"ROLE OF MULTI-DETECTOR COMPUTED TOMOGRAPHY INDICES IN PREDICTING EXTRACORPOREAL SHOCKWAVE LITHOTRIPSY OUTCOME IN PATIENTS WITH NEPHROLITHIASIS"

By

Dr. AASHISH

DISSERTATION SUBMITTED TO SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, KOLAR, KARNATAKA

In partial fulfilment of the requirements for the degree of

DOCTOR OF MEDICINE
IN
RADIODIAGNOSIS

Under the Guidance of

Dr. ANIL KUMAR SAKALECHA, MBBS, MD,
PROFESSOR & H.O.D. OF RADIODIAGNOSIS

DEPARTMENT OF RADIODIAGNOSIS,

SRI DEVARAJ URS MEDICAL COLLEGE,

TAMAKA, KOLAR – 563103.

2022

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, TAMAKA, KOLAR, KARNATAKA

DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation entitled **"ROLE OF MULTI-DETECTOR COMPUTED TOMOGRAPHY INDICES IN PREDICTING EXTRACORPOREAL SHOCKWAVE LITHOTRIPSY OUTCOME IN PATIENTS WITH NEPHROLITHIASIS"** is a bonafide and genuine research work carried out by me under the guidance of **Dr. ANIL KUMAR SAKALECHA**, Professor & HOD, Department of Radiodiagnosis, Sri Devaraj Urs Medical College, Kolar, in partial fulfilment of University regulation for the award "**M.D. DEGREE IN RADIODIAGNOSIS**", the examination to be held in 2022 by SDUAHER. This has not been submitted by me previously for the award of any degree or diploma from the university or any other university.

Dr. AASHISH,
Postgraduate in Radiodiagnosis,
Sri Devaraj Urs Medical College,
Tamaka, Kolar.

Date:

Place: Kolar.

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, TAMAKA, KOLAR, KARNATAKA

CERTIFICATE BY THE GUIDE

This is to certify that the dissertation entitled **"ROLE OF MULTI-DETECTOR COMPUTED TOMOGRAPHY INDICES IN PREDICTING EXTRACORPOREAL SHOCKWAVE LITHOTRIPSY OUTCOME IN PATIENTS WITH NEPHROLITHIASIS"** is a bonafide research work done by **Dr. AASHISH,** under my direct guidance and supervision at Sri Devaraj Urs Medical College, Kolar**,** in partial fulfilment of the requirement for the degree of "**M.D. IN RADIODIAGNOSIS**".

Dr. ANIL KUMAR SAKALECHA, MBBS, M.D.,
Professor & HOD,
Department Of Radiodiagnosis,
Sri Devaraj Urs Medical College,
Tamaka, Kolar.

Date:
Place: Kolar.

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH TAMAKA, KOLAR, KARNATAKA

CERTIFICATE BY THE HEAD OF DEPARTMENT

This is to certify that the dissertation entitled "**ROLE OF MULTI-DETECTOR COMPUTED TOMOGRAPHY INDICES IN PREDICTING EXTRACORPOREAL SHOCKWAVE LITHOTRIPSY OUTCOME IN PATIENTS WITH NEPHROLITHIASIS"** is a bonafide research work done by **Dr. AASHISH,** under direct guidance and supervision of **Dr. ANIL KUMAR SAKALECHA**, Professor & HOD, Department of Radiodiagnosis at Sri Devaraj Urs Medical College, Kolar**,** in partial fulfilment of the requirement for the degree of "**M.D. IN RADIODIAGNOSIS"**.

Dr. ANIL KUMAR SAKALECHA, MBBS, M.D.,
Professor & HOD,
Department of Radiodiagnosis
Sri Devaraj Urs Medical College,
Tamaka, Kolar.

Date:

Place: Kolar.

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH TAMAKA, KOLAR, KARNATAKA

ENDORSEMENT BY THE HEAD OF THE DEPARTMENT AND PRINCIPAL

This is to certify that the dissertation entitled **"ROLE OF MULTI-DETECTOR COMPUTED TOMOGRAPHY INDICES IN PREDICTING EXTRACORPOREAL SHOCKWAVE LITHOTRIPSY OUTCOME IN PATIENTS WITH NEPHROLITHIASIS"** is a bonafide research work done by **Dr. AASHISH** under the direct guidance and supervision of **Dr. ANIL KUMAR SAKALECHA,** Professor & HOD, Department of Radiodiagnosis, Sri Devaraj Urs Medical College, Kolar, in partial fulfilment of University regulation for the award "**M.D. DEGREE IN RADIODIAGNOSIS**".

Dr. ANIL KUMAR SAKALECHA,
Professor & HOD,
Department Of Radiodiagnosis,
Sri Devaraj Urs Medical College,
Tamaka, Kolar.

Date:
Place: Kolar.

Dr. P. N. SREERAMULU,
Principal,
Sri Devaraj Urs Medical College,
Tamaka, Kolar.

Date:
Place: Kolar.

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION

AND RESEARCH, TAMAKA, KOLAR, KARNATAKA

ETHICAL COMMITTEE CERTIFICATE

This is to certify that the Ethical committee of Sri Devaraj Urs Medical College,

Tamaka, Kolar has unanimously approved

Dr. AASHISH,

Post-Graduate student in the subject of

RADIODIAGNOSIS at Sri Devaraj Urs Medical College, Kolar

to take up the Dissertation work entitled

"ROLE OF MULTI-DETECTOR COMPUTED TOMOGRAPHY INDICES IN PREDICTING EXTRACORPOREAL SHOCKWAVE LITHOTRIPSY OUTCOME IN PATIENTS WITH NEPHROLITHIASIS"

to be submitted to the

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION

AND RESEARCH, TAMAKA, KOLAR, KARNATAKA.

Member Secretary,

Sri Devaraj Urs Medical College,

Kolar – 563 101.

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION AND RESEARCH, TAMAKA, KOLAR, KARNATAKA

COPY RIGHT

Dr. AASHISH

POST-GRADUATE

DEPARTMENT OF RADIODIAGNOSIS

Date:

Place: Kolar.

Drillbit Softtech India Pvt. Ltd

Certificate of Plagiarism Check for Dissertation

Author Name	Dr. AASHISH
Course of Study	MD Radiodiagnosis
Name of Guide	Dr. Anil Kumar Sakalecha
Department	Radiodiagnosis
Acceptable Maximum Limit	10%
Submitted By	librarian@sduu.ac.in
Paper Title	ROLE OF MULTI-DETECTOR COMPUTED TOMOGRAPHY INDICES IN PREDICTING EXTRACORPOREAL SHOCKWAVE LITHOTRIPSY OUTCOME IN PATIENTS WITH NEPHROLITHIASIS
Similarity	10%
Paper ID	423361
Submission Date	2021-12-04 12:08:26

Signature of Student

Signature of Major Advisor

Prof. & HOD,
Dept. of Radio Diagnosis,
R.L.J. Hospital & Research Centre
Tamaka, KOLAR-563 101.

Head of the Department

Prof. & HOD,
Dept. of Radio Diagnosis,
R.L.J. Hospital & Research Centre
Tamaka, KOLAR-563 101.

University Librarian

University Library Learning Resource Centre
Sri Devaraj Urs Academy of Higher Education & Research
Tamaka, KOLAR-563103

Coordinator, UG & PG Program

Co-Ordinator,
UG&PG Program, Faculty of Medicine,
Sri Devarj Urs Academy
of Higher Education & Research,
Tamaka, Kolar- 563103

* This report has been generated by DrillBit Anti-Plagiarism Software

ACKNOWLEDGEMENT

I owe my debt and gratitude to my parents ***Dr. BACHITTAR SINGH*** *&*
Dr. RITA JUSSAL, *my wife* ***Dr. APURVA SINGH,*** *my in laws* ***Mr. AVINASH KUMAR SINGH*** *&* ***Mrs. POONAM SINGH*** *and my brother* ***Mr. ANISH*** *for their moral support and constant encouragement during the course of the study.*

With humble gratitude and great respect, I would like to thank my teacher, mentor and guide, ***Dr. ANIL KUMAR SAKALECHA****, Professor & HOD, Department of Radiodiagnosis, Sri Devaraj Urs Medical College and Research Institute, Kolar, for his able guidance, constant encouragement, immense help and valuable advices which went a long way in moulding and enabling me to complete this work successfully.*

I have great pleasure in expressing my deep sense of gratitude to ***Dr. N. RACHEGOWDA,*** *Professor, Department of Radiodiagnosis, Sri Devaraj Urs Medical College and Research Institute, Kolar.*

I would also like to thank ***Dr. HARISH KUMAR G.****, Assistant Professor, Department of Urology, Sri Devaraj Urs Medical College for his wholehearted support, constant encouragement and guidance.*

*I would like to thank **Dr. DEEPTI NAIK,** Professor and **Dr. RAJESWARI, Dr. BUKKE RAVINDRA NAIK & Dr. DARSHAN A.V.,** Assistant professors, Department of Radiodiagnosis, Sri Devaraj Urs Medical College and Research Institute, Kolar, for their constant support and encouragement during the study period.*

*I am thankful to my seniors **Dr. Parameshwar Keerthi B.H**, **Dr. Anshul Singh**, **Dr. E. Vineela, Dr. Sahana N. Gowda, Dr. Amrutha Ranganath** & my fellow **postgraduates** **Dr. Chaithanya A., Dr. Varshitha G.R., Dr. Yashas Ullas L., Dr. Suraj H.S., Dr. Monisha V.** and all other **postgraduates** for having rendered all their co-operation and help to me during my study.*

I am extremely grateful to the patients and their families who volunteered to this study, without them this study would just be a dream.

*I am also thankful to **Mr. Ravi, Mr. Aleem, Mr. Chandrasekhar,** and **Mr. Subramani** with other **technicians** of Department of Radio diagnosis, R.L Jalappa Hospital & Research Centre, Tamaka, Kolar for their help.*

*I am also thankful to staff nurse **Mrs. Radha & Mr. Munipillappa, Mrs. Munivekatamma** and other **technicians** of Department of Radiodiagnosis, R.L Jalappa Hospital & Research Centre, Tamaka, Kolar for their help.*

My sincere thanks to ***Mr. Sunil, Mrs. Naseeba,*** *and* ***Mrs. Shobha,*** *along with rest of the computer operators.*

Last but not the least I would be failing in my duty if I do not express my gratefulness to the ***Almighty,*** *who helped me to successfully complete this study*.

Dr. AASHISH

POST-GRADUATE
DEPARTMENT OF RADIODIAGNOSIS

LIST OF ABBREVIATIONS

ACR	-	American College of Radiology
AUA	-	American Urological Association
AUC	-	Area Under Curve
BMI	-	Body Mass Index
BUN	-	Blood Urea Nitrogen
CI	-	Confidence Interval
CSA	-	Cross Sectional Area
CT	-	Computed Tomography
DUC	-	Distal Ureteric Calculi
EAU	-	European Association of Urology
ESWL	-	Extracorporeal Shockwave Lithotripsy
HD	-	Hounsfield Density
HU	-	Hounsfield Unit
HUC	-	Hounsfield unit at the center of stone
HUD	-	Hounsfield Density
IV	-	Intravenous
KUB	-	Kidney, Ureter, Bladder
kV	-	kilovolts
MDCT	-	Multi-detector Computed Tomography
MET	-	Medical Expulsive Therapy
m-PCNL	-	micro-percutaneous nephrolithomy
MRI	-	Magnetic Resonance Imaging

mSv	-	millisievert
NCCT	-	Non-contrast Computed Tomography
NSAIDs	-	Non-steroidal anti-inflammatory drugs
OR	-	Odds Ratio
PCNL	-	Percutaneous Nephrolithotomy
RIRS	-	Retrograde Intrarenal Surgery
ROC	-	Receiver Operator Curve
ROI	-	Region of Interest
SAV	-	Stone Attenuation Value
SD	-	Standard Deviation
SFA	-	Subcutaneous Fat Area
SFR	-	Stone Free Rate
SSD	-	Skin to stone distance
SWL	-	Shockwave Lithotripsy
TFA	-	Total Fat Area
URSL	-	Ureteroscopic Lithotripsy
VAS	-	Visual Analogue Scale
VFA	-	Visceral Fat Area

ABSTRACT

BACKGROUND: Nephrolithiasis is a common renal pathology in which calculi are formed within the kidneys. Non-contrast Computed Tomography is gold standard imaging investigation to diagnose nephrolithiasis. We evaluated nephrolithiasis on Multidetector Computed Tomography to prognosticate the outcome of Extracorporeal Shockwave Lithotripsy.

