.8, N21.9, N22, N22.0, N22.8, N23, and N23.0 for urolithiasis; N40, N40.0, N40.1, N40.2, N40.3, and N40.9 for BPH(8).

Statistical analyses

The ASR (per 100,000 population), which can reflect the differences between different groups composed of different ages or age composition changing over time more accurately, calculated on the basis of the formula: $ASR = \frac{\sum_{i=1}^A a_i w_i}{\sum_{i=1}^A w_i} \times 100,000$ (a_i , where i denotes the i^{th} age class, and the number of persons (or weight w_i) in the same age subgroup i of the selected reference standard population.). Estimated annual percentage changes (EAPC) value can reflect the trends in ASR within a specified time interval, assuming that the natural logarithm of ASR is linear along with time(9). Thus, $Y = \alpha + \beta X + \epsilon$, where Y refers to $\ln(ASR)$, X represents calendar year, and ϵ represents error term. Based on this formula, β determines the positive or negative trends in ASR. The formula for calculating EAPC is: $EAPC = 100 \times (\exp(\beta) - 1)$ and 95% CI (confidence intervals) are obtained from the linear model. It is shown that when EAPC and the lower boundary of the 95% CI are positive, then ASR is in an upward trend. Conversely, when EAPC and the upper boundary of the 95% CI are negative, the ASR is in a descending trend. All statistical analyses were performed using the R software (Version 3.6.1).

Table 1. Global incidence, mortality and DALYs of the three urologic benign diseases from 1990 to 2019

	Urinary tract infections			Urolithiasis			Benign prostatic hyperplasia
	Both	Male	Female	Both	Male	Female	Male
1990Δ							
Incident case($\times 10^5$)	2522.46(2233.14 to 2792.97)	488.47(437.22 to 536.93)	2033.99(1795.48 to 2259.36)	777.76(622.39 to 951.27)	527.82(421.54 to 644.73)	249.94(199.72 to 305.78)	54.76(42 to 71.16)
Deaths($\times 10^3$)	98.59(89.03 to 106.32)	46.79(39.61 to 52.73)	51.8(46.42 to 56.17)	11.34(7.28 to 13.78)	6.15(3.08 to 8.03)	5.18(3.51 to 6.12)	
DALYs($\times 10^3$)	3079.89(2651.63 to 3381.62)	1471.72(1224.73 to 1656.34)	1608.17(1362.18 to 1807.36)	516.73(374.13 to 635.72)	308.57(207.19 to 392.88)	208.16(152.47 to 249.07)	884.19(526.63 to 1337.22)
ASIR	4989.87(4434.39 to 5499.05)	1984.8(1784.33 to 2175.01)	4989.87(4434.39 to 5499.05)	1696.18(1358.11 to 2078.11)	2353.15(1878.96 to 2879.17)	1066.85(851.17 to 1305.09)	285.46(221.45 to 370.09)
ASMR	2.77(2.51 to 3.02)	3.14(2.67 to 3.59)	2.56(2.31 to 2.77)	0.3(0.2 to 0.37)	0.38(0.2 to 0.5)	0.25(0.17 to 0.29)	
ASDR	67.73(59.96 to 73.45)	69.74(59.16 to 78.72)	67.42(58.34 to 74.51)	11.75(8.57 to 14.39)	14.76(9.92 to 18.82)	9.11(6.73 to 10.91)	50.76(30.39 to 76.18)
2019Δ							
Incident case($\times 10^5$)	4046.12(3594.25 to 4465.48)	871.9(780.14 to 954.2)	3174.22(2809.71 to 3512.61)	1155.52(930.45 to 1401.8)	761.05(610.28 to 921.68)	394.47(316.44 to 479.04)	112.65(87.9 to 144.55)
Deaths($\times 10^3$)	236.79(198.43 to 259.03)	104.88(82.41 to 117.43)	131.91(111.61 to 145.72)	13.28(10.62 to 16.27)	6.93(4.5 to 9.14)	6.35(5.17 to 8.29)	
DALYs($\times 10^3$)	5201.67(4454.04 to 5704.84)	2407.94(1949.07 to 2706.29)	2793.74(2402.91 to 3098.75)	604.31(477.35 to 745.19)	362.3(274.44 to 454.56)	242.01(193.91 to 299.06)	1861.78(1127.72 to 2782.26)
ASIR	5075.89(4516.65 to 5594.1)	2211.69(1988.65 to 2420.05)	7945.83(7045.47 to 8792.4)	1394.03(1126.4 to 1688.16)	1856.87(1495.27 to 2245.34)	947.22(761.21 to 1148.43)	280.4(219.62 to 360.32)
ASMR	3.13(2.61 to 3.43)	3.27(2.54 to 3.65)	3.05(2.58 to 3.37)	0.17(0.14 to 0.21)	0.2(0.13 to 0.26)	0.15(0.12 to 0.19)	
ASDR	66.17(56.56 to 72.5)	65.64(52.8 to 73.33)	67.21(57.89 to 74.67)	7.35(5.82 to 9.04)	9.1(6.92 to 11.34)	5.72(4.58 to 7.07)	48.9(29.68 to 72.63)
1990-2019*							
Incident case (%)	60.4	78.5	56.06	48.57	44.19	57.82	105.7
Deaths (%)	140.18	124.17	154.64	17.12	12.62	22.46	
DALYs (%)	68.89	63.61	73.72	16.95	17.41	16.26	110.56
ASIR (EAPC, 95%CI)	0.08(0.04 to 0.11)	0.39(0.37 to 0.41)	0(-0.04 to 0.04)	-0.83(-0.92 to -0.74)	-1.01(-1.09 to -0.92)	-0.47(-0.59 to -0.36)	-0.03(-0.05 to -0.01)
ASMR (EAPC, 95%CI)	0.55(0.47 to 0.62)	0.28(0.23 to 0.34)	0.7(0.62 to 0.78)	-2.05(-2.24 to -1.86)	-2.32(-2.47 to -2.18)	-1.88(-2.15 to -1.61)	
ASDR (EAPC, 95%CI)	-0.08(-0.11 to -0.04)	-0.17(-0.21 to -0.12)	-0.04(-0.09 to 0.01)	-1.77(-1.91 to -1.64)	-1.83(-1.94 to -1.72)	-1.76(-1.96 to -1.56)	-0.06(-0.08 to -0.03)

