Urolithiasis in a Rural Wisconsin Population From 1992 to 2008: Narrowing of the Male-to-Female Ratio

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Purpose: Urolithiasis is a common disease with multiple etiologies and risk factors. Studies suggest an increased incidence in developed nations in recent decades as well as differential geographic incidence and prevalence rates, and differences between the genders. We updated urolithiasis epidemiological data by examining the incidence and prevalence rates in a stable rural Wisconsin population.

Materials and Methods: Data were obtained from the Marshfield Epidemiologic Study Area database, a surveillance tool created in 1991 to track disease in residents of an area of 24 ZIP Codes including approximately 85,000 individuals, of whom most receive care at Marshfield Clinic and affiliates. Urolithiasis cases were identified using ICD-9 codes. Incidence, prevalence and recurrence rates were determined.

Results: The mean age adjusted incidence of new onset urolithiasis per 100,000 person-years was 202 (95% CL 168–235) in 1992 and 289 (95% CL 253–325) in 2008. In women the increase per 100,000 person-years was higher than in men, that is 171 (95% CL 129–213) and 289 (95% CL 238–340) vs 238 (95% CL 184–290) and 296 (95% CL 244–348), respectively. The male-to-female incidence ratio decreased from 1.4 to 1.0. The age adjusted prevalence per 100,000 individuals was 1,968 (2%) and 3,554 (3.5%) in 1992 and 2008, respectively. The increase in women was higher than in men (52% vs 26%). The age adjusted recurrence rate per 100,000 individuals was 553 (0.72%) and 676 (1.0%) in 1992 and 2008, respectively. The increase in women was higher than in men (88% vs 20%).

Conclusions: Since 1992, urolithiasis incidence, prevalence and recurrence rates in this rural Wisconsin population have increased with higher increases noted in women. While prevalence increased, it was lower than reported in other geographic areas in the United States.

Key Words: kidney, urolithiasis, Wisconsin, male, female

Abbreviations and Acronyms

MC = Marshfield Clinic

MESA = Marshfield Epidemiologic Study Area

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UROLITHIASIS is a debilitating and often chronic condition with a reported annual incidence of 10% to 15% in the United States[1,2] and an increasing prevalence.[3] Recent reports suggest increased occurrence in women.[4–7] The annual direct cost of urolithiasis in the United States is estimated at $2.1 billion or greater[8] with some estimates more than twice that amount.[9] The lifetime recurrence risk is 50% with an estimated time to recurrence of within 1 year in 10% of cases, within 5 years in 35% to 50% and by 10 years in 50% or greater.[10] The true population incidence and prevalence of urolithiasis are difficult to study.

Prior groups used data of variable accuracy, eg individual self-reports,

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hospital discharge data and databases of specific health care organizations, referral populations or ethnic groups. Many quantified only symptomatic calculi, potentially decreasing overall estimates, especially since the advent of computerized tomography and other imaging modalities has made diagnosing asymptomatic stones common.

Knowledge of the true urolithiasis occurrence, that is the sum of incidence and recurrence, is crucial to determine the total disease burden and develop health care policy. Knowledge of the regional urolithiasis burden is important to develop regional policies and allocate health care resources appropriately. Epidemiological research will help clarify the natural history of urolithiasis so that preventive measures can be advanced, and the health impact and economic burden on those affected decrease. Given reported geographic differences in incidence, careful local/regional studies are needed. Together regional data will provide greater understanding of the nationwide picture of urolithiasis.

Johnson et al performed a seminal study in a well-defined population,[1] which was recently followed up by Lieske et al.[11] To our knowledge no assessment of the incidence and prevalence of urolithiasis in Wisconsin has been published to date. Our study was designed to estimate the incidence of the initial diagnosis of urinary tract calculi and describe urolithiasis prevalence and recurrence in a stable, nonreferral population from 1992 to 2008. We hypothesized that women would have an increased incidence compared to men.

