



higher prevalence of asymptomatic renal stones in diabetic population: do we need to screen routinely?

Medicine

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ABSTRACT

Introduction: Worldwide, renal stone disease is an important cause for morbidity. This is true in case of symptomatic renal stone disease causing hospital admissions, healthcare expenditure as well as in case of asymptomatic renal stones. Asymptomatic renal stones are also a matter of serious concern due to their potential for causing symptomatic disease and silently causing kidney damage and progressing towards chronic kidney disease. Type 2 diabetes mellitus is a known risk factor for renal stone disease. In our cross-sectional study, we investigated whether asymptomatic renal stone disease, which may be an additional risk factor for kidney damage is more prevalent in diabetic patients.

Aims of the study: To test our hypothesis that, like symptomatic kidney stones, asymptomatic stones are also more prevalent in diabetic subjects as compared to matched non-diabetic controls.

Materials and methods: In this cross sectional observational study, 123 diabetic patients were compared with 129 non-diabetic subjects on the basis of routine abdominal ultrasound for the diagnosis of asymptomatic kidney stones. Patients with any history of renal stone disease or any other kidney disease including diabetic nephropathy were excluded. Presence of any other micro or macro-vascular complication including coronary artery disease were also considered as exclusion criteria. Measurements of serum calcium, phosphorus, uric acid were also done. Statistical analysis was done by calculating the chi-square between the study groups.

Result: Nearly nine percent (8.9%) subjects inside the diabetic group were found to have renal stones as compared to 2.3% ($p < 0.05$) subjects in the control group detected in ultrasonographic screening. Although obesity was more common in the diabetic group, it was not statistically significant. Mean serum calcium and uric acid levels were comparable in both the groups.

Conclusion: On the basis of the finding of our original investigation, we propose for routine ultrasonographic screening of diabetic patients for detecting asymptomatic renal stones. Although the long-term benefit of such intervention will only be proved by an interventional study.

KEYWORDS:

Asymptomatic, renal stone disease, chronic kidney disease, ultrasound, Type 2 diabetes.

Introduction:

Renal stone worldwide is one of the commonly found kidney disease. Although the lifetime risk of having a kidney stone is estimated to be 1% to 15%, the exact prevalence, which is defined as a history of any kidney stone is highly variable. The highest reported prevalence is seen in northern Thailand, Turkey and Greece (16.9%, 14.8% and 15.2%). The non-weighted global average is close to the prevalence in United States (5.46% versus 5.2%). [1][2][3][4]

With the progressive increase in global prevalence of the renal stone disease, the annual economic burden of the disease only in United States of America exceeds 5 billion. Since the disease mostly affects people of the productive age group i.e., 20-60 years, there is also a great indirect economic burden of stone disease in the form of loss of working days and overall productivity. [5]

One of the most feared complication of nephrolithiasis is the evolution to chronic kidney disease. The symptomatic stone formers are at a higher risk as compared to asymptomatic renal stone disease. The association is stronger in patients with underlying diabetic nephropathy having asymptomatic kidney stones. Renal stones damage the parenchyma by obstruction, recurrent urinary tract infection, micro-calculi in the duct of belini as well as during extracorporeal shock wave lithotripsy (ESWL). [6]

There is paucity of data regarding the follow up of asymptomatic kidney stone disease and their short and long term influences on renal functions. Long He et al. in their recent study was able to

demonstrate that after surgical procedure, asymptomatic renal stone disease patients suffer a greater amount of glomerular filtration rate (GFR) loss as compared to symptomatic renal stone disease. The effect in multivariate analysis is also positively influenced by presence of diabetes mellitus. [7]

Type 2 diabetes mellitus carries the intrinsic risk of developing nephropathy. Although at any given point in time about 20% of the patients will have microalbuminuria, significant amount of them will end-up in developing overt diabetic nephropathy (35%-40%). [8][9][10] Renal stone disease is also more prevalent in type 2 diabetes mellitus as compared to the general population. Since undetected renal stone disease will lead to additional renal damage over and above conventional risk factors for diabetic nephropathy, we planned a study to have a clear idea on the prevalence of asymptomatic renal stone disease in diabetic patients. Our hypothesis was that if we find out significantly more asymptomatic renal stone in type 2 diabetes, then routine screening for stone disease probably will be beneficial to the patients.