DALYs: disability-adjusted life-years; ASIR: age-standardized incidence rate; ASMR: age-standardized mortality rate; ASDR: age-standardized DALYs rate; EAPC: estimated annual percentage change; CI: confidence interval.

Δ All data reported as number or rate (per 100,000 persons with 95% uncertainty interval).

* Percentage represents the change of the cases, EAPC represents the change in rates.

Results

Global incidence, mortality, and DALYs

In 2019, the incident cases of UTI, urolithiasis, and BPH were 404.61 (95%UI: 359.43 to 446.55), 115.55 (95%UI: 93.05 to 140.18), and 11.27 (95%UI: 8.79 to 14.46) million. Compared with 1990, the incident cases of UTI, urolithiasis, and BPH increased by 60.40%, 48.57%, and 105.70%, respectively. The age-standardized incidence rate (ASIR) of UTI (5,075.89/100,000, 95%UI: 4,516.65/100,000 to 5,594.1/100,000) was 3.64 times higher than urolithiasis (1,394.03/100,000, 95%UI: 1,126.4/100,000 to 1,688.16/100,000) and 18.10 times higher than BPH (280.4/100,000, 95%UI: 219.62 to 360.32) in 2019 (Table 1). In addition, the ASIR of urolithiasis and BPH showed a decrease trend with an EAPC of -0.83 (95%CI: -0.92 to -0.74) and -0.03 (95%CI: -0.05 to -0.01) while the ASIR of UTI showed an increased trend (EAPC: 0.08, 95%CI: 0.04 to 0.11) (Fig. 1a).