AIMS & OBJECTIVES: To perform NCCT-KUB (non-contrast Computed Tomography of Kidneys, Ureter & Bladder) and evaluate following indices: Hounsfield unit, Hounsfield density, calculus size, location and skin-stone distance. To derive cut-off values for the above indices in predicting successful extracorporeal shockwave lithotripsy results.

MATERIALS & METHODS: In this prospective cross-sectional study, we analyzed 45 patients suffering from nephrolithiasis and referred to R.L. Jalappa Hospital & Research Centre, attached to Sri Devaraj Urs Medical College, Kolar, Karnataka for CT-KUB (kidneys, ureter, bladder). The duration of the study is 18 months.

RESULTS: Hounsfield units of 1179 and below had sensitivity of 97.62% and specificity of 100% with a total diagnostic accuracy of 97.78%. Hence, a mean HU value of ≤1179 has a favorable ESWL outcome ($p<0.05$). Based on location of calculus, there was 100% clearance (n=14) in renal pelvis while 1 failure case was observed each in upper, inter and lower pole; therefore, renal pelvis has better ESWL outcomes as compared to other locations.

Out of 3 cases having failed ESWL, the calculus size was <13.30 mm for 1 (33.33%) and >=13.30 mm for 2 (66.67%) participants. Skin-stone distance was >=7.55 cm for 1 (33.33%) and <7.55 cm for 2 (66.67%) cases in the failure group. Out of 3 cases with failed ESWL, the Hounsfield density was <89.65 for 1 (33.33%) and >=89.65 for 2 (66.67%) cases. Hounsfield density, calculus size and skin-stone distance did not demonstrate statistical significance to prognosticate ESWL outcome (p>0.05), hence cut-off values could not be derived for these parameters.

CONCLUSION: MDCT (multidetector Computed Tomography) evaluation of nephrolithiasis can predict the ESWL success and can help in selection of patients with good prognosis.

Keywords: Nephrolithiasis, Extracorporeal Shockwave Lithotripsy, Multidetector Computed Tomography, Urolithiasis.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

INTRODUCTION

Nephrolithiasis is a well-known entity for centuries and is a common pathology in which calculi are formed within the kidneys. Bladder calculi are known to exist for nearly 5000 years back[1]. The presence of renal calculi correlates with a higher susceptibility to chronic kidney diseases and end-stage renal failure, cardiovascular diseases[2]. Nephrolithiasis poses a substantial health burden besides greatly impacting the quality of life[3]. Approximately 7-10 % of people will get nephrolithiasis at least once during their lifetime[4, 5]. The incidence is approximately 12% in the Indian population and 50% of them may end up with loss of kidney function[4, 6, 7]. Nearly 2 million people are affected by affected with nephrolithiasis in India every year[8]. The calculus belt of India is formed by Gujarat, Rajasthan, Maharashtra, Delhi, Punjab, Haryana and few states of the Northeast[8, 9]. The occurrence of urinary calculi is also high in south India because of regular use of tamarind in diet[9]. Epidemiology supports occurrence of pediatric nephrolithiasis in the past few decades[10].

Calculi are typically formed in kidneys but can be found anywhere in the genitourinary tract. The four major types of renal calculi include calcium, uric acid, Struvite and cystine[4, 11, 12]. Majority (80% approximately) of calculi in adults comprise of calcium oxalate or calcium phosphate. The type, size and number of calculi are the ones that decide the duration and course of disease and its complications[13]. Patients with usually present with flank pain that can radiate to groin region. Pain is severe and colicky[11]. There can be associated nausea and sometimes vomiting. A renal calculus usually will not be symptomatic until it moves or passes through the ureter. The imaging modalities for nephrolithiasis include plain radiograph, fluoroscopy, ultrasound and Computed Tomography (CT) scan. X-ray of Kidney, Ureter and Bladder (KUB) can be done for significantly large calculi but may often miss the smaller ones and calculi hidden by bowel and calculi that are not calcified[14, 15].

The gold standard investigation to diagnose urinary calculi is a non-contrast abdomen and pelvis CT scan, which also provides additional findings such as hydroureteronephrosis, perinephric collection, fat stranding, etc[16, 17, 18]. Routine use of Non Contrast CT (NCCT) KUB has proved to be revolutionary for evaluation and management of nephrolithiasis, nearly completely replacing other modalities for the diagnosis of renal and ureteric calculi. The three most common treatment modalities for renal calculi include ESWL, retrograde ureteroscopic calculus fragmentation and Percutaneous Nephrolithotomy (PCNL). ESWL was first introduced by Chaussy C et al in the year 1980[19]. High-energy shock waves are used to disintegrate renal calculi. In SWL high-energy shock waves are delivered to a calculus. Since its introduction, it has now become treatment of choice for renal and ureteral calculi <2 cm. However, there is a wide range of success rates ranging 46% to 91% which is based on multiple factors[20, 21, 22].

NEED OF THE STUDY

The use NCCT-KUB for renal calculi can help in selecting patients with favorable prognosis which optimizes the ESWL result[23, 24]. HU value is utilized to prognosticate response to shockwave lithotripsy, as higher values are directly proportional to shocks required and also reduced success rates[25, 26].

Several CT indices are considered for ESWL treatment for patients with nephrolithiasis, which include HU (Hounsfield units) value, Hounsfield Density (HD), calculus size/volume, calculus location and skin-stone distance (SSD)[27-29]. These indices will help to select appropriate treatment option (ESWL v/s intervention), hence based on the above-mentioned CT indices, appropriate treatment can be determined[30-35]. In India, most of the studies are based on only HU value to predict ESWL outcome. Also, there are conflicting HU cut-off values. Various criteria and their association with ESWL success have been studied in the past, however, there are no standard cut off values of such parameters. There is a scarcity of literature for making evidence based decisions in India. Hence the data gap in different CT variables and their effects on the ESWL needs to be studied in more detail.

AIMS AND OBJECTIVES

1. To perform NCCT-KUB (non-contrast Computed Tomography of Kidneys, Ureter & Bladder) and evaluate following indices: Hounsfield unit, Hounsfield density, calculus size, location and skin-stone distance.

2. To derive cut-off values for the above indices in predicting successful extracorporeal shockwave lithotripsy outcome.

REVIEW OF LITERATURE

Embryology of Kidney:

Nephrogenesis is the process of development of urinary tract. The evolution of the renal system proceeds through a series of successive phases - pronephros, mesonephros, and metanephros[36, 37].

Embryonic folding that happens in the 4th intrauterine week is the beginning of urinary tract with development when the urogenital ridge is formed. The ridge divides depending on the system which it will form; the nephrogenic cord forms urinary tract and gonadal ridge will form the reproductive system. Beginning rostrally and progressing caudally, three structures will form over a few weeks within the nephrogenic cord: pronephros, mesonephros, and metanephros[36].

The intermediate mesoderm gives rise to urogenital ridge on both sides of aorta. The urogenital ridge forms 3 sets: pronephros, mesonephros and metanephros[37, 38, 39].

The Pronephros is the cranial most set of tubes, which mostly undergoes regression and is the most immature form of kidney.

Then the mesonephros develops into mesonephric tubules and the mesonephric duct. The mesonephric tubules carry out few renal functions at first, but later on undergo regression. But the mesonephric duct persists and opens into cloaca [40-41].

Ultimately, it is the metanephros that gives rise to formation of the kidney. It develops from an outgrowth of caudal part of mesonephric duct, ureteric bud and metanephric blastema[42, 43].

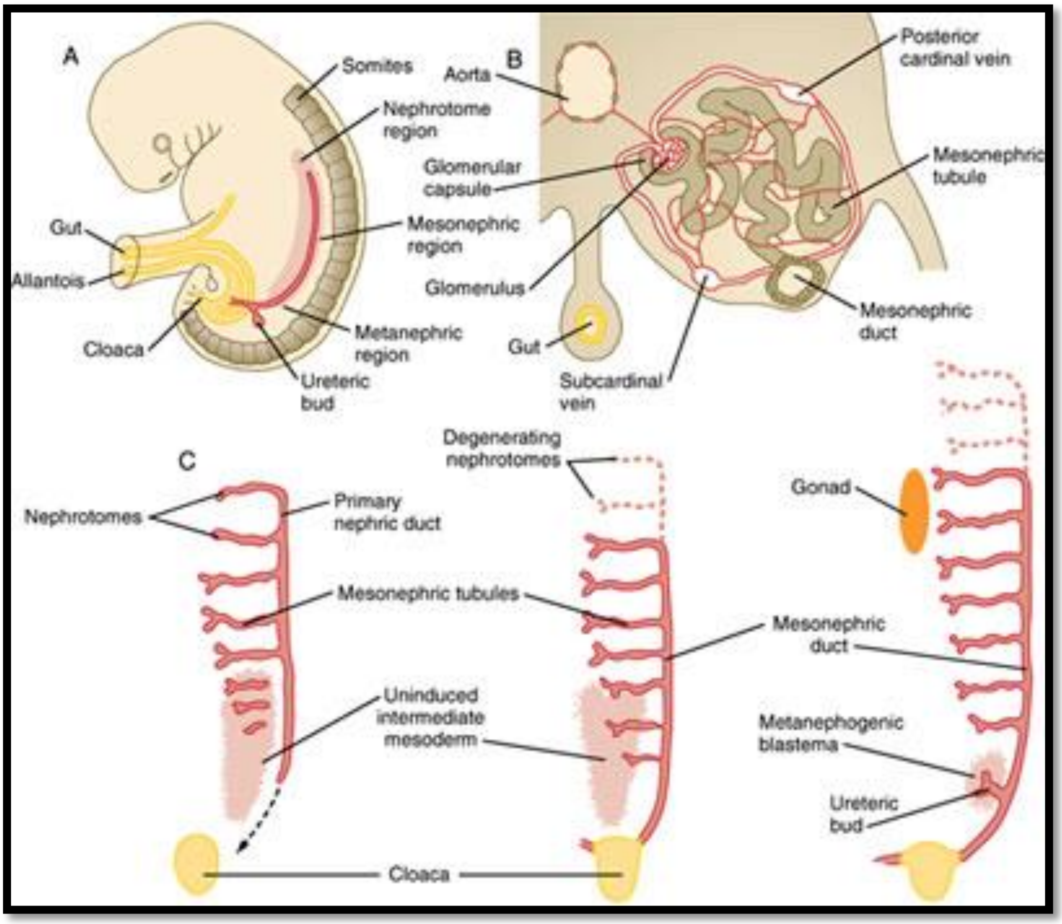


Figure 1: Embryology of Kidney:

Nephrolithiasis is a common urological pathology[1]. They are hard deposits which are comprised of various minerals and salts that form within the kidneys. The term urolithiasis is used in general for urinary tract calculi and if the calculi are located only in the kidneys, the term nephrolithiasis is used. Nephrolithiasis poses as a significant health burden causing debilitating pain which greatly impacts the quality of life[4]. According to recent estimates, the incidence of nephrolithiasis is 10.6 % in males and 7.1 % in females[8]. In addition, over the last few decades, there has been an increase in lifetime risk of having an episode of nephrolithiasis.

Radiological imaging plays a vital role in initial diagnosis of nephrolithiasis, treatment planning and post-procedural monitoring. Routine radiography and intravenous urography were considered the first line imaging modalities for nephrolithiasis. Currently, NCCT is the imaging investigation of choice for suspected cases of urolithiasis, since its introduction 1990[19].

NCCT also helps in differentiating nephrolithiasis from other conditions with similar clinical presentation such as pyelonephritis and ureteric obstruction. NCCT has a very high sensitivity (91 %) and specificity (98 %) when it comes to nephrolithiasis[8, 10].

Etiology:

The pathogenesis of calculus formation is a complex biochemical process, which is incompletely understood. Urolithiasis occurs due to solute crystallization from urine. It involves physicochemical changes and supersaturation of urine. Solutes precipitate in urine leading to nucleation and then subsequent crystal concretion. When the concentration of two ions in the solution surpasses their saturation point, crystallization occurs[44].

There are several factors responsible for Urolithiasis:

1. Anatomic factors causing stasis of urine, low urine volume.
2. Dietary factors such as high oxalate or high sodium content in the urine.
3. Urinary tract infections.
4. Medications such as Atazanavir, Overuse of silicate, Sulfonamide, Indinavir, Guaifenesin.

5. Systemic acidosis.
6. Genetic factors such as cystinuria.

Inadequate hydration resulting in low urine volume leads to formation of calculus[12]. The most common factors contributing to urinary calculus formation are hypercalciuria, hyperoxaluria, hyperuricosuria, and hypocitraturia[11, 45-48].

