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CORRELATION BETWEEN VASCULAR CALCIFICATION AND UROLITHIASIS AMONGST NON-DIABETIC YOUNG KIDNEY STONES FORMER AND ITS ASSOCIATION WITH TYPES OF STONES

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ABSTRACT **Introduction:** As per recent studies, an association between nephrolithiasis and cardiovascular disease is present, due to an unknown cause. The study hypothesizes that vascular calcification is common in young nondiabetic kidney stone formers and is mostly associated with calcium types of stones. It should be investigated, whether the young nondiabetic kidney stone formers have vascular calcification and whether calcium stones confirmed on stone analysis are related to vascular calcification in kidney stone formers. **Methods:** A matched case-control study that kidney stone formers attending in Department of Urology in GMCH, Guwahati from 2021 to 2022. Age and sex-matched nondiabetic stone formers without vascular calcification on CT were drawn. A total of 390 patients were investigated, of which 129 were kidney stone formers with vascular calcification and 261 were kidney stone formers without vascular calcification. We used computed tomography imaging for Abdominal aortic calcification and stone analysis for the type of stone. The prevalence, severity, and associations of abdominal aortic calcification were compared between calcium kidney stone formers with vascular calcification and kidney stone formers without vascular calcification. **Results:** Mean age was 32 years in non-diabetic calcium kidney stone formers with vascular calcification and 28 in abdominal aortic calcifications without vascular calcification. Men represented 17.17% and 82.82% of calcium kidney stone formers with vascular calcification and abdominal aortic calcifications without vascular calcification, respectively. A multivariate model adjusted for age, sex, high BP, diabetes, smoking status, and eGFR confirmed that calcium kidney stone formers have higher abdominal aortic calcification compared with other stone formers. 71.4% of patients have calcium stones on stone analysis. **Conclusions:** This study shows that young nondiabetic patients with calcium kidney stones suffer from significantly higher degrees of aortic calcification than age- and sex-matched other stone formers, suggesting that vascular calcification may explain reported associations between nephrolithiasis.

KEYWORDS : Nephrolithiasis, vascular calcification, CT KUB- Computed Tomography Kidney, Ureter and Bladder

INTRODUCTION

In our body, calcium is one of the essential elements. A large amount of calcium iron (Ca^{2+}) is stored in the human body in the form of calcium phosphate (CaP) in bones and vertebrae. In every cell of the body small quantity of calcium is present as calcium ions, which are necessary for the normal functioning of the heart, muscles, blood vessels, and neurons (1). The cells remain in a constant equilibrium of these elements to carry out their normal physiological functions (1). The Calcium ions function as signaling molecules both as 1st (2) and 2nd (3) messengers for various intracellular signal transduction pathways. This calcium can abnormally accumulate in various forms like Brushite, Hydroxyapatite, etc at various sites in the body known as "Ectopic calcifications". It may lead to various unwanted complications like nephrolithiasis and atherosclerosis (4,5). It is proposed that both the crystal disposition and stone formation may follow the same processes as the calcium phosphate deposits in tubular or hollow tissue microenvironments such as renal tubules and salivary gland ducts (5–7). Likewise, other factors such as Bone morphogenetic proteins (BMP) and Osteopontins(OPN) help in calcium phosphate crystallization in blood vessels as well as renal tubules through the regulation of various transcription factors, eg Runt related transcription factor 2 and msh homeobox 2(Msx2)(8). The pH level along with high calcium and phosphate remains the main fundamental influencer of calcium deposition. But even now it is not clear what is the main cause of calcium phosphate deposition and the specific process of stone formation.

Some studies suggest microcrystals bind to the surface of various tubular structures which increases the deposition of further crystals and leads to the formation of stones (9). A concept called the free solution crystallization mechanism explains the continuous crystallization process of Leads to nucleus formation from which stone forms and this process can be blocked by organic molecules (9,10). Various other processes also influence the crystal formations are lack of inhibitors and supersaturation of pre-calcium ions and phosphate ions (11,12). These various factors may influence crystal deposition and stone formation in various manners like-(i) influencing physiological processes (ii) Influencing calcium and phosphate ion concentration in blood and tissue, and (iii) Influencing bone formation and resorption (13,14). Few studies show similar calcification osteogenic transformation in vascular smooth muscles by increasing BMP 2 and osteopontin expressions (13–15).

