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To determine risk factors associated with nephrolithiasis in patients suffering from Diabetes type II

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Abstract— **Objective:** The aim to conduct this study is to see the patients suffering from diabetes type II having nephrolithiasis and the relationship of different risk factors that can also contribute to cause nephrolithiasis. **Introduction:** Nephrolithiasis is the condition in which stones are present in the kidneys. We studied nephrolithiasis in diabetes type II patients. We also examined different risk factors that are associated with nephrolithiasis. Then we evaluate the size of the stone, location, and the number of stones using ultrasonography. **Material and Method:** We performed the cross-sectional study and took a sample of 100 patients and the study is done under ultrasound for the evaluation of the presence and size of stone for analysis of data, a software name SPSS version 20 was used. For the significance of data, P-value was used. **Results:** The result shows that the dependent variable size of stone has an association with different independent variables. It is cleared from the result that there was the association between obesity and size of stone as there result showed P-value as .000 and association is also seen with diet, hypertension, family history, previous surgery, fluid intake, and urea creatinine level as their P- values are 0.057, 0.047, .000, .000, 0.021, 0.048 respectively. The result also showed that there was no association between gut problem and medication with the size of stone as their P-value were 0.727,0 .687 respectively. **Conclusion:** As diabetes type II patients have a highly increased chance of nephrolithiasis due to having acidic urine and some other factors that can also contribute to the formation of stones. Not all nephrolithiasis patients are diabetic but having diabetes type II increases the risk of nephrolithiasis. This study shows a direct relationship of stone size in diabetic type II patients with obesity, hypertension, fluid intake, family history, high fiber and protein diet, urea creatinine level and is not directly related to previous surgery, medications, and gut problems.

Index Terms — Diabetes type II, Family history, Hypertension, Nephrolithiasis, Obesity, Ultrasound, Urea Creatinine level

1 Introduction

Nephrolithiasis is the condition in which the patient has stones in his kidney. It may be present in the single kidney or both kidneys. Nephrolithiasis is the most common and ancient disease known to medicine. [1] .Nephrolithiasis, although, is a common disease but difficult to understand because it is a multifactorial disease but in most economically developed countries like North America, Europe, Australia, and Japan, calcium oxalate is the most common stone type in the upper urinary tract. Numerous epidemiological components, containing age, gender, heredity, profession, body estimate, social class, affluence, geographic area, atmosphere, and diet, and fluid consumption, have been identified as contributing factors in Renal stone disease.

As men have a bigger body structure and therefore three times more chance of stone occurrence exists as compared to women because they have less overall body weight. So we can say men have more hazard of having stones in their kidneys especially common stone types like calcium oxalate [2]. Chances of kidney stones increases if there is a factor of family history is present in a person than others but there is very little data on how it can run in families although it is a common observation. Dietary calcium intake may expand the danger of stone arrangement, even among people without a family ancestry of kidney stones [3].

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Types of Renal stone:
Following are the different types of renal stones:

1. **Calcium** stones are the most common renal stones, typically calcium oxalate. Oxalate is a common substance present in our body and is made in the liver day by day.
2. **Struvite** stones are present when there is no severe disease like only urinary tract contamination.
3. **Uric acid corrosive stones** are present in patients who have liquid deficiency due to either not drinking enough water or due to loss of excess liquid, who eat a diet with excess protein, and gout patients.
4. **Cystine stones** structure in individuals with an inherited issue that causes the kidneys to discharge a lot of certain amino acids (cystinuria).

Type 2 DM is a common condition, which is characterized by hyperglycemia, insulin obstacle, and relative insulin insufficiency. Type II Diabetes mellitus outcomes from the connection between hereditary and ecological and, these are the hazard factors [4]. There is a close relationship between nephrolithiasis development and renal stone formation. As insulin resistance, metabolic syndrome characteristics, and diabetes type II result in pH lowering and aminogenesis becomes impaired. So pH lowering becomes the major factor in causing uric acid nephrolithiasis [5].

