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Original Article

Urinary stone disease burden is increased in patients with cognitive impairment

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Abstract: Mental illness and brain disorders such as dementia are commonly encountered in patients with cognitive impairment in urology. In this cohort study, we assessed the prevalence and outcomes of inpatient admissions for stone disease in patients with cognitive impairment. Using the National Inpatient Sample database, we identified adults (>18 years) with stone disease between 2015 and 2019. The patients were dichotomized based on the presence or absence of cognitive impairment. The groups were compared for baseline differences in inpatient admissions and hospital complications. We evaluated the independent factors associated with urinary complications in the population using multivariate logistic regression. We identified 223,072 patients with stone disease. Patients with cognitive impairment were significantly (P<0.001) older (68 vs. 62 years), female (55.7% vs. 47.4%), had government-issued insurance (77.5% vs. 64.4%), and were discharged to a nursing facility (31.7% vs. 14.2%). Patients with cognitive impairment had significantly higher rates of urinary tract infection (29.7% vs. 21.5%, P<0.001), pneumonia (5.6% vs. 4.6%, P<0.001), systemic sepsis (4.3% vs. 3.8%, P<0.001), and acute renal failure (0.9% vs. 0.7%, P = 0.008). Female sex, low income, and cognitive impairment were all independently more likely to experience a urinary complication, with significant differences (P<0.001). Patients with cognitive impairment have a higher prevalence of stone disease and urinary complications associated with inpatient admissions than the rest of the population. Health care inequities among cognitively impaired patients should be a topic of further study.

Keywords: Disparities, national inpatient sample, cognitive impairment, stone disease

Introduction

Cognitive impairment among urology patients, such as those with mental illness and brain disorders, represents a major public health concern [1]. In the United States, 21% of the population lives with a mental illness [2]. Stressors such as COVID have made a significant impact on these numbers, with nearly one in four adults experiencing significant distress secondary to the pandemic [3]. With an aging population in the United States, the total number of patients with dementia is also predicted to rise rapidly [3]. Patients with cognitive impairment, either from mental illness or brain disorders, are likely to have increased utilization of healthcare resources, higher costs, and in general, worse outcomes [4]. Studies to date have focused on the emotional impact of urologic malignancies on mental health; however, a significant gap in care exists regarding the impact of cognitive impairment in stone disease [5].

There is a lack of research available on how mental health impacts disease in urology even for common conditions such as nephrolithiasis, which has a prevalence of 10.6% in men and 7.1% in women, and represents one of the most commonly encountered problems by the urologist [6]. For patients with a history of either schizophrenia or bipolar disorder, patients have an increased prevalence of obesity, which is associated with greater severity of kidney stone disease due to increased urinary calcium, uric acid, and oxalate excretion [7]. Patients with cognitive impairment are also subject to certain risky behavior such as poor nutrition, physical inactivity, smoking, drinking, insufficient sleep, and a reluctance to seek medical care which may predispose this population to a higher stone disease burden [8]. Patients with cognitive impairment are also at higher risk of developing chronic conditions which may be exacerbated by stone disease [9]. In sum, patients with a cognitive impairment are likely at a higher risk for stone disease.

Research has shown that there may be a link between cognitive impairment and the incidence of urinary calculi, or kidney stones. A study published in the Journal of the American Geriatrics Society found that older adults with cognitive impairment had a higher risk of developing kidney stones than those without cognitive impairment [10]. Another study published in the journal PLoS ONE found that individuals with a history of cognitive impairment had a higher incidence of kidney stones than those without such a history [11]. The exact mechanism behind this link is not yet fully understood, but some theories suggest that cognitive impairment may be associated with decreased physical activity, increased dehydration, and changes in dietary habits, all of which can contribute to the development of kidney stones. These findings suggest that individuals with cognitive impairment may benefit from increased monitoring and interventions to reduce their risk of developing kidney stones. Using the National Inpatient Sample (NIS) database between 2015 and 2019, we aimed to explore the prevalence and healthcare utilization of urinary tract stone disease among patients with cognitive impairment compared with the general population.

Materials and methods

Data acquisition

As a component of the Healthcare Cost and Utilization Project, NIS represents the largest all-payer database. The NIS covers more than 97% of the U.S. population. As such, the NIS accounts for approximately 20% of all discharges from US community hospitals, with approximately 7 million hospital admissions. The NIS has been used extensively in urology to assess national trends in its utilization, treatment, and outcomes [12-14].

