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Evaluation of Renal Calculi with risk factors and proteins with treatment regimen in a Tertiary Care Teaching Hospital

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A B S T R A C T

A Kidney stones are mainly lodged in the kidney(s). Mankind has been afflicted by urinary stones since centuries dating back to 4000 B.C., and it is the most common disease of the urinary tract. Kidney stones have been associated with an increased risk of chronic kidney diseases.The study was a prospective observational study conducted in a Urology and Nephrology department of tertiary care teaching hospital.The study was conducted at Urology and Nephrology unit IP of Narayana Hospitals, Nellore.The data was analyzed and tabulated below like demographics, reasons for admissions, types of calculi, diagnosis, management, complications, ris factors, proteins, genes and outcomes were analyzed and tabulated.In our study out of 572 patients 414 are willing to provide information, from age group 18 to above 60 of both sexes are considered with their educational, nutritional, marital status was obtained from the patients case data, the reasons for admission into the hospital, types of renal calculi, diagnosis, risk factors, proteins, genes and treatment, treatment outcomes and reoccurrence of stones are also analyzed.Our study concluded that most of the patients admitted in the hospital with renal calculi were analyzed and found that due to the changes in life style, medical management and surgical management renal calculi is treated and symptoms are relived

Introduction

Kidney stones are mainly lodged in the kidney(s) [1]. Mankind has been afflicted by urinary stones since centuries dating back to 4000 B.C. [2], and it is the most common disease of the urinary tract. The prevention of renal stone recurrence remains to be a serious problem in human health [3]. The prevention of stone recurrence requires better understanding of the mechanisms involved in stone formation [4]. Kidney stones have been associated with an increased risk of chronic kidney diseases [5], end-stage renal failure [3, 6], cardiovascular diseases [7, 8], diabetes, and hypertension [9]. It has been suggested that kidney stone may be a systemic disorder linked to the metabolic syndrome. Nephrolithiasis is responsible for 2 to 3% of end-stage renal cases if it is associated with nephrocalcinosis [10].

The symptoms of kidney stone are related to their location whether it is in the kidney, ureter, or urinary bladder [11]. Initially, stone formation does not cause any symptom. Later, signs and symptoms of the stone disease consist of renal colic (intense cramping pain), flank pain (pain in the back side), hematuria (bloody urine), obstructive uropathy (urinary tract disease), urinary tract infections, blockage of urine flow, and hydronephrosis (dilation of the kidney). These conditions may result in nausea and vomiting with associated suffering from the stone event [12]. Thus, the treatment and time lost from work involves substantial cost imposing an impact on the quality of life and nation's economy.

The Urinary System and Stones

The urinary filtrate is formed in the glomerulus and passes into the tubules where the volume and content are altered by reabsorption or secretions. Most solute reabsorption occurs in the proximal tubules, whereas fine adjustments to urine composition take place in the distal

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tubule and collecting ducts. The loop of Henle serves to concentrate urine composed of 95% water, 2.5% urea, 2.5% mixture of minerals, salts, hormones, and enzymes. In the proximal tubules, glucose, sodium, chloride, and water are reabsorbed and returned to the blood stream along with essential nutrients such as amino acids, proteins, bicarbonate, calcium, phosphate, and potassium. In the distal tubule, the salt and acid-base balance of blood is regulated [13]. The location of stones may vary as indicated in

Types of Kidney Stones

The chemical composition of kidney stones depends on the abnormalities in urine composition of various chemicals. Stones differ in size, shape, and chemical compositions (mineralogy) [14]. Based on variations in mineral composition and pathogenesis, kidney stones are commonly classified into five types as follows [15].