1.1Anatomy of kidney

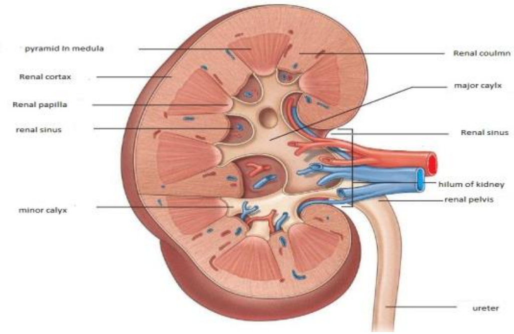


Figure: 1.1. Renal anatomy

1.2 There are the following risk factors that can cause kidney stone formation:

A **family history** of stones was essentially more typical among the stone-formers than among the controls, generally because of an expanded recurrence of stones among the dads and siblings of the person. This examination subsequently underpins past proposals that hereditary components influence the inclination to the stone arrangement. An expanded inclination was additionally noted, in any case, among the spouses of those whose relatives had stones, which proposes that natural elements are included. Subjects with a family ancestry of renal stones did not display specific attributes in their research center profiles, however, they seemed, by all accounts, to be increasingly inclined to grow early and visit repeats [6].

Hypercalciuria or hyperuricosuria was not over-represented among stone formers with a positive family ancestry [7]

Since men have heavy bodies and large structures and therefore have three times more risk of developing nephrolithiasis than women because of their small body structure. So this is concluded that body weight, size, and sex have some relationship with the development of nephrolithiasis [8].

There are two particular metabolic conditions representing kidney stone development in patients with metabolic disorder/focal weight.

(i) Abdominal corpulence inclines to insulin obstruction, which at the renal dimension causes diminished urinary ammonium discharge and therefore a low urinary pH; the result is more danger of uric corrosive stone development.

(ii) Bariatric medical procedure, the main intercession that encourages huge weight reduction in excessively fat individuals, conveys a more danger of calcium oxalate nephrolithiasis. The fundamental pathophysiological systems are significant enteric hyperoxaluria because of an intestinal official of calcium by malabsorbed unsaturated fats, and serious hypocitraturia because of delicate or watery stools, which lead to endless bicarbonate misfortunes and intracellular metabolic acidosis.

Kidney stones formation risk increases in the patients who have gastrointestinal tract resection issues. Patients with colon resection have more chances of developing uric acid stones and sometimes calcium oxalate stones can also develop. These patients should consume a high amount of liquids and water because there is a loss of water and salts in the diarrhoeal stool occurs and this promotes diminished volume of fluids in the body. They additionally have diminished retention, and along these lines lessened urinary discharge, of citrate and magnesium which inhibits calcium oxalate crystallization. Colon resection and ileostomy patients have more chances of developing uric acid stones because of the loss of bicarbonate in these patients. These conditions result in low liquid volume, decreases uric acid solvency, this causes crystallization, and in this way stones form in the kidney[9].

Nephrolithiasis is most commonly established in hypertensive patients than in others; however, the pathogenic connection somewhere in the range of hypertension and pebble malady is as yet not clear. A huge level of hypertensive subjects has a more danger of renal stone arrangement, particularly when hypertension is related with over the top body mass. Higher oxaluria and calciuria just as super saturation of calcium oxalate and uric corrosive have all the signs of being the most significant variables. Over the top weight and utilization of salt and proteins may likewise assume a significant job [10].

The primary connections hypertension to weight with expanded corrosive discharge as an insurance finding. The different proposes that expanded corrosive discharge and related low urinary citrate levels are markers of subclinical acidosis or a modified corrosive discharge system. A conceivable relationship between hypertension and modified corrosive base state is upheld by test proof. In creature models of hypertension, metabolic acidosis and expanded corrosive discharge were found before the advancement of hypertension. In two strains of immediately hypertensive rodents, plasma pH and bicarbonate fixation were lower than those in normotensive controls. Furthermore, salt affectability is by all accounts related to expanded metabolic corrosive generation in creatures and people. Therefore, stone framing may, similar to salt affectability, incline to hypertension [11].