Materials and Methods:

This cross-sectional observational study was conducted in the Outpatient and Inpatient departments of the Department of Internal Medicine, in active collaboration from the Department of Radiology, of a tertiary care hospital in Kolkata. Patients were divided into diabetic and non-diabetic groups as per present blood glucose reports or by the history of known diabetes. Diabetic Group was defined as those patients whose age group was more than 40 years

and was either taking oral hypoglycemic agents or under insulin replacement. A minimum duration of five years was decided as the cut-off. Diabetic patients with known micro or macrovascular complications were excluded from the study. Patients with known symptoms of Nephrolithiasis or previously diagnosed or operated for urinary calculi, patients with Bladder outlet obstruction, or patients with known surgical or medical diseases of the kidneys and urogenital system were excluded. One hundred and twenty three patients were recruited in the Diabetic Group as compared to 129 patients in the Non-diabetic Control Group. Detailed History and clinical examination of the recruited patients from both the groups were documented along with the following laboratory parameters: Serum Urea, Creatinine, FBS, PPBS, HbA1C, Complete Hemogram, Serum proteins, Calcium, Phosphorus and Uric Acid. Patients had also undergone ultrasound of whole abdomen for diagnosis and documentation of Nephrolithiasis. The collected Data was statistically analyzed as per protocol. The total duration of the study was about 24 months.

Result and Analysis:

The mean age of the patient population was just above 50 years (see table 1). Most of the subjects in both the group were overweight and there was no significant difference in BMI between these groups. Although the diabetic group contained significantly more number of subjects who smoked as compared to the control group, we had already excluded people with known coronary artery disease.

Table 1: Showing the clinico-demographic Profile of the Diabetic Group and the Non-Diabetic Group

Parameters	Diabetic group (n=123)	Non-Diabetic Group (n=129)	P value
Mean Age (in Years)	52.4±5.2	54.3±6.1	P=0.29 t=1.29
Male (%)	82 (66.6%)	84 (65.1%)	P=0.73
BMI (in Kg/M2)	26.1±2.3	25.8±2.1	P=0.28 t=1.08
Smokers (%)	37 (30%)	28 (21.7%)	P=0.04

The mean calcium and phosphorus levels in diabetic group was higher in the diabetic group as compared to the control group, however the difference was not statistically significant. Hyperurecemia was not seen in the majority of the patients in both the groups.

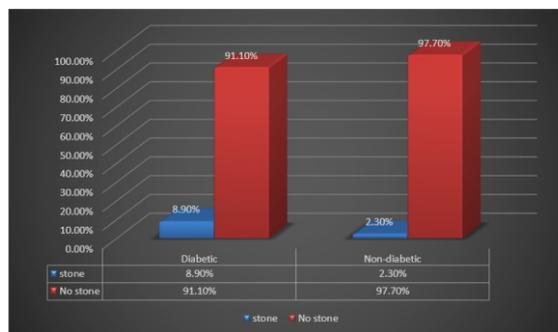
Table 2: Showing the laboratory parameters among the diabetic and non-diabetic population

Parameters	Diabetic group (n=123)	Non-Diabetic Group (n=129)	P value
Mean Hb Level	12.3±1.2	12.5±1.3	P=0.2 T=1.26
Urea (mg/dl)	44±12	46±17	P=0.05 T=1.94
Creatinine (mg/dl)	1.2±0.9	1.3±0.8	P=0.06 T=1.86
Calcium (meq/L)	5.2±1.4	4.9±1.5	P=0.1 T=1.63
Phosphorus (meq/L)	2.1±1.2	1.9±1.3	P=0.2 T=1.26
Uric Acid (mg/dl)	3.6±1.2	3.4±1.3	P=0.2 T=1.26
FBS (mg/dl)	166±3.2	96±3.6	p<0.00
PPBS (mg/dl)	220±3.6	134±13.1	P<0.00 T=317.32
HbA1C (%)	7.8±0.6	5±0.4	P<0.00

On routine USG screening, the prevalence of asymptomatic renal stone was significantly higher in the diabetic group as compared to

non-diabetic population (8.9% versus 2.3%, p=0.021).