Calcium Stones: Calcium Oxalate and Calcium Phosphate

Calcium stones are predominant renal stones comprising about 80% of all urinary calculi [9]. The proportion of calcium stones may account for pure calcium oxalate (CaOx) (50%), calcium phosphate (CaP, termed as apatite) (5%), and a mixture of both (45%) [10]. The main constituent of calcium stones is brushite (calcium hydrogen phosphate) or hydroxyapatite [11, 12]. Calcium oxalate is found in the majority of kidney stones and exists in the form of CaOx monohydrate (COM, termed as mineral names: whewellite, $CaC_2O_4•H_2O$), and CaOx dihydrate (COD, weddellite, $CaC_2O_4•2H_2O$), or as a combination of both which accounts for greater than 60% [13]. COM is the most thermodynamically stable form of stone. COM is more frequently observed than COD in clinical stones [14].

Many factors contribute to CaOx stone formation such as hypercalciuria (resorptive, renal leak, absorptive, and metabolic diseases), hyperuricosuria, hyperoxaluria, hypocitraturia, hypomagnesuria, and hypercystinuria [15]. Mostly, urinary pH of 5.0 to 6.5 promotes CaOx stones [16], whereas calcium phosphate stones occur when pH is greater than 7.5 [11]. The recurrence of calcium stone is greater than other types of kidney stones.

Struvite or Magnesium Ammonium Phosphate Stones

Struvite stones occur to the extent of 10–15% and have also been referred to as infection stones and triple phosphate stones. It occurs among patients with chronic urinary tract infections that produce urease, the most common being Proteus mirabilis and less common pathogens include Klebsiella pneumonia, Pseudomonas aeruginosa, and Enterobacter [1, 18, 19]. Urease is necessary to split/cleave urea to ammonia and CO_2, making urine more alkaline which elevates pH (typically > 7). Phosphate is less soluble at alkaline versus acidic pH, so phosphate precipitates on to the insoluble ammonium products, yielding to a large staghorn stone formation [17]. Women's are likely to develop this type of stone than the male. Escherichia coli are not capable of splitting urea and is not associated with struvite stones [18].

Uric Acid Stones or urate

This accounts approximately for 3–10% of all stone types [1, 19]. Diets high in purines especially those containing animal protein diet such as meat and fish, results in hyperuricosuria, low urine volume, and low urinary pH (pH < 5.05) exacerbates uric acid stone formation [11, 18, 19]. Peoples with gouty arthritis may form stones in the kidneys. The most prevalent cause of uric acid nephrolithiasis is idiopathic, and uric acid stones are more common in men than in women.

Cystine Stones

These stones comprise less than 2% of all stone types. It is a genetic disorder of the transport of an amino acid and cystine. It results in an excess of cystinuria in urinary excretions [1], which is an autosomal recessive disorder caused by a defect in the rBAT gene on chromosome 2 [19], resulting in impaired renal tubular absorption of cystine or leaking cystine into urine. It does not dissolve in urine and leads to cystine stone formation [11]. People who are homozygous for cystinuria excrete more than 600 millimole insoluble cystine per day [18]. The development of urinary cystine is the only clinical manifestation of this cystine stone disease [4].

Drug-Induced Stones

This accounts for about 1% of all stone types [1]. Drugs such as guaifenesin, triamterene, atazanavir, and sulfa drugs induce these stones. For instance, people who take the protease inhibitor indinavir sulphate, a drug used to treat HIV infection, are at risk of developing kidney stones [18]. Such lithogenic drugs or its metabolites may deposit to form a nidus or on renal calculi already present. On the other hand, these drugs may induce the formation of calculi through its metabolic action by interfering with calcium oxalate or purine metabolisms

Materials and methods:

Study design:

The study was a prospective observational study conducted in a Urology and Nephrology department of tertiary care teaching hospital.

Study site:

The study was conducted at Urology and Nephrology unit IP of Narayana Hospitals, Nellore.

Study population:

The study was done in 414 patients who are suffering with renal stones.