The mechanism of calculus formation involves the following steps:

1. Crystal nucleation
2. Crystal growth
3. Crystal aggregation
4. Crystal-cell interaction
5. Crystal retention/adhesion
6. Further aggregation/secondary nucleation for calculus formation

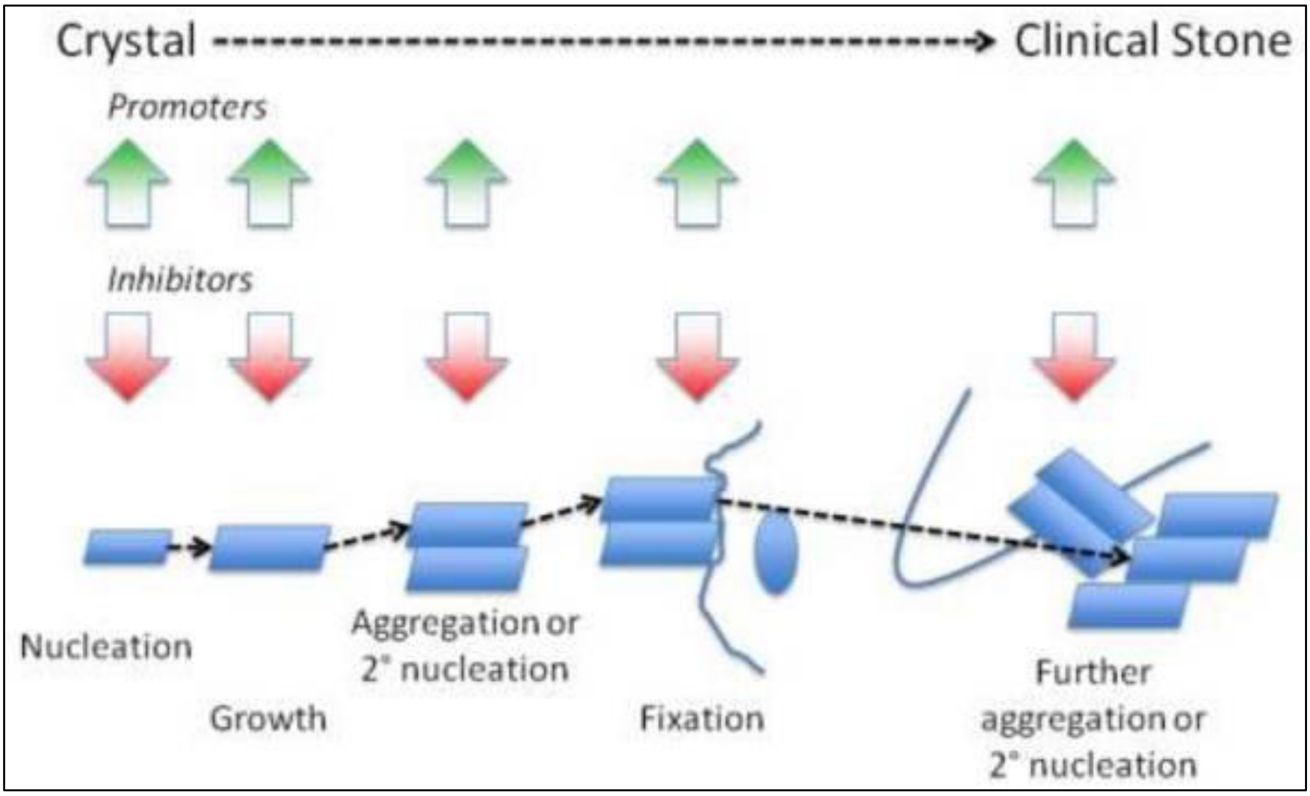


Figure 2: Mechanism of calculus formation

Figure 2 shows the steps of calculus formation such as nucleation of calculus constituent crystals, their growth or aggregation can interact with the intrarenal structures or retention within the kidney or renal collecting system to form the clinical calculus.

The 4 main types of renal calculi include[4, 11, 12]:

1. Calcium calculi (which can form due to hyperparathyroidism, hypomagnesemia and hypocitraturia).
2. Uric acid calculi, which are usually related to pH < 5, higher purine intake. These calculi can be associated with gout too.
3. Struvite calculi (mainly due to gram negative-urease organisms that result in breakdown of urea to ammonia. Organisms responsible for struvite include pseudomonas, proteus, and klebsiella. E coli is not a cause of this type of calculus.
4. Cystine calculi which are formed due to an intrinsic metabolic defect that results in failure reabsorption of cystine.

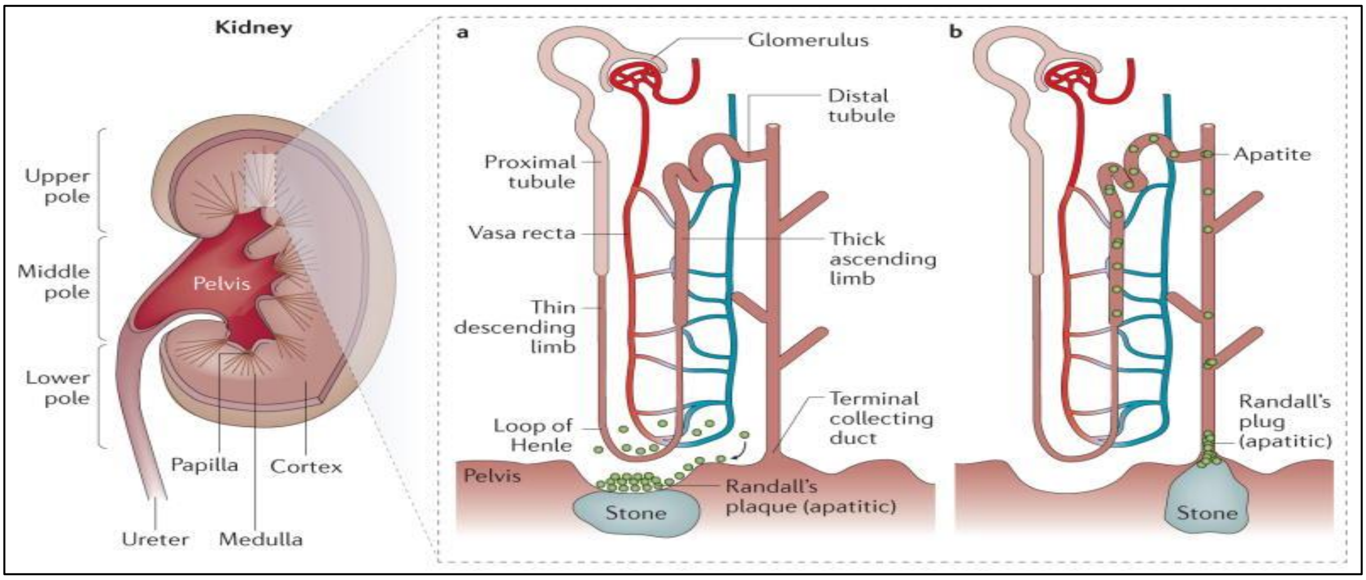


Figure 3: Morphology of human kidneys (Macroscopic and Microscopic) and location of calculi.

Left side: Macroscopic structure of human kidney.

Right side: Microscopic structure of human kidney.

a. Fixed particle mechanism of calculus formation, whereby calcium phosphate deposits in the renal interstitium grow outwards to renal papillary surface and pelvic urine, establishing a nucleus for deposition of calcium oxalate, forming renal calculi attached to calcium phosphate base/Randall's plaques.
b. Free particle mechanism of calculus formation, where crystals are formed in tubules followed by movement in urine. After this step there is aggregation of crystals which will plug collecting duct and will ultimately form Randall's plaque. Further calcium oxalate gets accumulated that will lead to formation calculus.

Majority (80% approximately) of calculi in adults consist of calcium oxalate or calcium phosphate. Around 10 to 15% is Struvite/magnesium ammonium phosphate calculi. 5 to 10% of calculi in adults are composed of uric acid while cystine calculi are infrequent (1%–2%)[9, 42, 49, 50]. In India, the calculus composition varies in different regions. Because of the lack of large population-based studies of prospective nature, there is no clear epidemiology[9]. Calcium oxalate incidence was more common in Bombay and Rajasthan among all the age groups[50], [51]. It was observed that mixed calculi occurred more commonly than the pure types. With increase in age, there is an increased occurrence of calcium oxalate calculi with decrease in occurrence of struvite, uric acid, and cystine[50]. Incidence of nephrolithiasis is higher in Manipur, especially cases of staghorn calculi[52].

CLINICAL PRESENTATION:

Urolithiasis most commonly presents with flank pain that often radiates to the groin and is severe and colicky[11]. Usually, there can be associated nausea and in some cases, vomiting. Pain radiation follows the dermatomes of T10 to S4 nerves[11].

At first, constant pain will wake up the patient from sleep. Following this, there will be bursts of extreme pain which may persist for 4 hours. There can be mild pain relief in later stages, however, it can stay for 4 to 16 hours[11].

The list of differentials include Appendicitis, Diverticulitis, Cholecystitis, Pelvic Inflammatory Disease, Acute epididymitis and Hernia. Smaller the calculus size and more distal location in the ureter at presentation favor greater likelihood of spontaneous passage. Spontaneous passage of calculus can occur in many cases but rarely does a struvite or a staghorn calculus of other composition (cystine, uric acid) pass spontaneously[13].

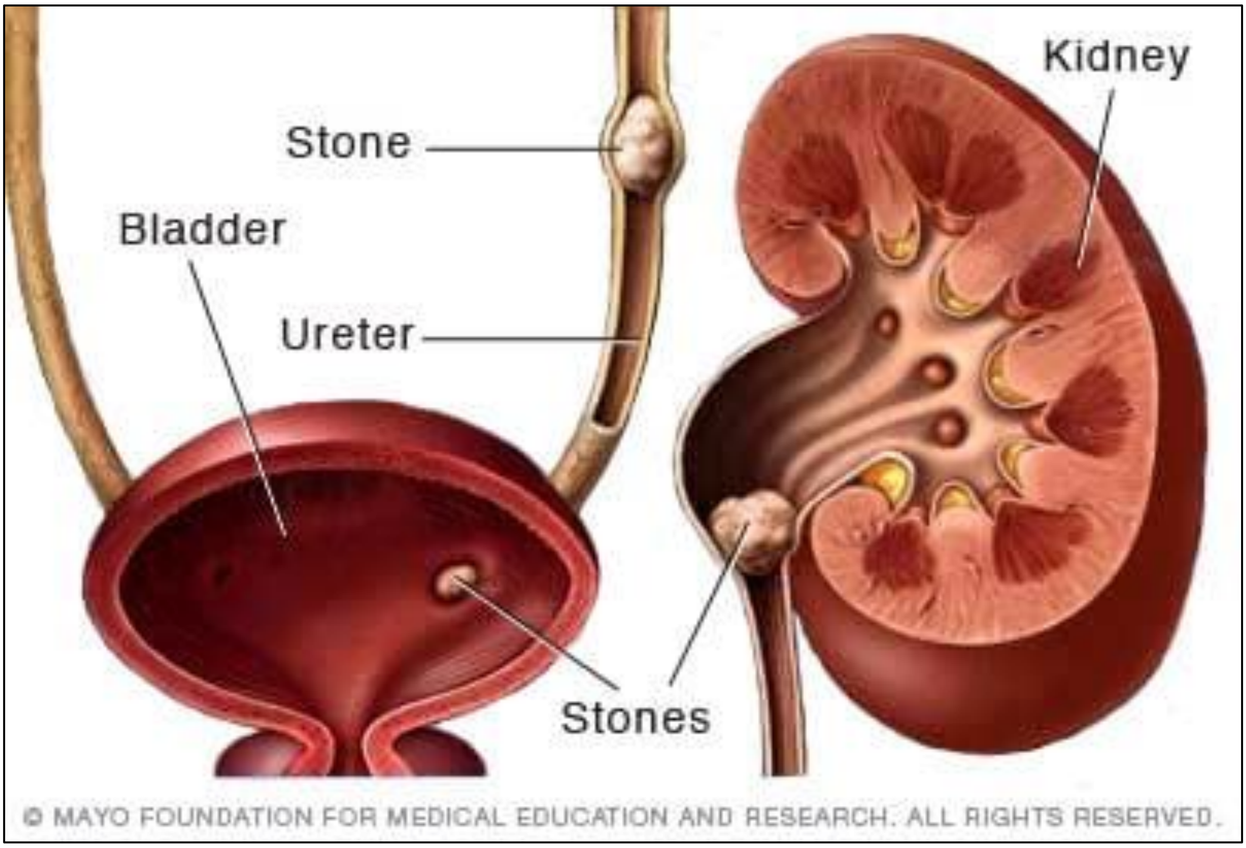


Figure 4: Presumptive clinical presentation based on composition of stones.

Clinical feature	Calcium	Uric acid	Struvite	Cystine
Crystalluria	+	+	-	+
Stone passage	+	+	-	+
Small discrete stones	+	+	-	+
Sludge and obstruction	-	+	-	+
Radiodense	+	-	+	+
Staghorn	-	+	+	+
Nephrocalcinosis	+	-	-	-

Figure 5: Renal calculi and surgical anatomy of the urinary tract.