After institutional review board approval, all adult patients (>18 years old) with stone disease were identified in the NIS between 2015 and 2019. A total number of 223,072 admissions for stone disease met the inclusion criteria. Patients admitted to the hospital for stone disease were included in the study. The cohort was dichotomized into two groups of patients with and without cognitive impairment. 40,094 (18.0%) patients were diagnosed with cognitive impairment and 182,978 (72.0%) without a cognitive impairment. Patients with missing data values in basic demographic data were excluded. Patients were identified based on the International Classification of Disease, Tenth Revision (ICD-10) by the presence of stone disease defined as a calculus of the kidney (N20.0), calculus of the ureter (N20.1), calculus of the bladder (N21.0), calculus of the urethra (N21.1), multiple stones (N20.2), or unspecified stone disease (N20.9, N21.8, N21.9, N22.0, N23.0, and N21.8). The cognitive impairment cohort was defined based on ICD-10 codes into three major categories: depression, psychosis, and dementia. Depression was further defined as post-schizophrenic depression (F20.4), bipolar disorder (F31.3-F31.5), depressive episode (F32), recurrent depressive episode (F33), dysthymic disorder (F34.1), mixed anxiety and depressive disorder (F41.2), and adjustment disorder (F43.2). Psychosis was further defined as schizophrenia (F20), delusional disorders (F22-F25), other psychotic disorders not due to a substance or known physiological condition (F28), unspecified psychosis not due to a substance or known physiological condition (F29), mania with psychotic symptoms (F30.2), and bipolar affective disorder (F31.2, F31.5). Dementia was further defined as dementia in Alzheimer's disease (F00-F03; G30) or delirium due to known physiological conditions (G31.1). For simplicity, due to the ambiguity of the ICD-10 codes, the procedures were defined as stone fragmentation (0TFxxxx) or drainage (0T9xxxx).

Endpoints

Inpatient demographics included age, sex, race, insurance status, income level, disposition, hospital region, hospital teaching status, length of stay, and total hospital charges.

The ICD-10 codes for complications were used based on the National Surgical Quality Improvement Program [15]. The complications are defined as superficial surgical site infection (SSI) [T81.41xA], Deep SSI [T81.42xA], perito-

Table 1. Baseline of patients demographics

n = 223,072		Cognitive Impairment Absent (182,978)	Cognitive Impairment Present (40,094)	*P*-value
Age		62 [18-90]	68 [18-90]	<0.001
Sex	Female	86,754 (47.4%)	22347 (55.7%)	<0.001
Obesity		27,776 (15.2%)	5,820 (17.0%)	<0.001
Race	White	128,851 (70.4%)	30,677 (76.5%)	<0.001
	Black	18,365 (10.0%)	3,407 (8.5%)	
	Other	35,762 (19.5%)	6,010 (15.0%)	
Diabetes		48,362 (26.4%)	11,120 (27.7%)	<0.001
Hypertension		94,462 (51.6%)	23,246 (58.0%)	<0.001
Metabolic syndromes		348 (0.2%)	82 (0.2%)	0.575
Drug abuse		11,786 (6.4%)	3,692 (9.2%)	<0.001
Insurance	Government	117,822 (64.4%)	31079 (77.5%)	<0.001
	Private	50,751 (27.7%)	7087 (17.7%)	
	Other	14,405 (7.9%)	1928 (4.8%)	
Income	Quartile 4	37,146 (20.3%)	8122 (20.3%)	0.845
	Quartile 1-3	145,832 (79.7%)	31972 (79.7%)	
Disposition	Home	152,126 (83.2%)	26235 (65.4%)	<0.001
	Nursing facility	26,035 (14.2%)	12712 (31.7%)	
	Other	4817 (2.6%)	1147 (2.9%)	
Location	Northeast	32,969 (18.0%)	7291 (18.2%)	<0.001
	Midwest	38,273 (20.9%)	9841 (24.5%)	
	South	74,281 (40.6%)	15415 (38.4%)	
	West	37,455 (20.5%)	7547 (18.8%)	
Bed size	Medium	55,307 (30.2%)	12031 (30.0%)	0.688
	Large	90,349 (49.4%)	19861 (67.6%)	
Hospital teaching status	teaching	124,432 (68.0%)	27088 (67.6%)	0.086
Length of stay (in days)		[0-332]	4 [0-306]	<0.001
Total Hospital charges		$34,902 [$116-$893,916]	#35,546 [$104-$3,194,869]	<0.001

neal abscess [K65.1], urinary tract infection (UTI) [N39.0], acute respiratory distress syndrome (ARDS) [J80], pneumonia [J18.9], acute renal failure [N17.9], systemic sepsis [R65.20], cardiac arrest [I46.9], bleeding [R58], and deep venous thrombosis (DVT) [I82.403]. Urinary complications were defined in our analysis as UTI, acute renal failure, and systemic sepsis.