METHODS

Setting and Population

MC is a large multispecialty system serving central and northern Wisconsin with more than 750 physicians on the main Marshfield campus or at 1 of the 42 regional centers. MESA is a geographic region of 24 ZIP Codes in central and northern Wisconsin, in which most residents receive medical care at MC, 1 of its satellite clinics or affiliated hospitals. Approximately 85,000 individuals are in the MESA population, including 60,000 in MESA central, the area surrounding Marshfield, and 25,000 in MESA north. This population is relatively stable with only 5% of the initial 1991 cohort lost to outward migration annually. According to the 2000 United States Census 97% of MESA residents were white and nonHispanic.

MESA was established in 1991 as a dynamic, population based cohort for disease surveillance and epidemiological research.[12] Clinical records of cohort members are available through an extensive electronic medical record system and data warehouse archive. Validation surveys indicate that MC data systems capture 97% of residents, 95% of inpatient stays, 90% of outpatient visits and 99% of deaths in the 14 MESA ZIP Codes immediately surrounding Marshfield with coverage slightly lower among the 10 MESA ZIP Codes to the north.[13] Automated review of MC computerized databases is performed regularly by MESA epidemiologists to track cohort membership, including routine examination of utility records, state and national death files, and other data in the public domain. In compliance with the Health Insurance Portability and Accountability Act this study was approved by our institutional review board and the statewide institutional review board consortium.

Database Verification and Data Validation

Detailed validation processes are done on MESA daily, monthly and annually. Validation confirms the resident status of individuals in the database and medical activity in the Marshfield health care system using previously detailed processes.[12] To verify our data we performed a pilot study before implementing the final query to determine the accuracy of the ICD-9 codes to be used and ensure data uniformity. This feasibility study identified 5,695 individuals with a total of 39,652 diagnoses of kidney stones from 1979 to 2008. Of the cases 26,347 (66%) were coded as 592.0, 12,172 (31%) were coded as 592.1 and 1,133 (3%) were coded as V13.01. Sample review determined that codes 592.0 and 592.1 had 90% specificity for kidney stones. Of cases coded with V13.01 only 100 did not have a concomitant 592.0 or 592.1 code. Record review indicated that many patients had a history of kidney stones but often at an earlier unknown date. Thus, we determined that eliminating V13.01 from the final query would result in acceptably small error. Similarly we found 288 patients diagnosed with other codes for urinary tract stones (592.9, 274.11 and 594.0-594.9) but not 592.0 or 592.1. However, manual review of a subset of these cases confirmed that only a few would be missed. Thus, we excluded these codes from the final query and from subsequent rate calculations.

Definitions

We used specific definitions for the terms incidence, prevalence and recurrent incidence (recurrence). Incidence was defined as the initial diagnosed stone event in an individual, whether or not it was symptomatic and whether or not it required hospitalization. Prevalence was defined as the proportion of the MESA population on a given day, eg December 31, who had had 1 or more lifetime stone events regardless of symptomatology and/or treatment. Finally, recurrent incidence (recurrence) was considered similar to incidence but allowed patients to be counted with additional stone events after the initial diagnosis.

Case Identification and Participants

MESA residency data are available from July 1, 1991, although patient diagnoses are archived back to 1979. We retrospectively identified all individuals in MESA who were first diagnosed from January 1, 1992 through December 31, 2008 with 1 or more of the 2 major ICD-9 codes (592.0 and 592.1) verified by our feasibility study. A random sample of 100 charts was manually reviewed by trained abstractors to evaluate validity. After eliminating 288 cases without the required ICD-9 codes, 3,212 incident diagnoses were identified during the study period, as were a total of 9,642 incident and recurrent events.

We separated them by year into appropriate case categories (fig. 1).