Renal calculi on getting lodged in the ureter, may block the flow of urine and cause swelling of kidneys and ureteric contraction, leading to severe pain. Characteristic presentation includes severe and sharp pain in the side and back and/or below the ribs, Pain that radiates to the lower abdomen and groin, Pain that comes in waves and fluctuates in intensity and Pain or burning sensation while urinating. Other signs and symptoms may include change in the color of the urine such as pink, red or brown urine, Cloudy or foul-smelling urine, increase in the frequency or persistent urge to urinate, urinating in small amounts, Fever and chills in case of associated Urinary Tract Infection, Nausea and vomiting. With movement of calculus in the tract, there can be change intensity and site.

DIAGNOSIS:

A urine analysis should be done for a suspected renal calculus[11, 53]. Imaging of nephrolithiasis include plain radiograph, fluoroscopy, ultrasound and CT scan. X-ray of Kidney, Ureter and Bladder can be done for significantly large renal calculi but may often miss the smaller ones, hidden by bowel and calculi that are not calcified[14, 15].

Ultrasound is a good screening tool for assessment of hydronephrosis, especially in the scenarios where X-ray/CT is contraindicated. Ultrasound is used to calculate the resistive index via Doppler studies[14, 15].

Resistive Index (RI) = (peak systolic velocity minus end-diastolic velocity) / peak systolic velocity.

RI<0.70 is normal. Increased RI is indicative of obstruction which can be due to a ureteric calculus (unilateral increase) or chronic kidney disease (bilateral increase). If the cause of obstruction is a ureteric calculus and the RI is within normal limits, there is a good possibility of the calculus to pass spontaneously[54, 55]. Ultrasound easily picks up nephrolithiasis, if >4 mm. Other investigations include WBC (white blood cell) count and urine culture.

IMAGING OF RENAL CALCULI:

Assessment of patients who present with flank pain and hematuria depends on patient age, BMI (body mass index) and whether the patient is pregnant.

Ultrasonography must be the first imaging investigation for patients <14 years of age and in pregnancy cases. This modality should be considered for all patients with potential nephrolithiasis when a strong suspicion of stones exists and in thin (BMI <30) patients. CT is currently considered by the AUA (American Urological Association) and ACR (American College of Radiology) to be the gold-standard modality for clinical suspicion of nephrolithiasis. CT is also recommended by the EAU (European Association of Urology) as the modality of choice after inconclusive ultrasonography. Regardless of the initial imaging modality, clinicians must attempt to reduce radiation exposure to as low as reasonably achievable. Some inconclusive results are to be expected when evaluating a patient using ultrasonography, and imaging with a low-dose CT in these circumstances is reasonable. In addition, advances in CT, ultrasonography, KUB radiography, and MRI (Magnetic Resonance Imaging) technologies are continuing and are likely to improve all modalities in the future.

Figure 6: KUB plain film radiography showing multiple bilateral renal calculi.

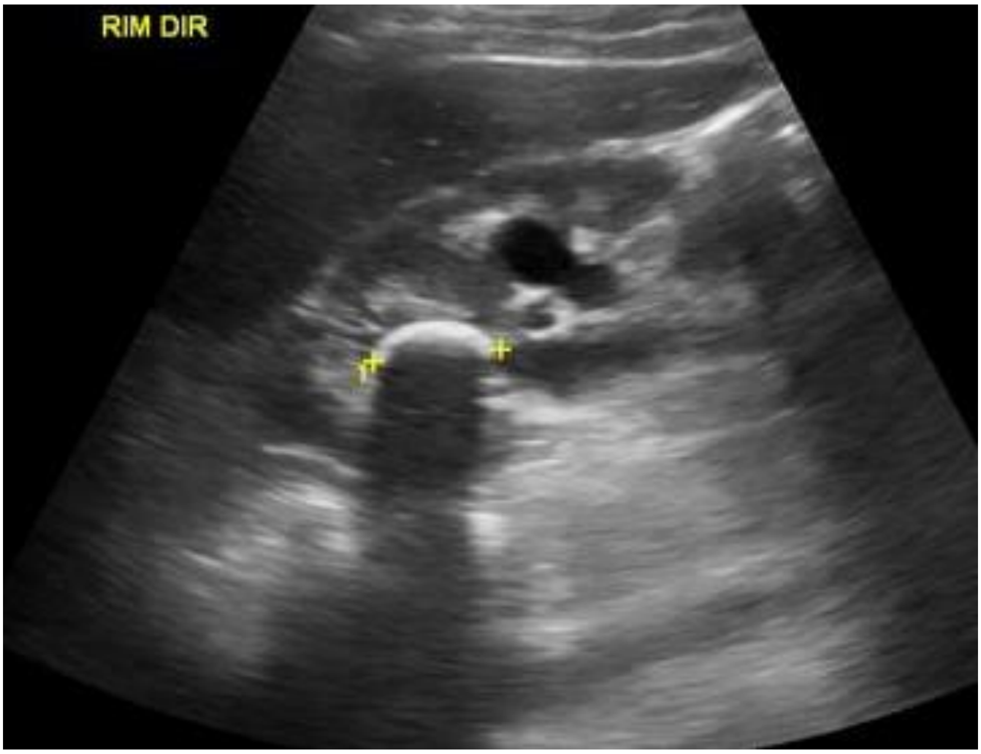


Figure 7: Ultrasound grey scale image of showing an upper pole calculus (measuring ~ 2.2 cm) in the right kidney casting a sharp posterior acoustic shadowing.

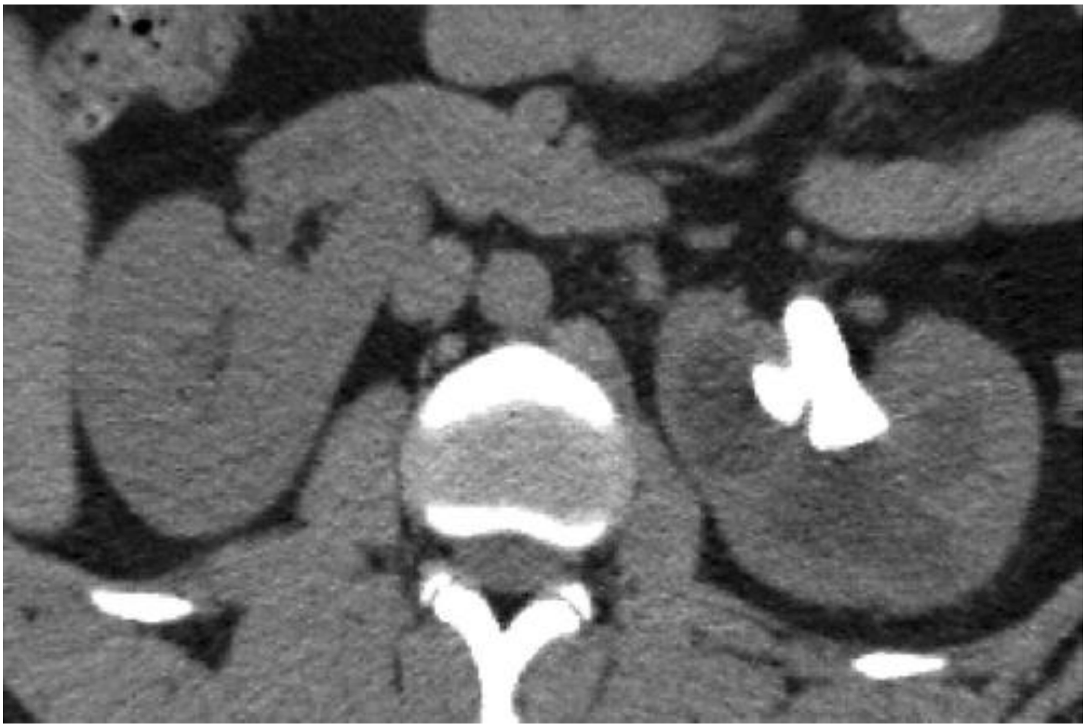


Figure 8. Unenhanced CT examination shows left hydronephrosis related to staghorn calculus.

Figure 9: Plain CT coronal reformatted image showing multiple microliths in bilateral kidneys.

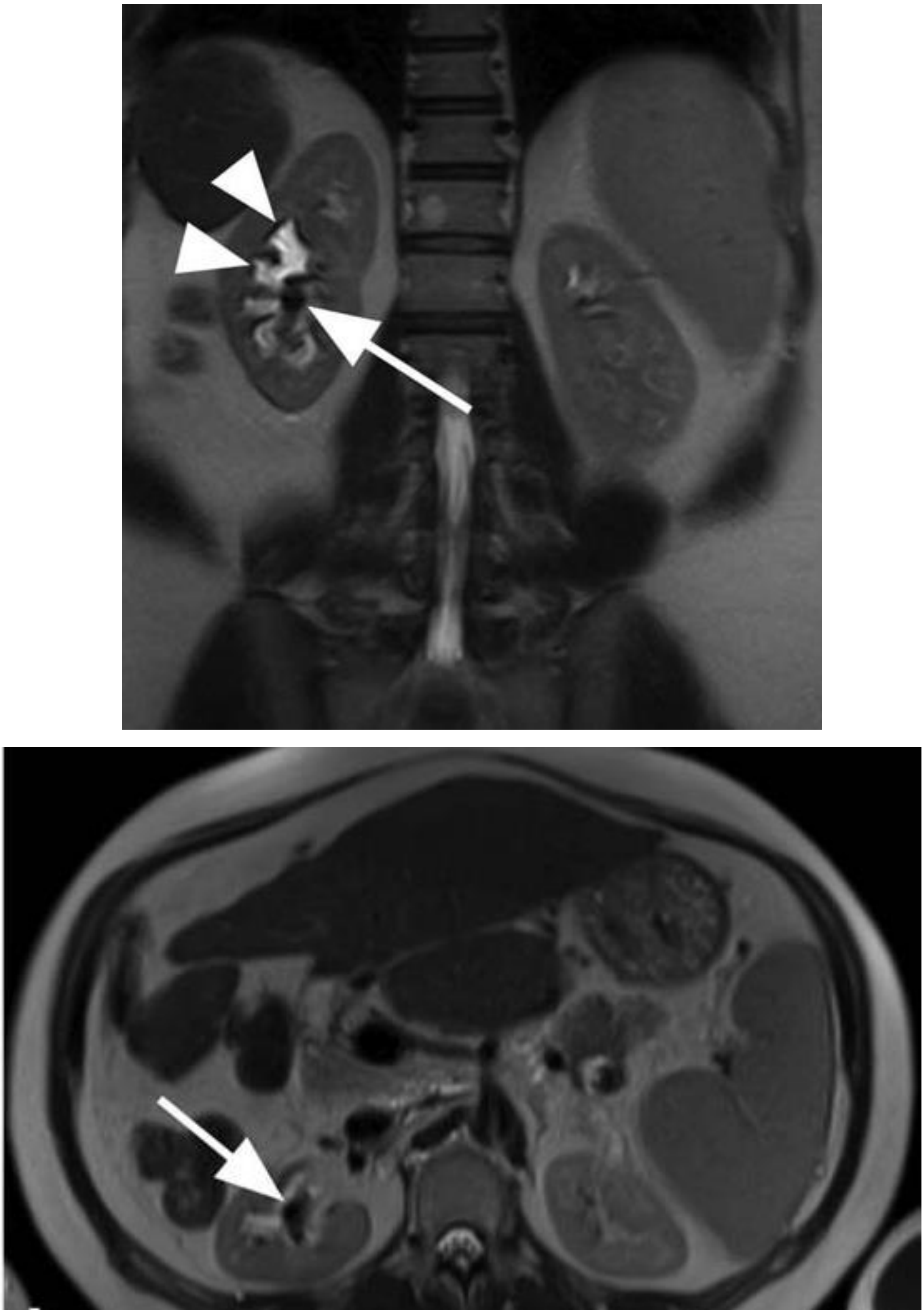


Figure 10: Coronal and axial T2W images demonstrate a staghorn calculus in the right renal pelvis (arrows). Visibility of the calculus is aided by hydronephrosis (a, arrowheads), with hyperintense fluid in the distended collecting system surrounding the hypointense obstructing calculus.

Computed Tomography (CT):

NCCT-KUB is highly sensitive and specific when it comes to diagnosing of urolithiasis. An advantage of NCCT is that it also provides additional information and findings which can be the cause of underlying patholgy[16-18].