The main outcome measured was the prevalence of admission complications in patients with cognitive impairment compared with the general population.

Statistical analysis

Patient demographic differences were assessed using Fisher's exact test for categorical variables and Student's t *test* for continuous variables. The median and interquartile range (IQR) were used to record continuous variables, whereas frequencies and percentages were used to record categorical variables. A multivariate logistic regression analysis was performed using patient-described characteristics (**Table 1**). Variables that were significant in the univariate analysis were included in the multivariate logistic regression analysis. For all tests, significance was defined based on a two-tailed *p*-value of <0.05. The analysis was conducted using the Statistical Package for the Social Sciences version 28.0 (IBM Corporation). R version 4.1.0 was utilized with the RCommander package and EZR PlugIn [16].

Results

A total of 223,072 admissions for stone disease met the inclusion criteria, with 40,094 (18.0%) patients diagnosed with cognitive impairment and 182,978 (72.0%) without a cognitive impairment. In the cognitive impairment cohort, depression was documented in 25,636 cases, dementia in 14,994, and psychosis in 2,428. A summary of the population in **Table 2** shows that the total prevalence of stone disease in the cognitive impairment cohort was significantly higher than in the general population (0.7% vs. 0.8%, P<0.001). The types of treatments described in **Table 2** included were stone fragmentation and drainage procedures. Our study shows that among patients who received stone fragmentation therapy, patients with no cognitive impairment had a higher rate of treatment compared to cognitive impairment patients subgroups (1.9% vs. [1.5%, 1.4%, 1.1%], P<0.001). Additionally, among the patients who underwent drainage therapy, patients with no cognitive impairment had higher treatment rates compared to the cognitive impairment patients with an exception to patients diagnosed with dementia (5.1% vs. [4.3%, 5.4%, 4.6%], P<0.001). Patient demographics (**Table 1**) showed that compared to the population without cognitive impairment, patients with cognitive impairment were significantly more likely to be older (68 years old vs. 62 years old, P<0.001), female (55.7% vs. 47.4%, P<0.001), have insurance issued by the government (77.5% vs. 64.4%, P<0.001), and be discharged to a nursing facility (31.7% vs. 14.2%, P<0.001). Patients with cognitive impairment had a significantly longer hospital stay (4 days vs. 3 days, P<0.001). Patients with cognitive impairment had significantly higher total hospital charges ($35,546 vs. $34,902, P<0.001).

Inpatient complications were also reported in our population (**Table 3**). Patients with cognitive impairment were significantly more likely to have UTI (29.7% vs. 21.5%, P<0.001), more likely to develop pneumonia (5.6% vs. 4.6%, P<0.001), and systemic sepsis (4.3% vs. 3.8%, P<0.001). Moreover, patients with cognitive impairment were significantly more likely to develop acute renal failure (0.9% vs. 0.7%, P = 0.008). Patients with cognitive impairment experienced higher rates of complications, except that they were significantly less likely to have either peritoneal abscess (0.2% vs. 0.3%, P = 0.003) or bleeding (5.0% vs. 5.5%, P< 0.001).

Multivariate logistic regression analysis was performed for variables associated with urinary complications of stone disease (**Table 4**). Age was a significant factor associated with urinary complications (P<0.001). Female patients were 1.5 times significantly (P<0.001) to develop urinary complications. Patients with diabetes were slightly more likely to develop urinary complications with significant differences (P = 0.010). Patients from the lowest income quartile were 1.1 times significantly (P<0.001) more likely to develop urinary complications than the rest of the population by income. Patients with cognitive impairment were 1.3 times significantly (P<0.001) to develop urinary complications.

Discussion

In our cohort, patients with cognitive impairment had a higher prevalence of stone disease than that in the general population. Patients with cognitive impairment had higher rates of longer hospital stay, higher total hospital charges, and discharge to a nursing facility. Patients with cognitive impairment have a shorter life expectancy than the general population. The lower survival rates in these patients can be partly ascribed to the higher incidence of physical illness, lifestyle, side effects of medications, and disparity in health care access and utilization [17].