Compared with 1990, the deaths of UTI and urolithiasis increased by 140.18% and 17.12% in 2019. The number of deaths and age-standardized mortality rate (ASMR) of UTI were 17.83 times and 18.53 times that of urolithiasis, respectively (Table 1). From 1990 to 2019, The ASMR of UTI increased from 2.77/100,000 (95%UI: 2.51/100,000 to 3.02/100,000) to 3.13/100,000 (95%UI: 2.61/100,000 to 3.43/100,000) with an EAPC of 0.55 (95%CI: 0.47 to 0.62), while the ASMR of urolithiasis decreased from 0.30/100,000 (95%UI: 0.20/100,000 to 0.37/100,000) to 0.17/100,000 (95%UI: 0.14/100,000 to 0.21/100,000) with an EAPC of -2.05 (95%CI: -2.24 to -1.86) (Table 1 and Fig. 1b).

Globally, UTI was attribute to the most DALYs among these three diseases, which was 8.61 times and 2.79 times that of urolithiasis and BPH, respectively. The largest increase of DALYs was found in BPH with 110.56%, followed by UTI (68.89%) and urolithiasis (16.95%) during the study period. Generally, age-standardized DALYs rate (ASDR) of these three diseases showed a decrease trend (Fig. 1c). The largest decrease was recorded in urolithiasis with an EAPC of -1.77 (95%CI: -1.91 to -1.64).

Regional incidence, mortality, and DALYs

In 2019, more than one fifth UTI cases occurred in South Asia, Western Europe and Tropical Latin America. The top five regions with incident cases of urolithiasis were South Asia, East Asia, Eastern Europe, Southeast Asia, and Western Europe, which were the same as BPH (Table S1). Indeed, Eastern Europe showed the highest ASIR in urolithiasis (4,433.72/100,000, 95%UI: 3,542.49/100,000 to 5,414.66/100,000) and BPH (629.82/100,000, 95%UI: 500.32/100,000 to 790.3/100,000). The highest ASIR of UTI recorded in Andean Latin America (13,163.85/100,000, 95%UI: 11,554.82/100,000 to 14,741.08/100,000) and Tropical Latin America (13,085.96/100,000, 95%UI: 11,490.17/100,000 to 14,608.79/100,000). Overall, the EAPC of ASIR for these three benign urologic diseases in most regions were over than zero (Fig. 2). Nevertheless, East Asia and High-income North America showed significant decrease of ASIR for urolithiasis with an EAPC of -2.68 (95%CI: -2.95 to -2.42) and -2.02 (95%CI: -2.33 to -1.71), respectively.

Regionally, the most deaths from UTI occurred in South Asia, almost twice as many as in Western Europe. The deaths of urolithiasis were mainly distributed in East Asia, Southeast Asia, and South Asia. The highest ASMR of UTI and urolithiasis was recorded in Tropical Latin America (9.38, 95%UI: 5.71 to 10.45) and Eastern Europe (0.55, 95%UI: 0.45 to 0.66) (Table S2). The region with the largest increase of ASMR in UTI and urolithiasis were Southern Latin America and Tropical Latin America with an EAPC of 4.92 (95%CI: 4.29 to 5.56) and 4.00 (95%CI: 3.76 to 4.24), respectively. In addition, East Asia and Central Europe showed the most significant decrease trend of ASMR both in UTI and urolithiasis (Figure S1).

Consistent with the incident cases and deaths, the region with the highest DALYs of UTI and urolithiasis was South Asia, and the highest DALYs of BPH was East Asia. The highest ASDR of UTI were found in Tropical Latin America (167.29, 95%UI: 114.4 to 183.79), and the highest ASDR of urolithiasis (23.61, 95%UI: 18.69 to 29.23) and BPH (128.09, 95%UI: 76.46 to 189.95) were found in Eastern Europe (Table S3). The largest increase of ASDR in UTI was observed in Southern Latin America with an EAPC of 4.12 (95%CI: 3.6 to 4.64) from 1990 to 2019. The EAPC of ASDR in urolithiasis and BPH in most regions was higher than the global level (Figure S2).