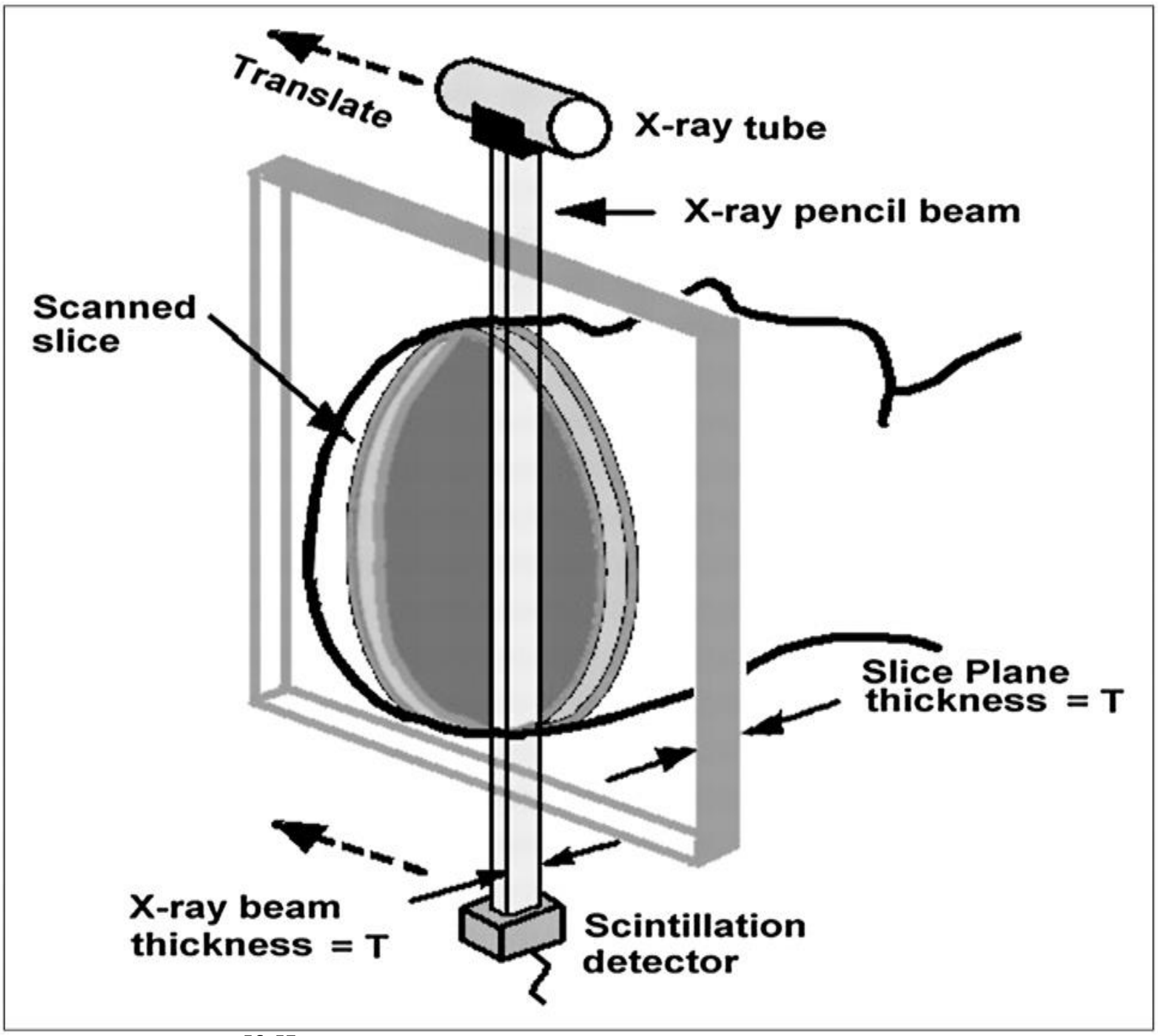
Modern CT scanners are rapid which can scan the abdomen and pelvis in under 7 seconds.

CT scan combines a series of X-ray images taken from multiple angles surrounding the body and uses computer processing to acquire cross-sectional slices of different parts of the body. CT provides more-detailed information than plain radiography.

The term ***computed tomography*** derives from *computed* (with computer), *tomo* (to cut), *and graph(y)* (pictures)[55]. CT utilizes ionizing radiation to record different densities and create images of a "slice" or "cut" of tissue. The x-ray beam rotates around the object within the scanner such that multiple x-ray projections pass through the object[56, 57].

With every single full rotation, scanner makes use of mathematical algorithms to construct a 2D slice. The thickness of each slice varies depending on the CT machine (ranges from 1-10 millimeters). When a full slice is gets completed, the image is stored and the bed will move forward into the gantry. The scanning process is then similarly repeated to produce another slice. This process continues till enough images are created for completing the study [57].

The CT image is composed of a grid of tiny squares which are known as pixels. The grays assigned to each pixel represent the attenuation of x-rays by the tissues in the slice. Manipulation of the gray scale allows optimal visualization of different tissues. The steps used to acquire the final CT image are collection of data, computer processing (mathematical calculation of attenuation of each structure in the tomographic slice), image display and storage of the acquired data. Common image artifacts that must be identified and interpreted as such include aliasing, ring artifacts, beam hardening effect, metal, motion, partial volume averaging, and streaking from



out-of-field objects[56, 57].

Figure 11: Principles of CT scan. CT arrangement. Axial slice through patient is swept out by narrow (pencil-width) x-ray beam as linked x-ray tube–detector

apparatus scans across patient in linear translation. Translations are repeated at many angles. Thickness of narrow beam is equivalent to slice thickness.

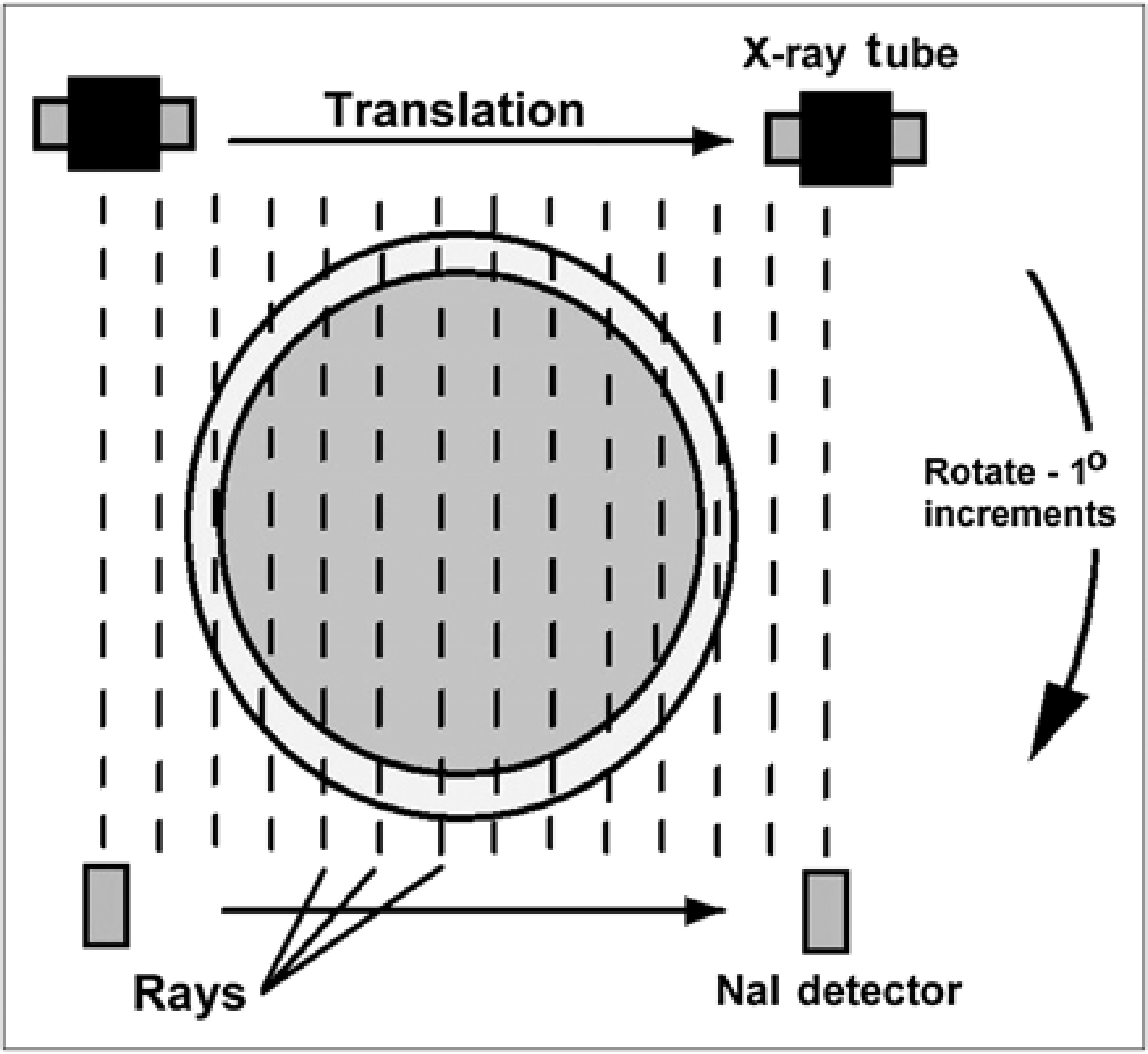


Figure 12: X-ray transmission measurements. Measurements are obtained at many points during translation motion of tube and detector. x-Ray path corresponding to each measurement is designated a ray, and set of rays measured during translation is designated a view. Views are collected at many angles (in 1° increments in this example) to acquire sufficient data for image reconstruction.

Figure 13: Slip-ring technology in Siemens Somatom Emotion CT scanner

Use of contrast in CT:

Same as in x-rays, bones are easily imaged, whereas soft tissues vary in their abilities to obstruct x-rays, thus resulting in changes in appearance and density. Because of this reason, intravenous (IV) contrast agents are used which are easily appreciable in an x-ray or CT scan and are also safe to use in patients. Contrast agents are composed of materials which stop x-rays and, thus, are more readily seen.

IV contrast for patients presenting with abdominal pain is not recommended initially and should be given only after examining the plain study. In most of the scenarios, an atypical abdominal pain ultimately would be a result of calculus that has moved. Even without IV contrast, correct diagnosis can be made. If contrast is absolutely necessary, doing the non-contrast study first eliminates urinary calculi from consideration. If the urinalysis comes out as abnormal, NCCT abdomen can be done before using IV contrast media which hinders diagnosing urinary stones. Obscuring urinary calculi with IV contrast can make it much more difficult to determine optimum treatment and possible surgery[16-18].

Classification of patients after diagnosis:

Patients with renal calculi can be put into different categories based on the composition of calculi and the previous history. This classification affects the diagnosis and treatment. However, both of these aspects have limitations[49]. Classifying according to composition has the disadvantage that chemical methods are imprecise and do not distinguish the crystalline forms[58]. Infrared spectroscopy or X-ray diffraction are the preferred methods[49]. Classification according to previous episodes of nephrolithiasis is easier because a single stone former is defined as a patient seeking advice for a single episode while a recurrent stone former is defined as a patient who has passed multiple calculi over a period of time.

MANANAGEMENT:

Nephrolithiasis requires emergency management which can include surgical interventions where indicated, and also medical therapy.

Medical management: Treatment of the pain associated with renal calculi includes the use of NSAIDs (non-steroidal anti-inflammatory drugs) as a first choice. The use of antispasmodics has not proved to be beneficial[59]. α-Adrenergic receptor antagonists (tamsulosin) and calcium channel blockers have been demonstrated to be an effective medical expulsive therapy[60]. Oral dissolution is usually recommended for uric acid calculi. 2/3rd of these calculi maybe partially dissolved [61]. The major aim of medical management is to treat the cause and prevent recurrence besides the symptomatic management.

Surgical management of nephrolithiasis can be non-invasive such as ESWL or invasive such as Percutaneous Nephrolithotomy. Common treatment options are:

1. Extracorporeal SWL (40–50% worldwide use),
2. Retrograde ureteroscopic fragmentation & retrieval (30–40%)
3. Percutaneous Nephrolithotomy (PCNL) (5–10%).

According to the EAU (European Association of Urology) guidelines, PCNL should be considered for large renal calculi (>20 mm) and also for smaller calculi (10–20 mm) in the lower pole when ESWL is unfavorable or fails but PCNL can be associated with significant complications[62].