Statistical Analysis

The incidence rate of newly detected urolithiasis from 1992 to 2008 was estimated as the number of subjects with an initial diagnosis divided by the sum of accrued person-time at risk in the MESA population. Cases with a confirmed diagnosis at any point before 1992 were considered prevalent cases and, thus, excluded from incidence analysis. Prevalence rates were estimated as the number of subjects with previously diagnosed urolithiasis divided by the total number of MESA residents in the corresponding age and gender specific categories on December 31 of each year from 1992 to 2008. Recurrence rates were calculated by including additional stone diagnoses made more than 3 months after a previous diagnosis. The 3-month cutoff was chosen as the best way to exclude complications or ongoing care from the incident diagnosis while still capturing additional stone recurrences. All prevalence and incidence rates were age adjusted to the 2000 United States Standard population using the direct method. We calculated the 95% CL for prevalence and incidence estimates using the Poisson distribution. The t and Wilcoxon 2-sample tests were used for continuous variables with significance considered at 0.05 in all analyses. SAS® was used for statistical analysis.

RESULTS

Incidence

Initial diagnosis. Using the ascertainment algorithm we identified 3,212 incident cases of kidney stones. The incident rate was 202/100,000 person-years (95% CL 168–235) in 1992 and 289/100,000 person-years (95% CL 253–325) in 2008. The overall incidence increased by 43% with an annual increase of 6.8/100,000 cases (2.5%). There was no gender difference with respect to the rate of increase (difference in incidence curve slopes p = 0.97, fig. 2). However, since men had a higher incidence than women at the start of the study period (p = 0.0004), the percent change in incidence in women was higher (69% vs 24%). The male-to-female ratio narrowed through the years from 1.4 in 1992 to 1.0 in 2008.

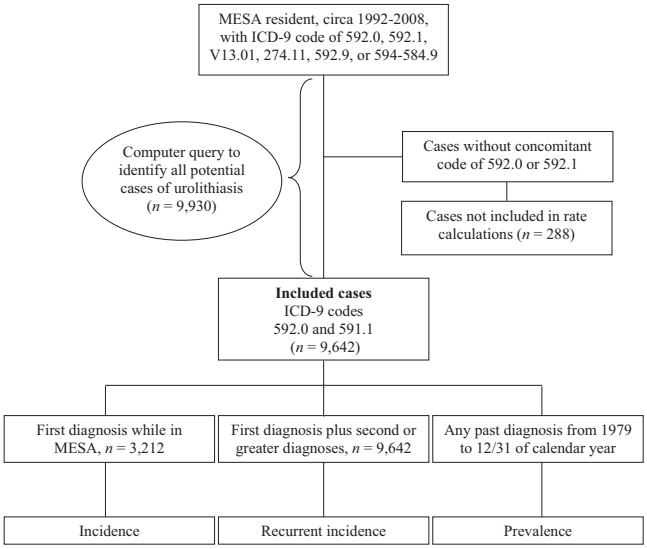

Figure 1. Case selection for study

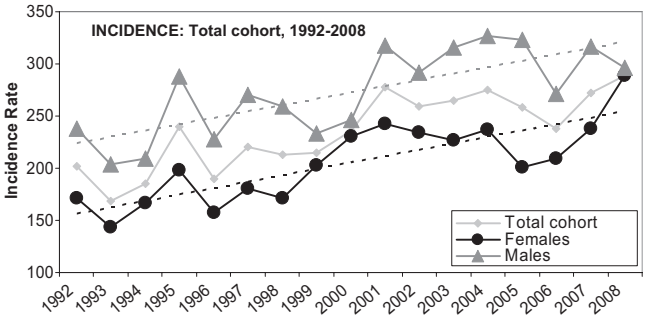

Figure 2. Age adjusted total incidence of urolithiasis per 100,000 person-years in MESA from 1992 to 2008.