National incidence, mortality, and DALYs

In 2019, three countries with the highest incident cases of UTI were India, Brazil and the USA. The most incident cases of urolithiasis and BPH were both found in India, China and Russian Federation. The highest ASIR for UTI, urolithiasis, and BPH was found in Ecuador (15,542.88/100,000, 95%UI: 13,708.11/100,000 to 17,401.43/100,000), Russian Federation (4,541.88/100,000, 95%UI: 3,648.94/100,000 to 5,522.00/100,000), and Lithuania (661.64/100,000, 95%UI: 547.15/100,000 to 790.35/100,000), respectively (Table S4). From 1990 to 2019, Ecuador (EAPC = 1.09, 95%CI: 0.95 to 1.24), Jordan (EAPC = 2.10, 95%CI: 1.74 to 2.47), and Mauritius (EAPC = 0.42, 95%CI: 0.38 to 0.46) had the largest increase of ASIR of UTI, urolithiasis, and BPH, respectively (Fig. 3).

India (55,558.41, 95%UI: 42,788.06 to 66,161.17) had the highest deaths of UTI and China (2,558.42, 95%UI: 1,733.75 to 3,527.82) had the highest deaths of urolithiasis in 2019. The highest ASMR of UTI and urolithiasis was recorded in Barbados (12.02/100,000, 95%UI: 8.50/100,000 to 14.55/100,000) and Armenia (1.82/100,000, 95%UI: 0.94/100,000 to 4.03/100,000), respectively (Table S4). Armenia (EAPC = 8.48, 95%CI: 7.28 to 9.69) and Portugal (EAPC = 8.28, 95%CI: 7.36 to 9.20) had the largest increase of ASMR in UTI. Costa Rica (EAPC = 7.18, 95%CI: 6.30 to 8.06) and Georgia (EAPC = 7.12, 95%CI: 5.62 to 8.64) had the largest increase of ASMR in urolithiasis (Figure S3).

The highest DALYs were recorded in India for UTI and urolithiasis, and in China for BPH. ASDR was highest in Tajikistan (242.35/100,000, 95%UI: 172.84/100,000 to 301.91/100,000) for UTI, in Lithuania (136.44/100,000, 95%UI: 85.33/100,000 to 200.10/100,000) for BPH and in Armenia (33.33/100,000, 95%UI: 21.71/100,000 to 61.27/100,000) for urolithiasis. The most significant increase of ASDR was found in Portugal for UTI with an EAPC of 6.44 (95%CI: 5.67 to 7.21), in Trinidad and Tobago (EAPC = 2.84, 95%CI: 2.30 to 3.38) for urolithiasis and in Mauritius (EAPC = 0.46, 95%CI: 0.42 to 0.49) for BPH (Figure S4).

Burden of the three urologic benign diseases by SDI

The incident cases, deaths, and DALYs of UTI were most distributed in middle and low-middle SDI regions, while the urolithiasis and BPH were most distributed in middle and high-middle SDI regions (Table S1-3). In addition, the ASIR and SDI of urolithiasis in regions with high SDI from 1990 to 2019 were negatively correlated, while the opposite trend was in regions with low SDI (Fig. 4). The ASDR and ASMR of urolithiasis were detective a negative correlation with SDIs in most GBD regions from 1990 to 2019 (Figure S5-S6). Nationally, generally positive correlations between ASIR of these three urologic benign diseases and SDI in 2019 were recorded (Fig. 4, Figure S7-S8). The ASDR and SDI for BPH in 2019 also presented a positive correlation (Figure S9). The ASDR and ASMR of UTI didn't showed obvious correlation with SDI value no matter from the regional level or the national level (Figure S10-S11).

Burden of the three urologic benign diseases by age and sex

In 2019, the incident cases of UTI mainly concentrated in 25–34 and 0–14 age group. The incident cases of urolithiasis concentrated in 50–54 age group both in female and male. The ASIR of UTI in female was 3.59 times that of male, while the ASIR of urolithiasis in male was 1.96 times higher than female in 2019. The incidence of UTI was highest in 30–34 and over 80 age group among female and male respectively. The incidence rate of urolithiasis in male was 1.96 times higher than female, and was highest in 55–59 age group in both sexes. For BPH, both incident cases and incidence were highest in 65–69 age group (Figure S12). The deaths and mortality rate of UTI and urolithiasis increased with age both in female and male. ASMR was 1.36 times more common in male (0.2/100,000, 95%UI: 0.13/100,000 to 0.26/100,000) with urolithiasis than in female (0.15/100,000, 95%UI: 0.12/100,000 to 0.19/100,000), while male and female with UTI had roughly the same ASMR across age groups (Figure S13). The DALYs of UTI mainly focus on 0–14 and over 80 age groups, urolithiasis was mainly in 45–54 age group, and BPH was mainly in 65–69 age group. The rate of DALYs was increased with age for UTI and urolithiasis while highest in 75–79 age group for BPH (Figure S14).