Patients with kidney stones are routinely encouraged to expand their liquid admission to diminish the danger of stone repeat. Be that as it may, there has been no nitty gritty examination to decide if the impact on repeat shifts by the kind of drink devoured [12]. Stone formers exhibited a transient ascent in serum creatinine and pee egg whites that therefore settled [13].

1.3 Medical Imaging:

Ultrasonography (US) is an available, moderately reasonable imaging strategy that comes without the dangers of presentation to ionizing radiation. With a capacity to show radiopaque and radiolucent stones, hydronephrosis, renal inflammation, burst fornices, ureteric planes, and resistive lists, the US can give important clinical data. Stone nearness and size assume a basic job in the directing of patients. The exact location and estimation of renal calculi are basic for controlling administration choices and clinical basic leadership. The US is frequently utilized in both the underlying evaluation and line up of patients with kidney stones. To distinguish a stone in the US, there necessities to exist a hyperechoic center with an acoustic shadow. The acoustic shadow can be debilitated on account of the impedance of interceding tissue or unseemly choice and parity of the transducer control and central length. Two regular strategies for stone recognition, expanding US profundity and increase, the estimation of stone shadow width rather than the stone itself prompted significantly progressively exact stone estimations [14].

Figure: 1.2 Ultrasound Image showing renal stone

The utilization of ultrasonography for kidney stones identification goes back to 1961 when Schlegel and associates originally gave an account of intraoperative adequacy (A) mode ultrasonography for renal calculi. Before ultrasound, kidney stones were analyzed for the most part utilizing plain radiographs of the kidney, ureter, and bladder (KUB) alongside intravenous pyeloureterograms. Given the powerlessness of these tests to distinguish radiolucent stones, ultrasound before long rose as a methodology fit for recognizing these kidney stones that were at the time hard to picture. Little case arrangement by Edell and Zegel just as Pollack and associates exhibited the capacities of grayscale ultrasound by demonstrating how it could distinguish radiolucent uric corrosive and framework stones, separately, the two of which were not acknowledged on regular plain-film urography As ultrasound machines developed, they decreased, compact, and were soon able to do ongoing imaging. This meant the working room as urologists began utilizing ultrasound to encourage stone limitation and evacuation. Cook and Lytton were the first to depict intraoperative ultrasound utilizing a splendor (B)-mode examining test to restrict a stone and guide their nephrolithotomy.

For pediatric and pregnant patients, ultrasound is generally acknowledged as the standard starting symptomatic imaging methodology for both of these helpless patient populaces. For pediatric patients, past reports have shown ultrasound to have 70% affectability, 100% particularity, 96% positive prescient esteem, and 62% negative prescient incentive to distinguish a renal stone. Ultrasound has a diminished affectability in pregnant patients, assessed to be ~34%, given that the physiologic changes of pregnancy make it hard to recognize physiologic ureteral widening from deterrent due to a ureteral stone. Be that as it may, these are two patient populaces for whom presentation to ionizing radiation is especially hindering[15].

Around 80% of stones are made out of calcium oxalate and calcium phosphate, 10% of struvite, 9% of uric corrosive; and the remaining 1% are made out of cystine or ammonium corrosive urate or are analyzed as medication-related stones. Stones eventually emerge due to an undesirable stage change of these substances from fluid to strong state [16].

Renal ultrasound Is the itemized examination of renal and urological frameworks performed by the radiological technologist or radiologist[17]. The US is exceptionally delicate and explicit for renal stones in patients with renal disappointment, it needs affectability for ureteric calculi especially when they are in the center ureter [18].

Various irregularities exist between flow speculations of the underlying occasion in nephrolithiasis development and exact observational information on stone disease [19].

The main lane is abundance on interstitial apatite plaque as observed in idiopathic calcium oxalate stone formers, just as stone formers with essential hyperparathyroidism, ileostomy, little inside resection, and in brushite stone formers.