In our cohort, we assessed the factors associated with the increased prevalence of urinary tract stone disease among patients with cognitive impairment compared to the general population. We found that patients with cognitive impairment had a higher prevalence of obesity than that in the general population. It has been postulated that there is an overlap between cognitive impairment and obesity [18]. People diagnosed with schizophrenia have up to 3.5 times increased likelihood of being obese (BMI≥30) [19]. Other studies have reported that the rates of obesity among the US and Canadian populations with schizophrenia ranging from 42% to 60% [19, 20]. In addition, patients with bipolar or major depressive disorder have up to 1.5 times an increased likelihood of obesity [21]. Several authors have shown a strong positive association between obesity and stone formation. In a cohort of 84,225 women, elevated BMI is associated

Table 2. Baseline stone disease in patients with cognitive impairment

n = 223,072		Normal	Cognitive Impairment subgroup			Total*	*P*-value
			Depression	Dementia	psychosis		
Inpatient prevalence of stone disease		182,978 (0.7%)	25,636 (0.8%)	14,994 (0.9%)	2,428 (0.3%)	40,094 (0.8%)	<0.001
Total		24.959,954	3,318,194	1,666,143	758,828	5,300,399	
Type of stone	Kidney Stone	128,981 (70.5%)	19,293 (75.3%)	10,616 (70.8%)	1,954 (80.5%)	29,638 (73.9%)	<0.001
	Ureter Stone	19,236 (10.5%)	2,303 (9.0%)	1,235 (8.2%)	136 (5.6%)	3,462 (8.6%)	
	Bladder Stone	11,533 (6.3%)	1,173 (4.6%)	1,677 (11.2%)	128 (5.3%)	2,751 (6.9%)	
	Urethra	663 (0.4%)	70 (0.3%)	50 (0.3%)	8 (0.3%)	119 (0.3%)	
	Multiple Stones	18,347 (10.0%)	2,270 (8.9%)	1,195 (8.0%)	150 (6.2%)	3,382 (8.4%)	
	Unspecified	4,218 (2.3%)	527 (2.1%)	221 (1.5%)	52 (2.1%)	742 (1.9%)	
Treatment	Stone fragmentation	3,494 (1.9%)	391 (1.5%)	210 (1.4%)	27 (1.1%)	2,446 (6.1%)	<0.001
	Drainage	9,415 (5.1%)	1,098 (4.3%)	803 (5.4%)	112 (4.6%)	582 (1.5%)	

*Total is reported with overlap between the Cognitive Impairment Subgroups. *P*-value is based on normal and Cognitive Impairment total.

Table 3. Admissions complications in stone disease

n = 223,072	Cognitive Impairment Absent (182,978)	Cognitive Impairment Present (40,094)	Total (223,072)	*P*-value
Superficial SSI	176 (0.1%)	43 (0.1%)	219 (0.1%)	0.537
Deep SSI	83 (0%)	18 (0%)	101 (0%)	1.00
Peritoneal abscess	616 (0.3%)	99 (0.2%)	715 (0.3%)	0.003
UTI	39.414 (21.5%)	11,900 (29.7%)	51,314 (23.0%)	<0.001
ARDS	213 (0.1%)	51 (0.1%)	264 (0.1%)	0.574
PNEUMONIA	8,333 (4.6%)	2,239 (5.6%)	10,572 (4.7%)	<0.001
ARF	1,330 (0.7%)	343 (0.9%)	1,673 (0.7%)	0.008
SYSTEMIC SEPSIS	6,892 (3.8%)	1,717 (4.3%)	8,609 (3.9%)	<0.001
CVA	4 (0%)	0 (0%)	4 (0%)	1.00
MI	30 (0%)	5 (0%)	35 (0%)	0.825
CARDIAC ARREST	580 (0.3%)	116 (0.3%)	696 (0.3%)	0.401
BLEEDING	10,112 (5.5%)	1,992 (5.0%)	12,104 (5.4%)	<0.001
DVT	153 (0.1%)	34 (0.1%)	187 (0.1%)	0.924

Abbreviations: SSI = surgical site infection, UTI = urinary tract infection, ARDS = acute respiratory distress syndrome, ARF = acute renal failure, CVA = cerebrovascular accident, MI = myocardial infarction, DVT = deep venous thrombosis.

Table 4. Multivariate factors associated with urinary complications in stone disease

		OR	95% CI	*P*-value
Age		1.02	1.00-1.16	<0.001
Sex (Male)	Female	1.53	1.50-1.56	<0.001
Obesity (Absent)	Present	0.92	0.90-0.95	<0.001
Diabetes (Absent)	Present	1.03	1.01-1.05	0.010
Hypertension (Absent)	Present	0.99	0.96-1.01	0.320
Drug Abuse (Absent)	Present	0.85	0.82-0.89	<0.001
Income (Quartile 1-3)	Quartile 4	1.10	1.07-1.12	<0.001
Cognitive Impairment (Absent)	Present	1.31	1.28-1.34	<0.001

Reference group in Parentheses. Abbreviations: OR = odds Ratio and 95% CI = 95% Confidence Interval.

with a 1.30-fold increased risk of stone disease compared with women with a normal BMI [22]. Taylor and colleagues concluded that weight, BMI, and waist circumference are positively associated with an increase in the risk of kidney stones [23]. Eisner et al. showed that higher BMI is associated with changes in urinary composition predisposing to stone formation in the form of a decrease in pH, an increase in urinary sodium, uric acid, and decreasing urine citrate [7].