By age group. An increased incidence with time was observed for each gender starting at age 15 years but it was higher in women (fig. 3). At age 30 years the incidence was relatively equal in men and women with the rate in men increasing steadily thereafter. The incidence acceleration in women was steady from ages 10 to 20 years with a sharp decrease at age 40 years. The incidence in men was stable at the younger and early adult ages, followed by a steady increase from ages 50 to 80 years (fig. 3). The incidence in men attained a peak in the 65 to 69-year age group with a rate of 568.5/100,000 person-years. In women a bimodal peak incidence was observed with the highest incidence in the 70 to 74 and 25 to 29-year age groups with a rate of 327.3 and 305.2/100,000 person-years, respectively. From 1992 to 2008 the increase in women was driven largely by the increased incidence in the 15 to 19, 40 to 44 and 20 to 24-year-old groups. In men the increase was driven by the increased incidence in much older age groups, ie ages 80 to 84 and 60 to 64 years. Figure 4 shows the incidence rate by gender and 10-year age groups.

Prevalence

Overall. The overall prevalence, that is individuals with a history of 1 stone or greater at a given time point, increased from 2.0% in 1992 to 3.5% in 2008. Prevalence was higher in men during the entire study period. The male-to-female ratio for prevalent urolithiasis was 1.8 in 1992 and 1.5 in 2008.

By age group. There was a sharp acceleration in prevalence in women and men (data not shown). In

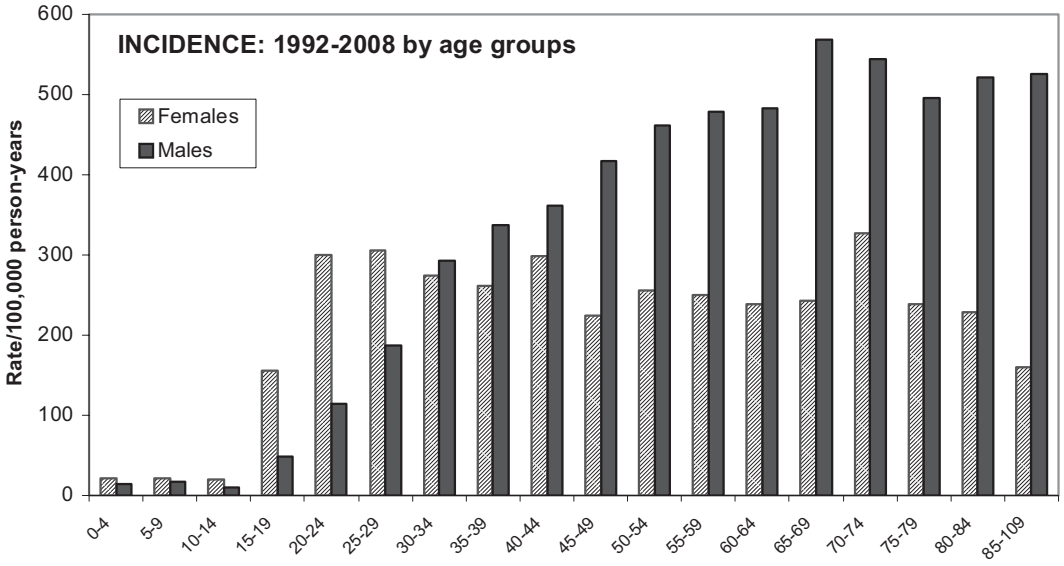

Figure 3. Urolithiasis incidence per 100,000 person-years in MESA from 1992 to 2008 by 5-year age groups, including ages 0 to 109 years.

women this occurred from ages 15 to 35 years and then again from ages 40 to 65 years. A decrease in prevalence was then noted with a final steep increase from ages 70 to 80 years. In men an accelerated increase in the prevalence rate with time was observed from ages 25 to 35 years. After decreasing, a sharp and steady acceleration in prevalence was observed at age 40 years, which persisted to age 75 years. After age 75 years a steep acceleration in prevalence occurred at age 80 years and thereafter. The age groups contributing most to the steady increase in prevalence with time were the 15 to 19 and 60 to 64-year-old groups for women, and the 10 to 14 and 85 years old or older groups in men.

Recurrent Incidence

Overall. We identified a total of 9,642 incident and recurrent cases. The overall recurrence rate, which included second or greater diagnoses that occurred 90 days or more after the prior diagnosis, increased from 553 to 676/100,000 person-years from 1992 to 2008.