Moreover, patients with chronic kidney disease have vascular calcification and they are also susceptible to various cardiological complications, like stroke and myocardial infarction, vascular calcification of the heart, and atherosclerosis (16,17). Now it is shown by a few studies that symptomatic stone disease is more likely to develop chronic kidney disease (18,19). Kidney stones are associated with various metabolic diseases like obesity, diabetes Mellitus, cardiovascular disease, and metabolic syndromes.

Hence various processes or mechanisms need to be examined that can influence kidney stone formation and calcification along with the high production of calcium phosphate crystals.

MATERIAL AND METHODS

Institutional ethical board clearance Taken with no MC/190/2007/pt-ii/march 2022/26.

we took all the patients who have given consent for study in the age group of 10 to 60 years and diagnosed urolithiasis on non-contrast computed tomography of the kidney, ureter, and bladder (NCCT-KUB). We have excluded the patient who does not fit into the study age group, who has diabetes mellitus, and who does not want to be taken part in the investigation.

A total of 390 patients fulfilled the inclusion criteria out of 667 patients listed and each patient was labeled with a unique identification number to reduce overlapping of data.

We have compiled a database with the information collected from the patient like the complete history and thorough examinations. The information about the chief complaint, history of Lithuria, history of

lower urinary tract symptoms, family history, drug history, occupational history, and habits like alcohol, smoking, and tobacco chewing. Body mass index is calculated with weight and height. Details from NCCTKUB extracted like stone- number, size, site, and site of involvement along with the site and extent of vascular calcification. We sent stones for stone analysis post-operatively

Statistical Analysis

We used IBM SPSS version 26 for Windows for various calculations like mean, and percentage calculations. The chi-square test was used for the test of significance to compare variables. We have taken $P < 0.05$ as significant.

RESULTS

In our study majority of the patient was male 246 (63.07%) out of 390 and the male-to-female ratio was 1.7:1. (Table 1)

Table 1: Sex Distribution of the study population		
Gender	Number of patients (n=390)	Percentage
Male	246	63.07
Female	144	36.92

The majority of patient 148(37.94%) belongs to the age group of 51 to 60. (Table 2)

Table 2: Age distribution of the study population		
Age group (Years)	Number of patients (n=390)	Percentage
10-20	24	6.15
21-30	30	7.69
31-40	76	19.48
41-50	112	28.71
51-60	148	37.94

The majority of the patient was a farmer by occupation 98(25.12%). (Table 3)

Table 3: Occupations of the study population		
Occupation	Number of patients (n=390)	Percentage
Student	54	13.84
Housewife	83	21.28
Office Workers	57	14.61
Retired	16	4.1
Business	82	21.02
Farmer	98	25.12

Most of the patient was not having the habit of using tobacco, drinking alcohol, or smoking 124(31.79%) however 47(12.5%) of the patient was alcoholic 108(27.67%) was tobacco chewers, and about 12(3.07%) was a smoker. (Table 4)

Table 4: Habits of the study population		
Habits	Number of patients (n=390)	Percentage
Alcohol	47	12.05
Tobacco	108	27.69
Smoking	12	3.07
No	124	31.79
Alcohol + Tobacco	62	15.89
Alcohol + Tobacco + Smoking	37	9.48

We have found the majority of our patient was overweight 195(50%) with a body mass index between 25 to 29.9.(Table 5)

Table 5: Body mass index of the study population		
BMI (Kg/m2)	Number of patients (n=390)	Percentage
<18.5	29	7.43
18.5-24.9	78	20
25-29.9	195	50
≥30	88	22.56

DISCUSSION

Urolithiasis is more common in males and the precise percentage varies among the various studies(10). In the present study, we have found that male suffers more from urolithiasis 63.07% with a male-to-female ratio of 1.7 to 1. However, worldwide issue varies from 1.82 to 3:1(11,13). Our study showed there are changes in the distribution of urolithiasis in genders.