In a second way, there are precious stone stores in renal tubules That was found in all stone framing gatherings aside from the Idiopathic calcium oxalate stone formers.

The third pathway is free arrangement crystallization. Clear instances of this pathway are those patient gatherings with cystinuria or Hyperoxaluria is related to detour medical procedures for corpulence. Even though the last items might be fundamentally the same as the methods for creation are different to the point that in Endeavoring to make creature and cell models of the procedures one should be cautious that the subtleties of the human condition are incorporated [20].

Uric corrosive nephrolithiasis might be the last indication of different pathophysiological forms. Late advances in renal urate transport have clarified instruments by which hyperuricosuria happens. Notwithstanding, in most uric corrosive stone formers the essential pathophysiologic deformity is an unreasonably acidic pee pH instead of hyperuricosuria. Insulin obstruction may add to the advancement of acidic pee by enlarging endogenous corrosive creation and diminishing renal ammonium discharge [21].

Results demonstrate that of stone formers patients with sort II diabetes mellitus discharge fundamentally more prominent urinary oxalate and altogether lower pee pH than those without diabetes mellitus. These discoveries are significant for treating nephrolithiasis since they may impact dietary directing, medicinal administration, and stone counteractive action [22].

2 MATERIALS AND METHODS

2.1 Study area: This study was accomplished in the province Punjab in DHQ hospital Faisalabad, Pakistan. My study includes all the patients referred by the doctors or referred by the Emergency Department. This study includes the patients of nephrolithiasis for ultrasonography from December 2018 to May 2019. It includes both males and females patients of adult to old age presented with nephrolithiasis.

2.2 Sample size: the sample size was 100 patients of age from 8 years to 80 years.

2.3 Study duration: the duration of my study was about 6 months from December 2018 to May 2019.

2.4 Study design: Cross-sectional study was conducted.

2.5 Inclusive criteria: the selected patients were suffering from

- Type II Diabetic patient with nephrolithiasis
- all the patients that came to the ultrasound departments presenting with severe pain in their back and abdominal area
- Those have face difficulty with voiding or blood with urine.

2.6 Exclusive criteria: Patients that are excluded were those

- who were not presented with diabetes type II
- Patients with diseases other than nephrolithiasis and diabetes type II
- Pediatrics were not added in this study

2.7 Equipment used: Toshiba Xario 100 ultrasound Machine was used for my research purpose installed at the radiology department DHQ Hospital Faisalabad. For the visualization of deeper structure, a curvilinear array was used. The crystals are aggregate along a **curved** surface and cause a fanning out of the ray, which results in a field of view that is extensive than the **probe's** footprint.2.5Mhz lower frequency ultrasound probe allowing a deep penetration and an extensive depth of field, which is exceptional for viewing intra-abdominal structures.

2.8 Patient preparation: For **KUB ultrasound** 4 to 6 hours fasting is required. 1 hour before the procedure the **patient** is also usually instructed to drink a liter of water. **KUB ultrasound** involves a full bladder so that the urinary bladder can be accurately evaluated especially since the bladder volume is measured throughout the scan.

3.9 Method:

2.9.1 Patient position: Patient lies supine on the imaging table.

2.9.2 Positioning of probe: The kidney is scanned **in** longitudinal and transverse scan planes with the probe placed **in** the margins. When insonation of the **kidney** is hidden by intestinal air, the **supine** scan **position** is shared with the lateral decubitus **position** with the probe moved dorsally.

2.9.3 Procedure: The patient will be requested to change into a cloth dress and lie on a table. The room is normally dark so the images can be perceived clearly on the processor screen. A technician qualified in ultrasound imaging will spread a clear, warm gel on the belly over the kidneys area. This gel aids in the transmission of the sound waves. The probe is tilted to make an 11'o clock position to evaluate the right kidney and about 2'o clock position to evaluate the left kidney.