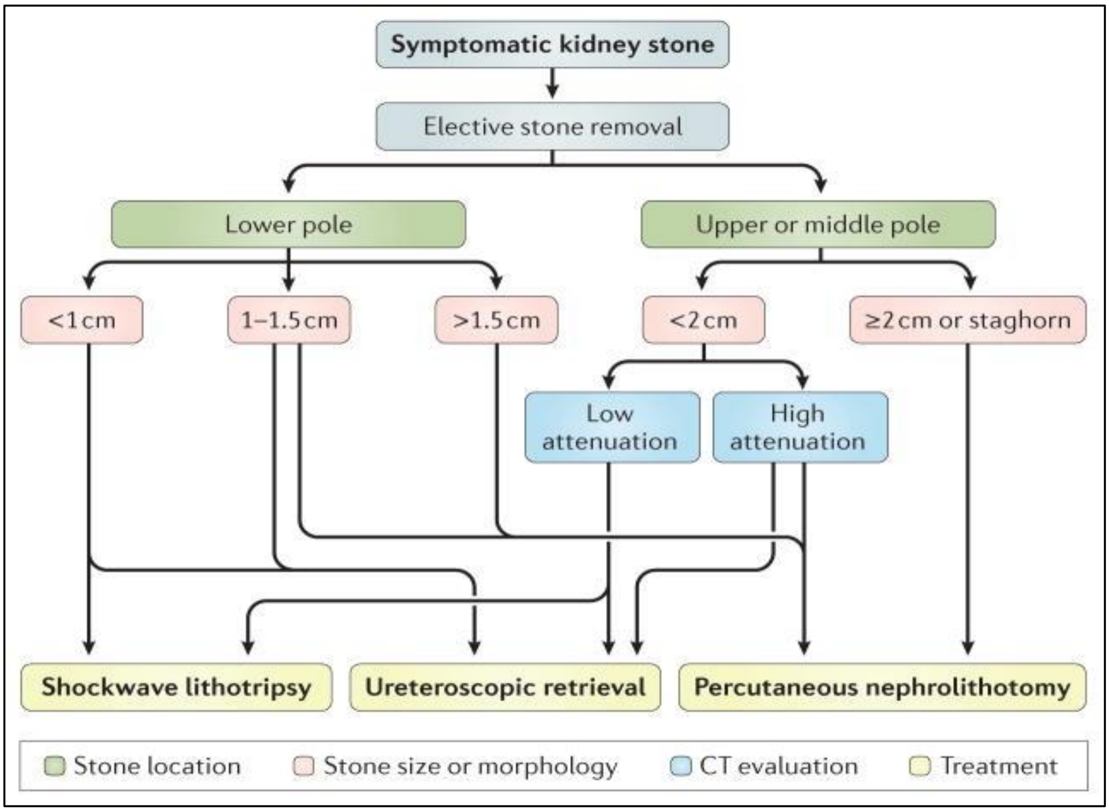


Figure 14: Algorithm for the most common approaches to surgical treatment of kidney stones.

EXTRACORPOREAL SHOCKWAVE LITHOTRIPSY:

Definition:

ESWL (Extracorporeal shock wave lithotripsy method) is a non-invasive treatment of nephrolithiasis in adults. ESWL should be considered as first option for renal calculi before opting for any surgical procedure[33, 63]. ESWL is inoperable disintegration and destruction of calculus in urinary tract by applying extracorporeal shock wave, through the tissues of the body.

History:

ESWL was first introduced in 1980 by Chaussy C et al[19]. The concept of shock waves use for fragmentation of calculi started in 1950 in Russia during the investigation of the supersonic aircraft[33, 63]. They found that shock waves coming from passing debris

into the atmosphere could break something solid.

Figure 15: Technique of ESWL.

Principle:

Shockwaves are used to disintegrate calculi. The shockwaves generated by the lithotripter are directed at the calculus. After these waves strike the calculus, there is release of energy which further results in the disintegration of the calculus.

Effectiveness, Indications and contra-indications:

ESWL has become the 1st choice of therapy for renal and ureteral calculi <2 cm in diameter[23]. Contraindications include coagulopathies (as there can be micro hemorrhages during the procedure), pregnancy, obesity, etc.

ESWL, even though a noninvasive technique has good clearance when compared to invasive procedures/surgery. However, these rates vary based on multiple factors[20-22]. It is important to select patients who will have a good prognostic outcome with EWSL, because of complications such as stone-street and hematoma formation and also need for surgery because of ESWL failure. The use of certain principles and the selection of favorable cases will enhance the results[23, 24]. Technical aspects such as type of lithotripter, energy and frequency, coupling of the patient to the lithotripter, calculus location have a vital role to play in the outcome. Other factors such as patient built, calculus size and density, skin-stone distance, anatomy anomalies are also important.

Procedure of ESWL:

Sedation or anesthesia can be given for pain tolerance and also to reduce renal movement with respiration. Antibiotic prophylaxis is not necessary. Alpha-blockers, particularly tamsulosin, are useful for stones >10 mm. Minor complications may occur following ESWL, which generally respond well to clinical interventions[23].

Outcome, success and complications:

Following factors play a major role when it comes to the prognosis of ESWL:

1. The calculus (size, location, composition-density),
2. The renal anatomy (obstruction/stasis, hydronephrosis, stenosis of the ureteropelvic junction, calyceal diverticula, horseshoe kidney, ectopic kidney/renal fusion) and
3. The Patient (skin-stone distance, renal failure, high BMI).

ESWL success is determined after 1–3 months from the procedure. This can be achieved by a follow-up radiograph or ultrasound KUB. Patients with residual fragment size <4 mm are declared as free from calculus as such as small fragment is usually asymptomatic and can pass spontaneously[64]. Lower pole calculi are the biggest challenge for the surgeon as the clearance of such calculus is very poor.

Minor complications may occur following ESWL, which generally respond well to clinical interventions. Pain in the costo-vertebral angle and flank, the appearance of petechiae or subcutaneous bruising at the entry and exit point of the shock waves are common, requiring analgesics in up to 40% of cases[65]. Microscopic hematuria occurs in virtually all cases, however gross hematuria appears only in about one third of patient[66].

In relation to late complications, there has been an inconsistent association between ESWL and the development of hypertension and diabetes[23].

NONCONTRAST ABDOMINAL COMPUTED TOMOGRAPHY (NCCT):

NCCT KUB is the gold-standard imaging investigation for diagnosis and pre-operative assessment of nephrolithiasis. NCCT has previously used in the past for assessing calculi since a long time. Compared with other imaging modalities, NCCT is fast and accurate in confirming the diagnosis. Besides, NCCT provides accurate assessment of intra-abdominal fat and it is considered to be the optimal method over other anthropometric measurements, such as BMI or waist circumference[67]. In addition to this, previously few studies have proven that total fat area (TFA), visceral fat area (VFA), and subcutaneous fat area (SFA) that has been obtained from NCCT KUB around L4 & L5 vertebrae, related closely to the abdominal fat volume[68, 69].

CT has high a sensitivity & specificity for imaging calculi in patients presenting with renal colic. The ACR (The American College of Radiology) and AUA (The American Urological Association) both recommend CT as the first-line investigation for adult patients presenting with symptoms suggestive of obstructive nephrolithiasis[15]. Data is obtained by rotation of radiation source and opposite detector around the patient. This data is processed by a computer which does post-processing for obtaining 3D images. The sensitivity of NCCT is as high as 95% for diagnosing calculi[70, 71]. Even though, larger calculi are easily noticeable on CT, but sometimes, smaller calculus might be missed. Detection for smaller calculi can be improved by evaluation of thin slices[71. 72].

HOUNSFIELD UNIT:

The Hounsfield unit (HU) measures attenuation and density of different tissues in body. In the HU scale, water corresponds to 0 HU, air −1,000 HU and bone 1,000 HU. Sir Godfrey Newbold Hounsfield introduced the concept of quantifying the X- and created this Hounsfield scale. CT images are made up of pixels. These pixels will have value ranging from 1-256 (1 represents black and 256 represents white). These values correspond X-rays that are passing through the human body which are then estimated by detector. This estimation of X-rays provides the final HU value. This helps in differentiating the different values from 1-256 which is not possible with ordinary naked eye[73].

HU is of great value for diagnosing and evaluating nephrolithiasis. It can not only help in determining the calculus composition but also helps in choosing among the treatment options.

HU can give a significant knowledge about radio-opacity. It helps urologists to select the appropriate intervention and imaging modality to use during follow-up.

HU has several roles such as:

1. Determining calculus type, composition.
2. Determining the strength of shockwave needed for fragmentation.
3. Predicting radio-opacity of stones, hence reducing the follow up exposure to radiation.
4. Predicting success of ESWL.
5. Predicting success of PCNL.

But its use is limited in predicting success of Ureteroscopic lithotripsy and medical expulsive therapy.

Calculus HU can determine the composition, as different calculus compositions will absorb varying amounts of radiation. Uric acid calculi typically have 200–400 HU, calcium oxalate calculi range from ~600–1,200 HU[74].

There exists a positive relationship between HU value and hemorrhage in PCNL, as it is related with an increased endoscopic manipulation to extract stones. HU value has been used as a parameter to prognosticate ESWL outcome. HU>1000 is considered unfavorable for ESWL[27-29]. A stone clearance rate of 55% following ESWL has been reported for stones with attenuation values >1000 HU, compared with 86% for those with attenuation levels of 500–1000 HU and 100% for those with attenuation levels < 500 HU[30].

Calculi with high HU, because of their compact structure will pass through the ureter slowly and with difficulty. But HU value cannot predict the likelihood of success for medical expulsive therapy and does not provide any additional benefit[73, 75]. The use of HU is also limited in Ureteroscopic lithotripsy.

Operational definitions to define outcome can also vary across studies. A study conducted by El Mahdy AM et al concluded that a successful ESWL is when there is complete clearance calculus or small residual gravels <4 mm. Failure of ESWL was considered when there was no fragmentation of the stone after three sessions[76].

CT attenuation values can predict outcome of ESWL. Higher HU values are directly proportional to the shockwaves required [25, 26] and also reduces the clearance rates. Dual-energy CT scanners have an advantage that patients are assessed at two different current settings followed by comparison of HU values on 2 detectors. The ratio of HU values at these two current settings also helps in evaluation of calculus composition[77, 78].

NCCT is preferred over ultrasonography in scanning obese subjects. NCCT is ideal for patients with high BMI (>30) according to various standard guidelines[70, 79]. Limitations of CT include cost and radiation exposure. A standard CT scan exposes patients to an effective dose of ionizing radiation of ~10 mSv[79].

Use of low-dose CT helps in reduction of radiation exposure as it lowers tube current. A standard NCCT scan uses 100 mAs tube current, while in low-dose ~30 mAs or lower current is used[80]. Alternatively, low-dose protocols can also make use of an automated current modulator that automatically adjusts current based on attenuation of different structures. Low-dose CT refers to the use of ionizing radiation <3 mSv. Low-dose CT has sensitivity of 99% and specificity of 94%[81]. There is no gross difference in the information when compared low dose with standard dose CT[82]. But there is a definite decline in the quality of image when lower doses of current are used[80]. Currently, the guidelines do not recommend low-dose CT for higher BMI(>30) cases[62, 70, 79].

CT is a highly sensitive and specific for diagnosing nephrolithiasis. The ACR (The American College of Radiology) and AUA (The American Urological Association) both recommend CT as the first-line investigation for adult patients presenting with symptoms suggestive of obstructive nephrolithiasis[15]. Routine use of NCCT-KUB has been revolutionary for evaluation and management of nephrolithiasis, near completely replacing other imaging methods for the diagnosis of renal and ureteric calculi.

Sengupta S et al (2021) evaluated the Triple-D scoring system to assess the stone free rate (SFR) in 120 individuals who were given ESWL for renal stones measuring 10-20 mm in diameter. Before performing ESWL, Triple-D scoring was done. The scoring observed was in the range starting from 0 (worst) to 3 (best). Follow-up was done by plain radiography after 3 weeks. Complete clearance was considered the "stone free status". Calculus size, density and location came out to be good prognostic factors of stone free rate. The (AUC) of Triple-D score turned out to be 0.598. They concluded that Triple-D scoring system has been successfully validated as the SFR showed a parallel increase with every positive component[34].

Ullah S et al (2021) studied the ESWL outcome in patients with high-density stone. A descriptive case series study was conducted in patients of either gender aged between 25-50 years, who presented with solitary renal and ureteric calculi of 0.5-2 cm in diameter and high-density renal stones [>750 Hounsfield units (HU)]. Favorable outcome was defined as complete clearance within 3 ESWL sessions. 51.6% male preponderance was noticed. Renal and ureteric stones were present in

69.7% and 30.3% of cases. 21.3% of patients showed stone clearance after two ESWL sessions, 27% of patients after three ESWL sessions, and 51.6% of patients after four ESWL sessions. Clearance was found in 58.2% and a satisfactory outcome was observed in 42% of patients. They concluded that the outcome with ESWL is satisfactory for high-density renal stone on NCCT[83].