Discussion

From 1990 to 2019, the global incident cases of these three urologic benign diseases showed a substantial increase. Meanwhile, we observed a decrease trend of ASIR in urolithiasis and BPH during the study period, which indicate the increased cases may due to the population growth and the general aging process. UTI is one of the most common microbial infections in humans. Our results showed that the incidence of UTI remained much higher than urolithiasis and BPH, and the ASIR showed an increase trend. The increased rates of antimicrobial resistance and the changes in population structure may partially explain this phenomenon(10, 11). UTI range in severity from mild self-limited to severe sepsis, with a mortality rate of 20–40%(12). In addition, for special populations of UTI such as the elderly, men, pregnant women, trauma patients, and patients who use urinary catheters in medical institutions, there are certain challenges in the management, and the risk of death also increases(13–15). Our results showed an increased ASMR for UTI over the past 30 years, which indicates that we need to pay more attention to those specific populations and improve treatment effect. The decrease of ASMR in urolithiasis over the past 30 years was inseparable from the innovation of surgical paradigm and the advancement of guidelines(7, 16). For another, it may be attributed to the early diagnosis and treatment of its comorbidities such as chronic kidney disease or end stage renal disease(17). In these urologic benign diseases, UTI had the highest DALYs and BPH had the most significant increase. Meanwhile, we found the ASDR of these three urologic benign diseases were decrease in the past decades. BPH often manifests as lower urinary tract symptoms (LUTS), which seriously affects the quality of life. On the one hand, the aging population may explain the increased disease burden of BPH(18). On the other hand, uneven allocation of medical resources in underdeveloped areas is still an important challenge, including the underdiagnose, undertreatment, and the disparate ratio of urologists and patients(18, 19). In this study, we explored the global burden of these three urologic benign diseases and provided evidence for the targeted formulation of health care policies and the allocation of medical resources in the future.

At regional and national levels, the number of incident cases, deaths and DALYs of UTI mainly distributed in South Asia and Western Europe, while the corresponding ASR were the highest in the Tropical Latin America. Consistently, the antibiotic resistance in Europe and Asia was significantly higher than before and multidrug-resistant *E.coli* was also increased steadily worldwide(20–22). Besides, lacking of antibiotic use surveillance systems in some undeveloped areas or inappropriate use of empirical antibiotics may further aggravate the antibiotic resistance problem(23, 24). As for urolithiasis and BPH, East Asia, Southeast Asia, and South Asia were recorded the most incident cases, deaths and DALYs, while Eastern Europe had the highest corresponding ASR. Even so, East Asia was recorded to have the largest decrease of ASMR in urolithiasis over the past three decades. In addition, we found India had the most incident cases of these three urologic benign diseases and China had the most deaths of urolithiasis and DALYs of BPH. China and India are the two most populous countries in the world, then the large population base and aging may relate to the most incident cases. In addition, urolithiasis has obvious geographical distribution characteristics due to the factors such as mineral distribution, climate, ethnicity, and dietary habits(7). Moreover, we found that the ASIR of these three urologic benign diseases was higher in those countries with high SDI in 2019, while the ASDR and ASMR of urolithiasis decreased with SDI in most regions from 1990 to 2019. High SDI regions and countries may mean more patients engagements in medical care and a more complete medical and healthcare system. Therefore, the development of artificial intelligence-assisted medical systems and online clinic services is an effective way to help underdeveloped areas directly obtain external medical resources, which is conducive to achieving universal health coverage.