We found that the prevalence of type 2 diabetes mellitus (DM) was higher among patients with cognitive impairment than among the general population. This agrees with prior studies that showed that the prevalence of DM in people with schizophrenia, schizoaffective, bipolar disorders & depression is 1-3 times higher compared with the general population [24-26]. The higher prevalence of DM among patients with a cognitive impairment could be explained by genetic, lifestyle factors, and treatment effects [27]. Taylor et al. in a large cohort of 200,000 patients, concluded that the risk ratio of stone disease in people with DM was 1.38, 1.67, 1.13 in older women, younger women, and men respectively [28]. Moreover, the authors found that DM was an independent predictor of stone disease irrespective of age, diet, and BMI [28]. Insulin resistance in patients with DM is associated with impaired renal amino genesis which lowers urine pH which predisposes to uric acid renal stone formation.

People with cognitive impairment have a higher incidence of comorbid conditions, higher rates of not opting, and non-adherence to treatment, which contribute to healthcare inequality among those populations. In addition, high-risk behavior and substance abuse are more likely to be encountered in patients with cognitive impairment, particularly those with mental health [29]. Moreover, people with cognitive impairment are more likely to be abandoned by their families and more likely to be admitted to nursing facilities, which may contribute to malnutrition and reduce access to proper healthcare services [30]. This agrees with our findings in the current study, which showed that people with cognitive impairment and stone disease are more likely to be institutionalized with a higher incidence of drug abuse and more likely to have a governmental type of insurance.

Moreover, these patients are less likely to undergo definitive treatment for stone disease, with a longer hospital stay and higher hospital charges. The treatment of urinary stones in patients with cognitive impairment may present unique challenges, as these patients may have difficulty understanding and complying with treatment recommendations [11]. Therefore, treatment plans should take into consideration the patient's cognitive status and may require additional support and education for both the patient and their caregivers. In some cases, medical management with medications like alpha-blockers and thiazide diuretics may be sufficient to manage urinary stones in patients with cognitive impairment. In other cases, more invasive procedures such as shock wave lithotripsy (SWL), ureteroscopy (URS), or percutaneous nephrolithotomy (PCNL) may be necessary. It is important to weigh the risks and benefits of these procedures carefully, as patients with cognitive impairment may be at higher risk for complications [31].

Inequality in healthcare for people with cognitive impairment has been reported in the management of other health conditions, including higher rates of mortality due to cardiovascular diseases and a lower chance of receiving proper management. For example, patients with schizophrenia are less likely to be diagnosed, treated for dyslipidemia, and less likely to have surgical interventions in the form of cardiac catheterization or coronary artery bypass grafting [32]. People with cognitive impairment are also less likely to be screened for metabolic abnormalities, including DM, which may prolong the period of poor glycemic control, contributing to the development of peripheral neurovascular disease with subsequent damage to kidneys with potential long-term renal failure and other organs damage [33]. Our results showed that treatment of stone disease in patients with cognitive impairment is associated with a higher rate of urinary complications in the form of urinary tract infections, acute renal failure, and sepsis, which could be explained by the higher rate of comorbid conditions among this population, including higher disease burden and late presentation.

The NIS database is the largest inpatient database in the United States, representing all types of hospitalizations within the US, and is not affected by payment type, practice, or geographical variation, which reflects real-world data and eliminates selection bias. However, this database is not without its limitations. NIS also lacks data on intraoperative details including operative time, intraoperative complications, and laboratory data, which precludes us from performing a more detailed analysis. Furthermore, we were unable to assess the rate of readmission, which reflects access to care and financial burden among the population with cognitive impairment. Additionally, NIS lacks detailed treatment information on stone fragmentation and drainage to further understand the differences among patients.

Conclusion

This is the first contemporary analysis to evaluate the nationwide prevalence of stone disease in patients with cognitive impairment. The prevalence of stone disease is significantly higher in the population with cognitive impairment than in the general population. This could be attributed to associated comorbid conditions, including diabetes mellitus, metabolic syndrome, and dietary factors. Inequality of health care among patients with cognitive impairment leads to significantly lower rates of proper treatment, including definitive surgical intervention, and higher rates of complications. These findings may be useful in developing new strategies to properly identify and treat stone diseases in patients with cognitive decline.

Disclosure of conflict of interest

None.

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