Sheikh AH et al (2020) determined the outcome of ESWL in 100 cases with renal calculi of 0.6 cm to 2 cm in size. ESWL was performed (Storz Medical Modulith SLX-F2). During each session 3000 shock waves were used. CT was performed to determine ESWL outcome, i.e. pain during procedure and clearance of the calculi. The mean age of patients was 37.7 ± 10.9 years. Of the 100 patients, 54 (54%) were male and 46 (46%) were female. About 44 (44%) had right renal calculus, 51 (51%) had left renal calculus and 5 (5%) had bilateral renal calculus. There were 11(15%) patients had 1 ESWL to 2 ESWL visits, 60 (60%) patients had 3 ESWL to 5 ESWL visits and 29 (29%) patients had 6 ESWL visits. Pain was observed in 8 (8%) cases while complete clearance was observed in 98 (98%) patients. They concluded that ESWL is a highly successful modality for removal of renal calculi in adult population[84].

Waqas M et al (2018) evaluated various CT scan-based factors for forecasting the ESWL (extracorporeal shock wave lithotripsy) outcome for renal stones. They did a retrospective study on 203 subjects undergoing ESWL with renal stones of size 5-20 mm. They evaluated BMI, stone attenuation value (SAV), stone location, skin-to-stone distance (SSD), diameter of the stone, Volume, area and Hounsfield density. 60% subjects showed clearance. Double J stenting, a lower pole, a high SAV, higher

Hounsfield density were negative predictors. The independent predictors of ESWL that were statistically significant were stone location, SSD, and SAV[85].

Yamashita S et al (2018) in their review article summarized the CT parameters for prognosticating ESWL outcome in stone cases in the upper urinary tract. They observed that “Shock wave lithotripsy (SWL) should be the first choice for upper ureter calculi which has advantages of safety and non-invasiveness, but with low success[86.]

Waqas M et al (2017) compared the NCCT scan-based parameters which influenced the ESWL outcome for calculi in ureter. They retrospectively evaluated CT of patients with calculi within ureter. They concluded that low SSD, HU and HD favored ESWL success[87].

Geng JH et al (2015) assessed the impact of calculus parameters and abdominal fat distribution on calculus-free after performing ESWL. They retrospectively reviewed 328 subjects with urinary stones who underwent SWL. The subjects were classified into stone-free (60%) or residual stone group (40%). Unenhanced CT variables like stone attenuation, abdominal fat area, and SSD were analysed. The mean age was 49.35 ± 13.22 years and 55.32 ± 13.52 years, respectively. On multivariate logistic regression, statistically significant factors influencing the result were stone size, stone attenuation, Total Fat Area and creatinine. [Adjusted odds ratios and (95% confidence intervals): 9.49 (3.72–24.20), 2.25 (1.22–4.14), 2.20 (1.10–4.40), and 2.89 (1.35–6.21) respectively, all $p < 0.05$]. They concluded that NCCT should be performed before subjecting patient for ESWL[69].

El Mahdy AM et al (2016) evaluated the role of MDCT for predicting ESWL outcome for urinary calculi. 54 symptomatic renal colic and hematuria subjects were evaluated. Overall percentage of success was 90.7. In 26 subjects (48.1%), ESWL success was achieved after second session of ESWL while 15 (27.8%), achieved after first session. They added that smaller size and density of urinary stones can increase ESWL success rate. They concluded that MDCT can provide valuable inputs in predict the outcome and deciding treatment for urinary stones such as ESWL[76].

Nasef A et al (2015) evaluated the relationship between renal stone density in NCCT and stone biochemical composition and success of ESWL. 60 subjects with solitary renal stones ≤20 mm size, were subjected for ESWL. Dornier SII lithotripter was used in all cases. Pre-ESWL NCCT was done. The expulsed stone fragment(s) underwent chemical analysis by chemical stone analysis kits. The Overall renal ESWL success rate was 93.33%. The ESWL success rate was significantly better in calculi ≤ 15 mm than larger stones (97.62% versus 83.33%; $p=0.042$). ESWL was effective in 47 of 48 (97.92%) cases with stone density < 1000 HU and only in 9 of 12 (75.00%) of those with stone density ≥1000 HU ($p=0.023$). The stones with density values ≥1000 HU needed more energy, shockwaves and ESWL sessions than stones with a density value < 1000 HU ($p<0.001$). The most common type of stone detected were calcium oxalate stone (29.63%), uric acid and mixed uric acid + calcium oxalate + calcium phosphate stones (20.37% for each). Calcium oxalate had the highest density values (902.73±425.23 HU) and uric acid stones had the lowest values (364.00±115.17). No significant differences were observed regarding stone compositions. They concluded that use of pre-ESWL NCCT will allow predicting stone composition and fragility [29].

Yazici O et al (2015) investigated the patient (age, sex, BMI, BUN) and stone related factors (laterality, location, longest diameter with density as CT HU and SSD on fragmentation) determining the final outcome of SWL in ureteral stones management. They evaluated 204 adult subjects undergoing SWL for single ureteral stone (between 5 to 15 mm). No significant variation was noticed in stone free rates for proximal (68.8%) and distal ureteral stones (72.7%) (p=0.7). Higher BMI (mean: 26.8 and 28.1, p=0.048) and density values were statistically significant factors influencing treatment failure for proximal ureteral stones. In distal ureteral stones, only higher SSD value was the significant deciding factor (median: 114 and 90, p=0.012)[88].

Elkholy MM et al (2014) evaluated the efficacy and safety of the Dornier lithotripter S II (ESWL) system on 97 subjects with ureteral stones (solitary radiopaque ureteral stones of radiological stone size of ≤1 cm). 54 were males and 43 were females Their mean age was 42.6 years. Procedure time, number of shocks, energy used, number of sessions, ESWL outcome and complications were recorded. Stones were in the abdominal (upper) ureter in 50% and in pelvic (middle ureter) in 47%. Mild hydronephrosis was found in 85% of cases. 49 were treated by a single session, while 35% required two sessions and 16% needed three sessions. The average shockwaves given was 3125. After 1 session, 49 patients were successfully treated. Clearance rates for upper, middle ureteral stones were 94% and 95.7%. They concluded that there was no serious complications[89].

Tanaka M et al (2013) investigated factors on NCCT that can predict SWL outcome by reviewing records of 75 subjects with urinary calculi (between 5 to 20 mm) who underwent SWL. They estimated the largest calculus dimension. Successful outcome was defined as stone-free or <4 mm stone in diameter. The success percentage was 73.3. Average stone attenuation value, stone length, and stone cross-sectional area 627.4±166.5 HU (Hounsfield unit) vs. 788.1±233.9 HU (p=0.002), 11.7±3.8 mm vs. 14.2±3.6 mm (p=0.015), and 0.31±0.17 cm^2 vs. 0.57±0.41 cm^2 (p<0.001) in successful and unsuccessful groups, respectively. SAV was the only independent predictor of SWL success (p=0.023) in multivariate analysis. Stone cross-sectional area (CSA) had a tendency to be related with SWL success (p=0.053). By using cutoff values of 780 HU for SAV and 0.4 cm^2 for CSA, the subjects were classified in 4 groups. Groups with a low SAV and a low CSA were more than 11.6 times likely to have a successful result on SWL compared to all other groups (odds ratio, 11.6; 95% confidence interval, 3.9 to 54.7; p<0.001)[90].

Park BH et al (2012) retrospectively reviewed 573 subjects who were subjected to ESWL for urinary stones sized from about 5 mm to 20 mm with no evidence of stone movement. They determined whether the SSD, as measured by CT scans, could affect the stone-free rate achieved via ESWL. They excluded patients with ureteral catheters and percutaneous nephrostomy patients; ultimately, only 43 patients fulfilled the inclusion criteria. They classified the success group as those patients whose stones had disappeared on a CT scan or simple X-ray within 6 weeks after ESWL and unsuccessful group as those patients in whom residual stone fragments remained on a CT scan or simple X-ray after 6 weeks. They analyzed variations among two groups in age, sex, size of stone, skin-to-stone distance (SSD), stone location, density (Hounsfield unit: HU), voltage (kV), and shockwaves delivered. The success group included 33 patients and the failure group included 10. In the univariate and multivariate analysis, age, sex, size of stone, stone location, HU, kV and the number of shocks delivered did not vary much among the groups. Only

SSD was a factor influencing success: the success group clearly had a shorter SSD (78.25±12.15 mm) than did the failure group (92.03±14.51 mm). The results showed SSD as the only index that influences the results of ESWL. They concluded that SSD may therefore be a useful clinical predictive factor of the success of ESWL on renal stones[27].

Abdelghany M et al (2011) evaluated the ESWL efficiency on 100 subjects with a solitary distal ureteric calculi (DUC) by a lithotripter (Lithostar Plus, Siemens, Erlangen, Germany). They also determined the factors that influenced outcome of treatment by evaluating after 3 months. They observed that after in situ ESWL, 84% were stone-free (after first session in 57, second session in 27). BMI, stone length and stone width were the statistically significant factors affecting the Stone Free Rate (SFR). The SFR was much less in obese subjects compared to normal and overweight subjects (P = 0.019). Stone width ⩾8 mm was associated with a SFR of 64% (14/22), compared with 89.7% (70/78) for those with a stone width of <8 mm (P =0.007). The SFR was 86.8% (66/76) for a stone length of ⩾10 mm and 71% (17/24) for a stone length of >10 mm (P = 0.016). BMI, stone width and stone length were the statistically significant factors on multivariate analysis. They concluded that in situ ESWL was effective for DUC. BMI, dimension of the stone were the significant predictors determining the overall success of ESWL[91].

Saygin H et al (2020) compared results of minimal invasive treatment (RIRS, m-PCNL) with the ESWL, Micro-Percutaneous Nephrolithotomy (m-PCNL), and RIRS in patients with nephrolithiasis (<20 mm). Preoperative renal ureter-bladder (KUB) film and computed tomography (CT) were used to image stone size and localization in all patients. 90 consecutive patients were randomized equally to three groups. After 1st month, stone-free rate for the lower calyx stones was 33.3% (3 patients out of 10) in ESWL, 83.3% (10 patients out of 12) in RIRS, and 90.9% (10 patients out of 11) in m-PCNL. ESWL's success was less in lower pole calculi. Our rates for the stones in renal pelvis, middle, and upper calyx were 85.7% (18 patients out of 21) in ESWL, 94.4% (17 patients out of 18) in RIRS and 94.7% (18 patients out of 19) in m-PCNL. No difference was observed in the duration of hospitalization undergoing RIRS and m-PCNL. They concluded that m-PCNL and RIRS methods were more effective than ESWL, with regards to stone free rates[92].

Chung DY et al (2019) performed review and network meta-analysis comparing stone-free rates following retrograde intrarenal surgery (RIRS), ESWL and percutaneous nephrolithotomy (PCNL) treatments of nephrolithiasis. They included clinical trials comparing RIRS, SWL, and PCNL. The quality scores within subscales were relatively low-risk. Network meta-analyses indicated that calculi-free rates of RIRS (OR 0.38; 95% CI 0.22-0.64) and SWL (OR 0.12; 95% CI 0.067-0.19) were lower than that of PCNL. In addition, stone-free rate of SWL was lower than that of RIRS (OR 0.31; 95% CI 0.20-0.47). Stone free rate of PCNL was also better in comparison to RIRS including ≥ 2 cm stone (OR 4.680; 95% CI 2.873-8.106), lower pole stone (OR 1.984; 95% CI 1.043-2.849), and randomized studies (OR 2.219; 95% CI 1.348-4.009). They observed that PCNL showed the highest success and stone-free rate among surgical procedures. In contrast, SWL had the lowest success and stone-free rate[93].

Gallioli A et al (2017) studied about the HU value and success of PCNL. They concluded that HD is an independent factor that can prognosticate the patients to determine whether PCNL will be successful or not. There was no correlation of the HU value with complications of the PCNL[94].

Niemann T et al (2008) evaluated the diagnostic performance of low-dose CT for urolithiasis diagnosis by a meta-analysis. They included 1,061 subjects from seven studies by searching on PubMed, Medline, and Cochrane Library databases for articles from 1995 to 2007 on low-dose CT (< 3 mSv dose during whole CT examination) for urolithiasis diagnosis. They reported the pooled sensitivity as 96.6% (95% CI of 95% to 97.8%) and specificity as 94.9% (95% CI of 92% to 97%) respectively. They concluded that low-dose CT should be utilized for the initial imaging workup in suspected urolithiasis[81].

MATERIALS & METHODS

Study site: This study was conducted in the department of Radiodiagnosis, R. L. Jalappa Hospital and Research Centre, affiliated to Sri Devaraj Urs Medical College.

Study population: All the Patients with clinically/sonographically suspected nephrolithiasis and referred for CT evaluation at Department of Radiodiagnosis, R. L. Jalappa Hospital and Research Centre were considered for study population.