Study duration:

The study was conducted for 12 months (2020- 2021)

Study criteria:

Patients are enrolled in the study based on inclusion and exclusion criteria

a) Inclusion criteria:

- All the patients suffering with renal calculi
- Patients age in between 18-80
- Patients of both sexes.

b) Exclusion criteria:

- Pregnancy women
- Lack of interest to give information
- Pediatrics
- Whose verbal communication was poor.
- Unconscious patients.

Study materials:

- Patients informed consent form.
- Renal Urinary medical questionnaire form

Study method

The study will be initiated after obtaining the permission from the Institutional ethical committee. The patient will be enrolled in the study after taking informed consent from them. The enrollment of patients will be done on the basis of inclusion and exclusion criteria. The data or the present study will be collected by "Patient interview and chat review method ", which is well suited to identify all the necessary and relevant baseline information, which will be collected on a specially design patient data collection proforma and Renal Urinary medical questionnaire form. Which includes patients demographics like age, socioeconomic status, family income, educational status, high risk factors, lab investigation data, radiographic data, physician medication order form, nurse's medication administration records (drug chart) and any other verbal communication data.

Results

The obtained results were categorized and tabulated as mentioned below. The demographic details; Reasons for admissions; diagnosis

details of the patients; types of calculi details of the patients; Genes involved in hypercalciuria, gene products, and renal phenotype; sizes of calculi details of the patients; Causes of calculi details of the patients; drugs used for calculi details of the patients; Treatment options for calculi; Treatment outcomes for calculi; Reoccurrence of stones calculi were tabulated in *Table 01; Table 02; Table 03; Table 04; Table 05; Table 06; Table 07; Table 08; Table 09; Table 10 and Table 11* respectively.

Demographics	Number of Patients	Frequency
Age		
18-30	90	21.73
30-45	63	15.21
46-60	207	50
>60	54	13.04
Sex		
Male	261	63.04
Female	153	36.95
Educational status		
Primary	207	50
Secondary	137	33.09
Tertiary	70	16.09
Nutritional status		
Poor	198	47.82
Average	135	32.60
Better	81	19.56
Marital status		
Married	279	67.39
Unmarried	135	32.60
Ethinicity		
Indian	414	100

Table 1: Shows demographic details of the patients with frequency.

Reasons for admissions	Number of patients	Frequency
	24	05.79
Blood in urine	76	18.35
Discoloured or foul smelling urine		
Frequent need to urinate	45	10.86
Burning mitchuration	61	14.73
Urinating small amounts with pain	25	06.03
Fever chills and pain		
Pain in the lower abdomen	54	13.04
Pain associated by nausea and vomiting	65	15.70
	64	15.45

Table 2: Shows reasons for the admissions with frequency.

Diagnosis for renal calculi	Number of patients	Frequency
Blood tests		
Calcium	65	15.70
Phosphorus	24	05.79
Uric acid	76	18.35
Electrolytes	45	10.86
Blood urea nitrogen	61	14.73
Creatinine	65	15.70
Abdominal X- ray	414	100
Intravenous pyelogram	75	18.11
Retrograde pyelogram	24	05.79
MRI	81	19.56
CT	127	30.67
USG abdomen	414	100

Table 3: Shows diagnosis details of the patients with frequency.

Types of calculi	Number of patients	Frequency
Calcium	152	36.71
Uric acid	82	19.80
Struvite	63	15.21
Cysteine	27	06.52
Drug induced stones	90	21.73

Table 4: Shows types of calculi details of the patients with frequency.