By age group. Age related recurrent incidence rates (data not shown) resembled the incidence rates (fig. 2). While recurrent incidence rates in men in the sixth and seventh decades of life were approximately double that in women, recurrence rates in females at ages 15 to 30 years were higher than in men of the same age (data not shown).

DISCUSSION

We identified the increasing incidence, recurrence and prevalence of urolithiasis from 1992 to 2008 in a stable cohort of residents in a largely nonurban section of northern Wisconsin. Higher increases in women were noted, resulting in a 1:1 gender incidence ratio in 2008. Results were calculated using United States Census data and support prior studies documenting an increased occurrence in women,[4–7,11] including during late adolescence through age 29 years.[14] Preventive strategies aimed at specific gender and age groups appear warranted.

Due to the significant implications for health care, factual data on urolithiasis epidemiology are needed. Accurate, reliable estimates are possible with adequately designed studies that use population data and appropriate statistical methodology. Assumptions leading to potential error include assuming that the proportion of urinary tract stones is uniform across regions, medical care facilities and/or health maintenance organizations; that data on gender and/or age specific cohorts may be generalized to the total population; that hospital discharges are surrogates for actual patients; and that data on individual self-reported stone events, such as from surveys or questionnaires, are accurate. Many groups have used designs with 1 or more of these assumptions. While some useful knowledge has been obtained, studies are needed that use population census data as the denominator in rate calculations.

Geographic differences in urolithiasis occurrence have been reported[15–17] but other series suggest decreased regional variation.[18] Assuming that geographic or regional differences exist, whether due to