Figure 1: Showing the prevalence of asymptomatic Renal Stones among Diabetics and Non-diabetic population:



Discussion:

Type 2 diabetes is a known predisposing factor for renal stone disease. The underlying patho-mechanism is insulin resistance. Insulin resistance predisposes diabetic population to stone formation by three different methods. Most importantly, insulin resistance produces decrease in ammonia production in proximal tubule. This is due to suppression of glutamine production and increased delivery of free fatty acids in the tubular cells. Because of decrease in urinary pH solubility of uric acid decreases leading to increase in uric acid stones. Low urinary pH also leads to hypocitraturia which in turn leads to more calcium stone formation. In vivo human studies have provided evidence that high plasma insulin levels, which is a common finding in type 2 diabetes mellitus due to insulin resistance, leads to hypercalciuria.[11]

It is now well established that type 2 DM is a risk factor for renal stone disease. There is however almost no data regarding the prevalence of asymptomatic stone disease in this special population. In our study, the prevalence of asymptomatic renal stone disease in general (non-diabetic) population was found to be 2.3%. This is comparable to the rate in United states (2.9% to 4%).[12] and even to a high prevalence “stone-belt” country like Pakistan (3%)[13]. The prevalence of asymptomatic kidney stone disease in diabetic population specifically was not very well known. Our study is first of its kind to systematically consider the prevalence of asymptomatic kidney stone disease in this special population. In our study population, the first glimpse of disease prevalence came out to be 8.9%.

Meydan N et al in their publication showed the prevalence of USD (Urinary Stone Disease) in diabetic population to be as high as 21% [14]. In another landmark study by Eric n. Taylor et al. the baseline prevalence of renal stone disease was higher in diabetic population irrespective of BMI.[11]

Asymptomatic kidney stones are not entirely innocuous. There is very scanty data regarding the natural history of asymptomatic kidney stone disease. Particularly in diabetic population. Only short term data is presented in the work of Long He et al. In this article, it was shown that after detection by ultrasonography and then surgical intervention, GFR decline in patients with asymptomatic stone disease was more as compared to their symptomatic counterpart (58.2% versus 31%, p < 0.05) [7].

The authors have proposed that the reason for accelerated GFR decline was probably the physical damage caused by long standing calyceal calculi. Burgher A et al in their study on asymptomatic renal stone disease demonstrated that 77% of patients experienced disease progression, with 26% requiring surgical intervention [15].

Asymptomatic ureteral stones are more notorious. Marchini et al. in their study showed that even asymptomatic ureteral stones are associated with less than normal GFR for that individual kidney and even after surgical intervention and correction of hydronephrosis

the GFR failed to improve to a normal value indicating chronic parenchymal damage[16].

Kidney stones not only increases the risk of CKD , which again is complicated by the presence of diabetes [17], it also increases the risk for complicated urinary tract infections. Diabetes mellitus and renal stones, both are significantly associated with poor outcome in acute pyelonephritis, even after treatment[18]. Complicated urinary tract infections associated with diabetes and renal stone disease is frequently associated with acute kidney injury or acute on chronic kidney disease with significant impact on mortality and morbidity.

Conclusion:

In our study, it is clearly established that significantly higher prevalence of asymptomatic renal stone disease exists in diabetic population. Considering the high incidences of chronic kidney disease in diabetes as well as long standing kidney and ureteric stones, untreated kidney stone disease may be an additional risk factor for chronic kidney disease in diabetes. Although very long term follow up of asymptomatic renal stone disease is not available, we have given existing evidence that they are not innocuous. We suggest routine use of ultrasound screening for diabetic patients for asymptomatic renal stone disease along with screening for nephropathy and retinopathy. This strategy may lead to early prevention of chronic renal damage and possibly can also reduce the incidences of acute pyelonephritis related kidney injury in diabetic patients.

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