In our study, most patients were farmers (25.12%) and office-going (14.61%). Sedentary lifestyle professionals had a higher incidence of urinary calculi (12). It may be related to differences in the diet but also may be because of physical inactivity. Physical activity may increase urine output and reduces crystal aggregation. In a study on urolithiasis patients, the most common symptom was loin pain (73% to 94%)(14).

A study done by Lohiya(3) suggests that the majority of patients diagnosed by ultrasound and asymptomatic at the time of presentation. We also had similar results and patients were diagnosed incidentally by radiographic or ultrasonographic techniques.

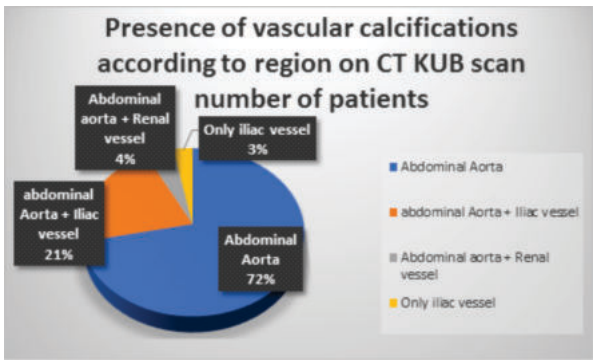
In our study, 12.5 % of patients had a history of regular alcohol consumption with 27.69% being tobacco chewers and 3.07% having a history of smoking.

We have found about 50% were overweight BMI between 25 and 29.9. these are similar to various other studies, that suggest high body mass index age has a positive association with urolithiasis.

The location of stones in the urinary tract in our study was kidney 286 (73.33%), followed by Upper 1/3 ureter 48 (12.3%), middle 1/3 ureter 6 (1.53%), lower 1/3 ureter 34 (8.71%), and bladder 11 (2.6%). (Table 6) These are almost similar to the study like renal stones at 75.08%, ureteric calculus13.62%, the vesicoureteric junction (VUJ) calculus at 9.56%, and bladder at 1.74% (20).

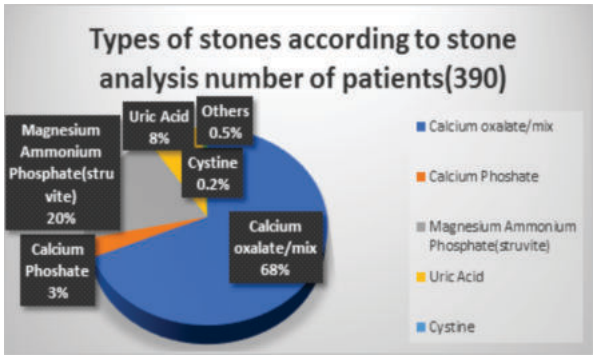
Table 6: Calculus presence according to the region on the CT KUB scan		
Site	Number of patients	Percentage
kidney	286	73.33
Upper 1/3 ureter	48	12.3
Middle 1/3 ureter	6	1.53
Lower 1/3 ureter	34	8.71
Bladder	11	2.82
Urethra	2	0.51
External meatus	3	0.76

In our study, the most common site of vascular calcification was the Abdominal Aorta 71.64% (48). Vascular calcification was generally in the elderly, however, we found about 37.17% (25) were less than 50 years, of which two patients were less than 30 years and six patients were in the age group of 31-40 years. Seven patients of the age group less than 50 years were having CKD, however only five patients of the age group of lesser than 50 years were Diabetic. Almost all the 20 patients, who were less than 50 years old, were having calcium oxalate or mixed type of renal or ureteric calculus. (Picture 1)



Picture 1: Distribution Of Vascular Calcifications On CT-KUB Scan

From stone analysis, it was found stones of Calcium oxalate/mix (68.4%), Calcium Phosphate (3%), Magnesium Ammonium Phosphate(struvite) (19.4%), Uric Acid (8.2%), Cystine (0.2%) and Others (0.5%). (Picture 2)



Picture 2: Different Types Stones On Stone Analysis

CONCLUSION

In our preliminary study, we report that vascular calcification has an association with renal calculus in a non-diabetic young patient. Hence better understanding is needed for the Physiology of renal and vascular calcification. Most patient remains asymptomatic and hence needs strict vigilance.

Appendices: It is a single-center study; hence it should be examined in further studies.

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