Genes	Gene product/function	Renal phenotype
VDR	Vitamin D receptor	Decreased calcium reabsorption leading to hypercalciuria and nephrocalcinosis
CLCNS	Cl/H antiporter	Inactivating mutation causes hypercalciuria, hyperphosphaturia, low molecular weight proteinuria, nephrocalcinosis, stone
CASR	Calcium sensing receptor	Gain of function mutation produces hypercalciuria, nephrocalcinosis, stone
CLDN16	Tight junction protein	Hypercalciuria, magnesium wasting, nephrocalcinosis, stone
NPT2a/c	Sodium phosphate cotransporter	Hypercalciuria, hypophosphatemia, phosphate wasting, nephrocalcinosis, stone
TRPV5	Calcium selective transient receptor potential channel	Hypercalciuria, hyperphosphaturia
sAC	Soluble adenylate cyclase/bicarbonate exchanger/	Hypercalciuria, stones
KLOTHO	Aging suppression protein/regulator of calcium homeostasis	Hypercalciuria

Table 5: Shows Genes involved in hypercalciuria, gene products, and renal phenotype.

Sizes of calculi	Passage	Number of patients	Frequency
1mm	87	14	2.5
2mm	72	27	4.82
3mm	83	42	7.5
4mm	72	107	19.10
5mm	60	119	21.25
6mm	72	61	10.89
7mm	47	53	9.46
8mm	56	28	5
9mm	33	32	5.71
10mm	27	77	13.75

Table 6: Shows sizes of calculi details of the patients with frequency.

Causes of calculi	Number of patients	Frequency
Increased drug concentration	84	11.49
Super saturation	72	09.84
Crystal aggregation	102	13.95
Bacterial infection	56	07.66
Defects in elements	82	11.21
Calcium intake	128	17.51
Salts and sugars	64	08.75
Procured meat	52	07.11
Spinach	91	12.44

Table 7: Shows Causes of calculi details of the patients with frequency.

Drugs used for calculi	Number of patients	Frequency
Thiazide diuretics		
Bendroflumethazide	65	15.66
Hydrochlorthiazide	54	13.04
Chlorthalidone	24	05.79
Trichlormethazide	17	04.10
Indapamide	4	0.96
Allopurinol	78	18.8
Antibiotics		
Ciprofloxacin	214	51.69
Cefalexin	57	13.76
Trimethoprim	84	20.28
Cystine binding thiol drugs		
D- Pencilamine	77	18.59
Tiopronin	83	20.04
Captopril	24	05.79
Bucillamine	17	04.10
Others		
Potassium citrate	317	76.57

Table 8: Shows drugs used for calculi details of the patients with frequency.

Treatment options for calculi	Number of patients	Frequency
Life style modifications	268	64.73
Medication Management	414	100
Surgical interventions	123	29.71
Diet management	315	76.08

Table 9: Shows Treatment options for calculi details of the patients with frequency.

Treatment outcomes	Number of patients	Frequency
Poor	35	08.45
Average	220	53.14
Better	159	38.40

Table 10: Shows Treatment outcomes for calculi details of the patients with frequency.

Reoccurrence of stones	Number of patients	Frequency
Reported	42	10.14
Not reported	372	89.85

Table 11: Shows Reoccurrence of stones calculi details of the patients with frequency.

Discussions:

In our study out of 572 patients 414 are willing to provide information, from age group 18 to above 60 of both sexes are considered with their educational, nutritional, marital status was obtained from the patients case data, the reasons for admission into the hospital, types of renal calculi, diagnosis, risk factors, proteins, genes and treatment, treatment outcomes and reoccurrence of stones are also analyzed. From the data the calculi are mostly developed due to calcium, discolored and foul smelling urine were reported and ultrasonography of abdomen was done to find out the renal calculi, sizes of 1mm to 10 mm were reported, the overall treatment outcome was average and better, some patients went for surgical procedures for removal of renal calculi, all the patients are under the medication management. After the treatment and surgical removal of calculi with life style changes only 42 patients reported reoccurance of stones in the study period.

Conclusion:

Our study concluded that most of the patients admitted in the hospital with renal calculi were analyzed and found that due to the changes in life style, medical management and surgical management renal calculi is treated and symptoms are relived, the physicians and clinical pharmacist should advice the patients about the foods to avoid, preventive care to be taken so the severity can be reduced. Some preventive measures and information leaflets has to be provided to create awareness to the public.

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