We found the 25 to 35 years old women had the highest incidence of UTI, which is consistent with previous studies(25, 26). Changes in behavioral factors and physiological functions may affect the incidence of UTI in women. First, the strongest risk factors for UTI in premenopausal women were sexual intercourse, use of spermicides, pregnancy, and previous UTI(27). Second, estrogen reduction, changes in vaginal microbial flora and pH and impairing of bladder emptying function in elderly women also increase the risks. Finally, diabetes, dyslipidemia, urolithiasis, long-term indwelling catheters and neurogenic bladder are comorbid conditions that increase risk in both sexes(27, 28). On the contrary, evidence revealed that the incidence of urolithiasis in male has been significantly higher than that in female over a century, and this sex gap is narrowing(29, 30). Our findings showed that the ratio of male to female in ASIR have dropped from 2.21 to 1.96 in the past 30 years. This may be related to the changes of diet, increase in metabolic syndrome, and the innovation of surgical intervention(31, 32). In addition, we observed the ASMR and ASDR of UTI and urolithiasis dramatically increases over 70 years old. This may be due to the poor tolerance of the elderly to severe infections and the prone to complications, including decreased bone mineral density, cardiovascular disease, and chronic kidney disease(32). To our knowledge, the prevalence of BPH increased with age, ranging from 50%-75% over 50 years old to 80% over 70 years old(33). We also found the ASDR of BPH increased with age while decreased over 80 years old. Therefore, we inferred that most patients were treated with drug or surgical intervention in the early stage of disease, and the symptoms of LUTS/BPH were improved or controlled, so the DALYs and ASDR in the age group older than 80 years were decreased compared to the pre-80 age group.

Although this article comprehensively analyzed the burden of these three urologic benign diseases in different regions and countries around the world, it still had certain limitations. First, GBD data sources are limited and cannot cover all populations or regions, so the data only represent the general situation of a certain region. Second, the quality of the data is uneven, and the heterogeneity of the data can be caused by the differences in the diagnostic standards,

detection methods and supervision systems in regions with different levels of development. Third, due to the limitation of the definition of disease given by GBD, the burden of diseases may be underestimated.

Conclusion

Over the past three decades, the disease burden remains increased in UTI, while decreased in urolithiasis and BPH. The allocation of medical resources should be more based on the epidemiological characteristics and geographical distribution of diseases.

Abbreviations

ASR, age-standardized rates

ASDR, age-standardized DALYs rate

ASMR, age-standardized mortality rate

ASIR, age-standardized incidence rate

BPH, benign prostatic hyperplasia

CI, confidence interval

DALYs, disability-adjusted life-years

EAPC, estimated annual percentage changes

GBD 2019, Global Burden of Disease Study 2019

ICD, International Classification of Diseases

SDI, socio-demographic index

UI, uncertainty interval

UTI, urinary tract infections

YLD, years lived with disability

YLLs, years of life lost

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated during the current study are available in the Global Health Data Exchange query tool (<http://ghdx.healthdata.org/gbd-results-tool>).

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

ZC, WDQ, and ZH collected and analyzed the data and was a major contributor in the writing of the manuscript. HQ was in charge of data analyzing and proofreading. GJM, LLY, GXP and LY participated in data collecting and analyzing. FC, LXD, and ZXT contributed to the study design and revised the manuscript. All authors read and approved the final manuscript.

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Figures

Figure 1

Global Trends of ASIR, ASMR, ASDR of the three urologic benign diseases from 1990 to 2019. a: ASIR. b: ASMR. c: ASDR. ASIR: age-standardized incidence rate; ASMR: age-standardized mortality rate; ASDR: age-standardized DALYs rate.

Figure 2

The EAPC of the ASIR of the three urologic benign diseases in global and 21 regions. a: urinary tract infections. b: urolithiasis. c: benign prostatic hyperplasia. ASIR: age-standardized incidence rate; EAPC: estimated annual percentage change.

Figure 3

The EAPC of ASIR of the three urologic benign diseases in 204 countries and territories. a: urinary tract infection; b: urolithiasis. c: benign prostatic hyperplasia. ASIR: age-standardized incidence rate; EAPC: estimated annual percentage change

Figure 4

ASIR of urolithiasis for 21 regions and 204 countries and territories by SDI. a: 21 regions from 1990 to 2019; b: 204 countries and territories in 2019. ASIR: age-standardized incidence rate; SDI: sociodemographic index.

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