The sonographer will then allocate a probe over the gel. The probe emits high-frequency sound waves and a computer processes how the sound waves bounce back from inside the body. The processor changes those sound waves into images to be examined. The test is painless. You feel a minor compression on the stomach as the probe is moved over it. You'll need to lie immobile during the technique so the sound waves can reach the area efficiently. The technician may ask you to lie in changed positions or hold his or her breath momentarily. The on-screen stone appears hyperechoic (bright) and has a shadow below the stone.

2.10 Statistical Analysis: After that data arranged in a pie chart, or bar or frequency tables, etc. For analyzing the data software that I would prefer was SPSS. Calculate the values and p-value that were significant for consideration.

3 RESULTS

In this study total number of females and males was 48 and 52 respectively. Their age range was 8-80 years and there was a minimum of 8 years, a maximum of 80 years age, and the average age was 1.83 years. All calculations were done on SPSS software. The **formulation** of **BMI** = kg/m^2 where kg is a person's weight in kg and m^2 is their height in meters squared. A **BMI** of 25.0 or more is weighty, while the healthy range is 18.5 to 24.9. The graph given below shows the age groups involved in this study.

Pie chart

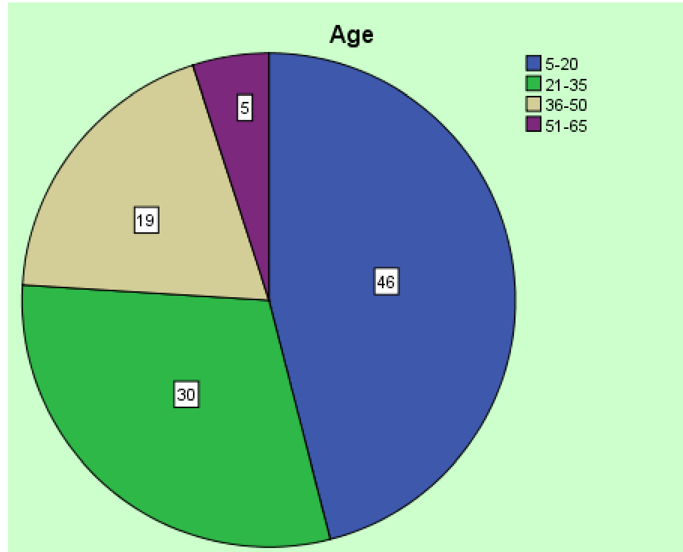
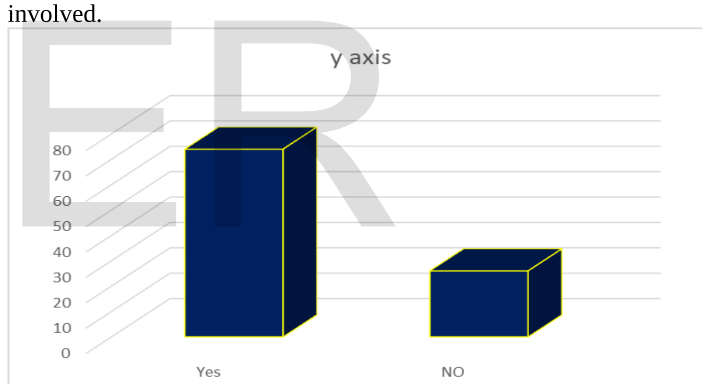


Fig # 3.1 Graph showing Age in groups

The graph given below shows the frequency distribution of sex in which 52 males and 48 female patients are involved.
The graph given below shows the frequency distribution of marital status in which 70 were married and 30 unmarried patients were involved.



Fig# 3.2 Graph showing a frequency distribution of Marital status.

Table # 3.1: Relation between size of stone and obesity

Obesity		Size of stone		X^2	p-value
		Equal &Less than 5 mm	Greater than 5mm	32.702	.000
	No	32	0		
	Yes	27	41		

The table showed that there was an association between obesity and the size of the stone.

Table # 3.2: Relation between diet and size of stone

Diet		Size of stone		X^2	p-value
		Equal &Less than 5	Greater than 5mm	3.616	.057

		mm			
	Low fiber and protein diet	30	13		
	High fiber and protein diet	29	28		

The table showed that there was an association between Diet and Size of stone.