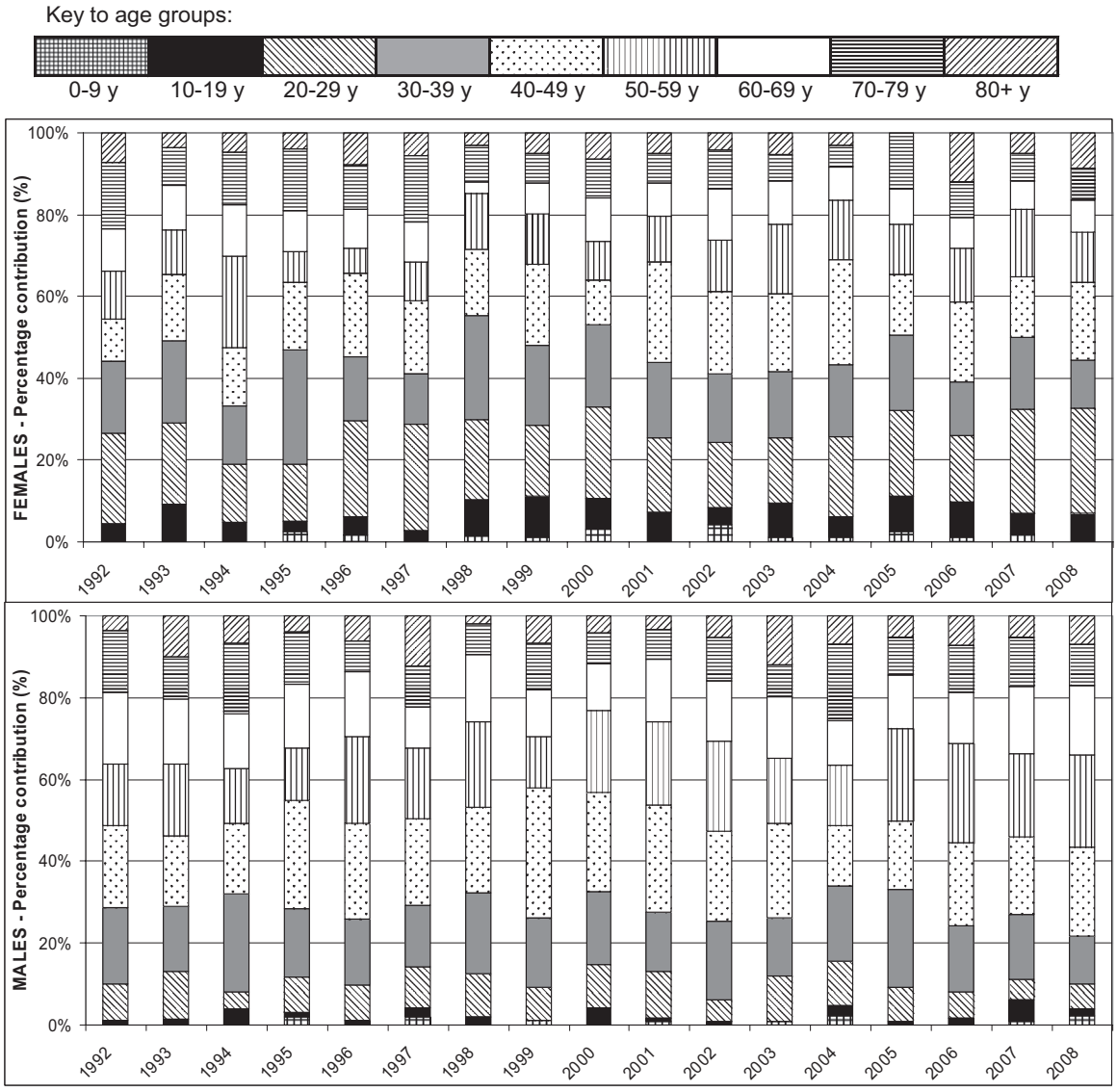

Figure 4. Relative percent of incident urolithiasis in MESA in each gender by 10-year age groups from 1992 through 2008

factors such as climate, socioeconomic status, race, heritability, diet and/or health status/comorbidities, regional studies using comparable methodologies must be done to piece together a national and eventually a global picture of the urolithiasis problem. Contributions toward the development of this broader picture have been made[19,20] and they warrant expansion.

What may contribute to an increase in the incidence rate in women compared to men? Typically a higher rate of urinary tract infection is thought to skew the gender distribution for urolithiasis. Our data did not allow us to rule this out but the changing gender distribution speaks more to social or environmental etiologies, as suggested by others.[4] One such reason may be diet related. Perhaps the diet of women has changed in the last decade or so to more closely resemble that of men. As women continue to enter professional occupations and work situations traditionally held by men, concomitant changes in dietary patterns could be a factor, especially in certain age groups. As the trend toward adolescent women to be involved in athletics and other sporting events grows commensurate to that of young men, perhaps changes in eating and/or hydration status accompanying this trend could explain changes in incidence.

Another factor accounting for a portion of the difference detected in the incidence in women vs men could be that health care utilization by women may be higher than by men, especially during the childbearing years. Due to increased health care utilization, disproportionate use of computerized tomography and other imaging could have led to the

increased detection of incidental or asymptomatic urinary calculi. On the other hand, because of the well-known propensity for lower urinary tract symptoms to develop in men later in life, due for example to an enlarged prostate, men may undergo more diagnostic testing of the urinary tract in later years than women. This may account in part for the differences in stone epidemiology in women vs men in the sixth decade of life and thereafter. Further regional studies and longer term followup may provide definitive explanations for changing gender trends.

There are potential limitations of our study. 1) While we did not exclude asymptomatic stones, as have earlier reports, our data nonetheless missed cases in which stones were not detected by the medical care system. This lack of detection would have contributed to an underreporting of incidence, recurrence and prevalence rates. 2) A few cases received alternate, nonspecific diagnosis codes only and were not included in rate analysis, which resulted in a mild underreporting of events. However, manual validation of a significant percent of these charts confirmed that this was a small source of error.

CONCLUSIONS

Since 1992, urolithiasis incidence, prevalence and recurrence rates in this rural Wisconsin population have increased. Higher increases were noted in women, resulting in a male-to-female incidence ratio of 1:1. While prevalence increased, it was lower than reported in other geographic areas.

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