Table # 3.3: Relation between size of stone and Medication

		Size of stone		X^2	p-value
medication		Equal &Less than 5 mm	Greater than 5mm	.163	.687
	No	38	28		
	Yes	21	13		

The table showed that there was no association between medication and the Size of the stone as the p-value is .678.

Table # 3.4: Relation between size of stone and Gut Problem

		Size of stone		X^2	p-value
Gut problem		Equal &Less than 5 mm	Greater than 5mm	.122	.727
	No	21	16		
	Yes	38	25		

The table showed that there was no association between Gut problem and the Size of the stone as their p-value is not equal to .000.

Table # 3.5: Relation between size of stone and Hypertension

		Size of stone		X^2	p-value
Hypertension		Equal &Less than 5 mm	Greater than 5mm	3.931	.047
	No	32	14		
	Yes	27	27		

The table showed that there was an association between Hypertension and the Size of the stone.

Table # 3.6: Relation between size of stone and Family history

		Size of stone		X^2	p-value
Family history		Equal &Less than 5 mm	Greater than 5mm	18.261	.000
	No	29	4		
	Yes	29	37		

The table showed that there was an association between Family history and the Size of stone as the result showing .000 p-values.

Table # 3.7: Relation between size of stone and Gut Previous surgery

		Size of stone		X^2	p-value
Previous surgery		Equal &Less than 5 mm	Greater than 5mm	13.455	.000
	No	57	29		
	Yes	2	12		

The table showed that there was an association between previous surgery and the Size of the stone.

Table # 3.8: Relation between size of the stone and Fluid intake

		Size of stone		X^2	p-value
Fluid intake		Equal &Less than 5 mm	Greater than 5mm	5.296	.021
	< 8 glasses	42	37		
	Equal & > 8 glasses	17	4		

The table showed that there was an association between fluid intake and the Size of the stone.

Table # 3.9: Relation between size of stone and Urea and Creatinine level

		Size of stone		X^2	p-value
Urea Creatinine level		Equal &Less than 5 mm	Greater than 5mm	6.066	.048
	Normal	38	17		
	Exceeded	21	23		

The table showed that there was an association between urea and creatinine level and the Size of stone.
It is cleared from the result that there was an association between obesity and size of stone as their results showed p-value as .000 and association is also seen with diet, hypertension, family history, previous surgery, fluid intake, and urea creatinine level as there p- values are 0.057, 0.047, .000, .000, 0.021 and 0.048 respectively. The result also showed that there was no association between gut problem and medication with the size of stone as their p-value were 0.727,0 .687 respectively.

4 DISCUSSION

Our examination results from a huge populace of more seasoned grown-ups show just because that metabolic disorder additionally connected with a twofold more prominent event of dispassionately shown Nephrolithiasis. Although among the individual segments of

Metabolic disorder, high BP essentially conveyed a huge relationship to Nephrolithiasis in the two people, the mix of high BP and at least one different segment of Metabolic disorder was related with a further increment in the danger of Nephrolithiasis [23].

Our outcomes affirm that body size is autonomously connected with the advancement of episode kidney stones. Since slender weight is decidedly corresponded with percent muscle to fat ratio and may assume a significant job in stone arrangement, it is conceivable that more noteworthy fit weight is in any event mostly in charge of the watched relationship between higher BMI and expanded hazard. Be that as it may, the solid relationship between weight gain since early adulthood and the danger of episode stone arrangement proposes that adiposity assumes a focal job in the connection between body size and nephrolithiasis [24].

In this investigation, we have demonstrated a relationship between expanding meat admission and the danger of hospitalization for stone illness. Generally, non-meat eaters (for example fish eaters and veggie lovers) and those expending under 50 g/day of meat had a decrease of somewhere in the range of 30 and 50 % in the danger of stone infection contrasted and meat-eaters who devoured 100 g/day or a greater amount of all-out meat items and which was autonomous of BMI, absolute vitality and liquor consumption, notwithstanding other potential confounders including sex, the technique for enlistment, area of living arrangement, long haul treatment, smoking, and self-detailed earlier diabetes. Our examinations demonstrate that while red meat and poultry were related with an expanded stone hazard, handled meat was not, although it is conceivable that the low variety in the admission of prepared meat prompted a decrease in capacity to recognize an affiliation, on the off chance that one exists [25].

The examination demonstrated that ingestion of cranberry squeeze positively and interestingly changed 3 key urinary danger features, for example, oxalate and phosphate discharge diminished, while citrate discharge expanded. A few other hazard variables were positively changed by the two conventions, for example, pH, capacity, ML, calcium discharge and relative supersaturation of calcium phosphate (brushite), uric corrosive, and CaOx. It is especially noteworthy that it diminished despite the high oxalate and ascorbic corrosive substance of the juice, as both of these exogenous components may have been required to enlarge oxalate release. The outcome subsequently concurs with that recently detailed investigation which demonstrated that oxalate in cranberry juice isn't promptly bioavailable. We propose that cranberry juice may restrain the assimilation of oxalate and that its conceivable practice in the preservationist management of hyperoxaluria may merit investigating [26].

This information bolsters past perceptions that men who have experienced kidney stones are around multiple times bound to have a family ancestry of renal stones. A family history of kidney stones likewise significantly expands the danger of stone development in men who never have had a stone, free of their dietary admission. The extent of the relationship between family ancestry and the danger of stones was more prominent in men more youthful than 60 yr of age. A few hereditary components are probably going to assume a job in calcium oxalate stone infection and may result in an unusual discharge of calcium, uric corrosive. Citrate, inhibitors, or advertisers [27].

Our outcomes demonstrated that a more seasoned period of pebble formers who present with uric corrosive stones contrasted with other stone sorts. Different examiners have related developed radiographic calculi weight to diminished renal work among patients undergoing shockwave lithotripsy [28].

This forthcoming information gives no help to the conviction that higher utilization of calcium from dietary sources builds the danger of symptomatic kidney stones; indeed, the information proposes that the connection may be reversed. Since most stones contain calcium28 and because hypercalciuria has been related to the development of stones, calcium limitation has been routinely prescribed for patients who have kidney stones. Be that as it may, we are uninformed of any information that exhibits that limitation of calcium admission diminishes the repeat of kidney stones. Also, in patients with idiopathic hypercalciuria dietary calcium limitation may prompt negative calcium parity and bone misfortune [29].

Instruments that reason nephrolithiasis may subsequently add to the advancement of hypertension at a more established age. As hypertension by and large will in general happen at a more seasoned age than does nephrolithiasis. Be that as it may, these indistinct elements are probably not going to be real reasons for hypertension, as a generous extent (near 90%) of hypertensive subjects have never given nephrolithiasis. The huge relationship between nephrolithiasis and hypertension does not suggest a causal relationship; rather, at least one pathogenic instrument basic to nephrolithiasis and hypertension might be in charge of the advancement of both. A few potential systems may connect nephrolithiasis and circulatory strain. Changes in calcium digestion have been recommended to assume a significant job in the pathogenesis of both nephrolithiasis and hypertension [30].

5 CONCLUSION

As diabetes type II patients have very acidic urine so there is an increased chance of nephrolithiasis and our study shows that there is a certain risk factor that increases the chance of stones in type II patients. However, not every diabetic patient needs to have a renal stone. This study shows a direct relationship of stone size with obesity, hypertension, fluid intake, family history, High fiber, and protein diet, urea creatinine level, and has no direct relationship with previous surgery, gut problem, and medication.

5.1 LIMITATIONS

The limitation of the study is a shortage of time and a small volume of examined population. I am unable to study by changing the condition of the patient having a particular risk factor like if a patient is taking a diet high in oxalic acid and has a kidney stone, due to lack of time, I cannot examine if a patient changes his dietary habits and then see the results of that changes. To remove the precision a large study population is required but due to the limitation of time.

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