Study design: The current study was a cross sectional analytical study

Sample size: Sample size is estimated by using the proportion of subjects with respect to the study done by **Nasef et al**, where *P* value is found to be 0.042.

$$\text{Sample size} = \frac{Z_{1-\alpha/2}{}^{2}\,p(1-p)}{d^{2}}$$

Using the above values at 95% Confidence level, a sample size of 37 subjects diagnosed with nephrolithiasis and undergoing extracorporeal shockwave lithotripsy were taken up for the study.

Sampling method: All the eligible subjects were recruited into the study consecutively by convenient sampling till the sample size is reached.

Study duration: The data collection for the study was done between December 2019 to July 2021 for 18 Months.

Inclusion Criteria:

1. Patients who are 18 years of age and above.
2. Patients with calculus size of 5-20 mm.

Exclusion criteria:

1. Pregnancy.
2. Coagulopathy.
3. Severe untreated hypertension.

Ethical considerations: Study was approved by institutional human ethics committee. Informed written consent was obtained from all the study participants and only those participants willing to sign the informed consent were taken in the study. The risks and benefits involved in the study and voluntary nature of participation were explained to the participants before obtaining consent. Confidentiality of the study participants was maintained.

Data collection tools: All the relevant parameters were documented in a structured study proforma.

Methodology:

Written Informed Consent was taken from all the individuals.

NCCT-KUB Protocol:

Individuals underwent NCCT-KUB on SIEMENS® SOMATOM EMOTION 16 CT machine and those who show presence of nephrolithiasis were subjected to ESWL.

- kV – 130 kV
- Tube current – Based on the BMI the tube current will vary as per the CARE 4D® software.
- Slice thickness – 5 mm acquisition done.
- Sagittal and coronal reformation were performed.

- After scan, all CT indices were recorded.

Figure 16: SIEMENS® SOMATOM EMOTION 16® CT scanner used in the study.

CT Indices:

Parameters included are as follows:

1. **Hounsfield unit**
   - Hounsfield unit is a measure of density of the calculus which provides information about the hardness. More the HU value, harder is the calculus and vice-versa. It is measured by drawing a ROI (region of interest) covering most of the calculus which will display minimum, mean and maximum HU values. Mean or the average HU value is considered. The measurement is taken at 5x zoom and in bone window setting.

2. **Calculus size**
   - The calculus was evaluated to find the largest dimension which was taken as the calculus size. The calculus size was measured at 5x zoom in bone window setting.

3. **Calculus location**
   - Based on the calyx in which the calculus is situated, renal calculi locations can be classified as upper, inter and lower poles.

4. **Hounsfield density**
   - Hounsfield density is also one of the measures of calculus density. It depends on the HU value of the calculus and additionally on the

calculus size. It is calculated as the ratio of HU value of calculus to largest dimension of calculus. Its unit is HU/mm.

5. **Skin to stone distance (SSD)**
   - SSD is self-explanatory which depends on factors such as BMI (body mass index), abdominal circumference and location of the calculus. 3 lines are drawn from the skin surface to the calculus; horizontal, vertical and 3rd line making a 45° angle with both earlier mentioned lines. SSD is taken as the mean of these 3 distances.

Lithotripter:

Patients were treated with extracorporeal shockwave lithotripsy with SIEMENS SIGMA® ORILITHO-CAL lithotripter. It is equipped with C-arm and Ultrasound (SIEMENS ACUSON X300). Depending on the calculus properties, the lithotripter parameters were set to ensure best outcome.

Patients underwent ESWL upto a maximum of 3 sessions. The parameters of the lithotripter were set at 60 shockwaves/min for 45 minutes at an energy of 20 kV.

Follow up ultrasound was performed to see for absence of calculus or fragmented calculus measuring 4 mm or less (which is considered successful treatment).

Statistical Methods:

Result (Success v/s failure) was considered as primary outcome variable. Hounsfield units, Hounsfield density, calculus size, location and skin to skin distance etc., were considered as secondary outcome variables.

Descriptive analysis was carried out by mean and standard deviation for quantitative variables, frequency and proportion for categorical variables. Data was also represented using pie charts, bar charts and clustered bar charts.

Cross tabulation was performed to determine the relation between categorical outcome parameters.

The utility of different indices in predicting successful outcome of ESWL was assessed by Receiver Operative curve (ROC) analysis. Area under the ROC curve along with its 95% CI and p value are presented. The sensitivity, specificity, predictive values and diagnostic accuracy with the decided cutoff values along with their 95% CI were presented. $P<0.05$ was taken as to be of statistical significance. IBM SPSS was used for statistical analysis.

RESULTS

A total of 45 participants were taken up for the final analysis.

Table 1: Descriptive analysis of age in the study population (N=45)

Parameter	Mean ± SD	Median	Minimum	Maximum
Age (in years)	41.62 ± 15.25	38.0	18.0	85.0

The mean age of participants among the study population was 41.62 ± 15.25 years, ranged from 18 years to 85 years.

Table 2: Descriptive analysis of gender in the study population (N=45)

Gender	Frequency	Percentages
Female	21	46.67%
Male	24	53.33%

Among the study population, there were 21 (46.67%) females and 24 (53.33%) males.

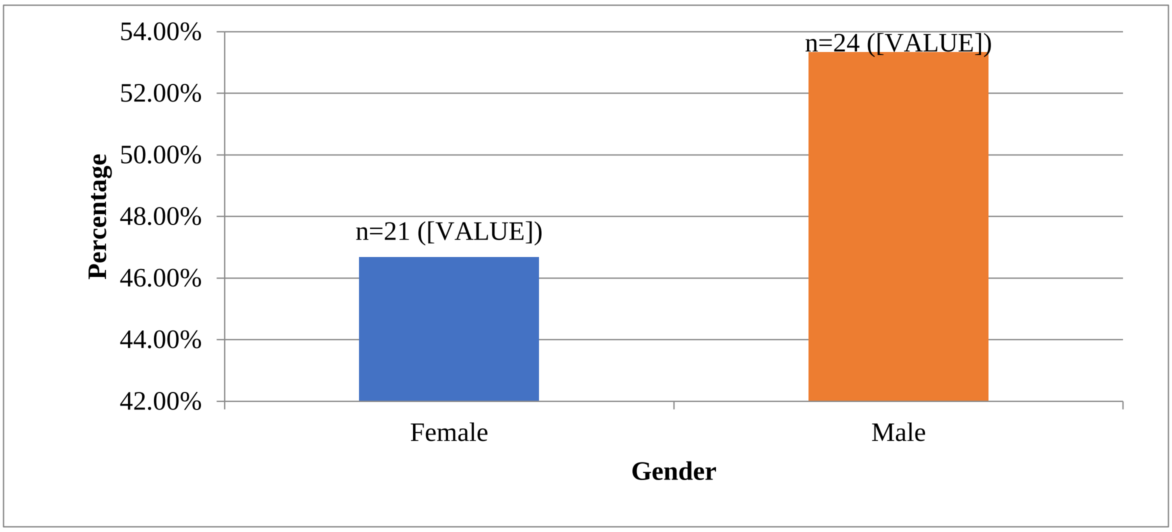


Figure 17: Bar chart for gender

Table 3: Descriptive analysis of kidney side in the study population (N=45)

Kidney side	**Frequency**	**Percentages**
Right kidney	26	57.78%
Left kidney	19	42.22%

Among the study population, calculus was present in right kidney for 26 (57.78%) participants and in left kidney for 19 (42.22%) participants.

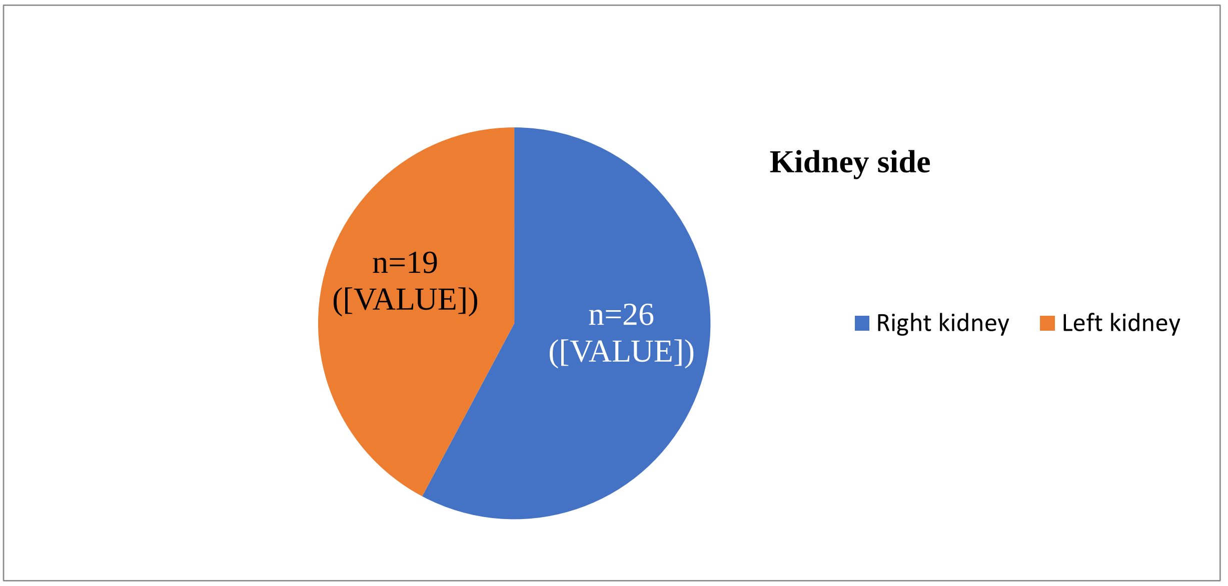


Figure 18: Pie chart for kidney side

Table 4: Descriptive analysis of calculus location in the study population (N=45)

Location	Frequency	Percentages
Pelvis	14	31.11%
Upper pole	12	26.67%
Lower pole	12	26.67%
Interpole	7	15.56%

The location of calculus was renal pelvis for 14 (31.11%) participants, upper pole for 12 (26.67%) participants, lower pole for 12 (26.67%) participants and interpole for 7 (15.56%) participants.

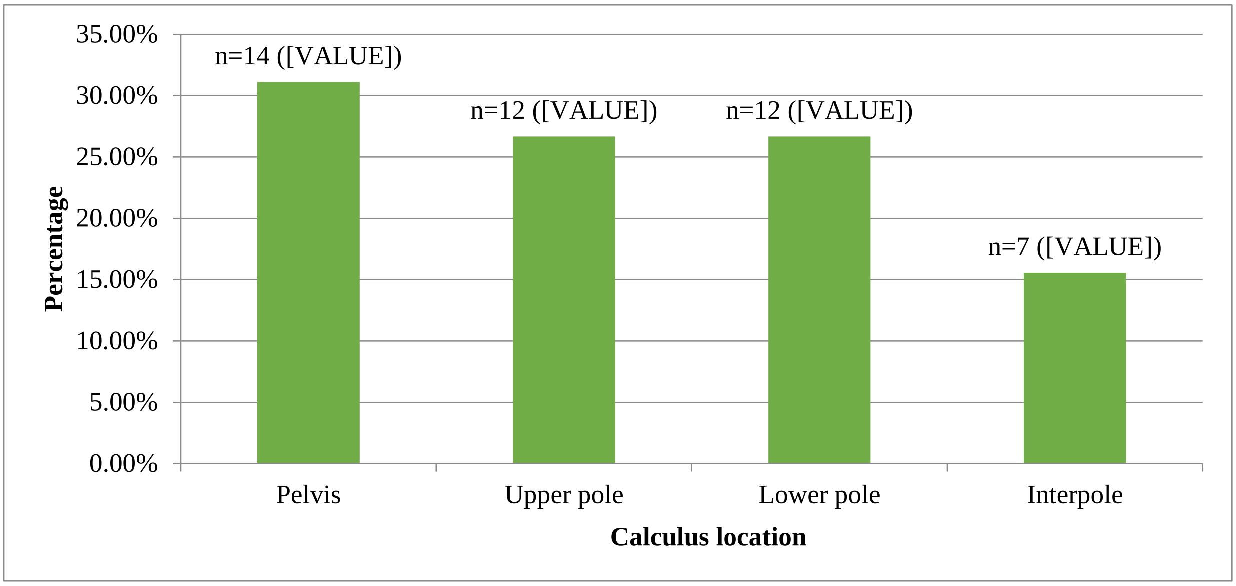


Figure 19: Bar chart for calculus location

Table 5: Descriptive analysis of calculus size in the study population (N=45)

Parameter	**Mean ± SD**	**Median**	**Minimum**	**Maximum**
Calculus Size (in mm)	11.46 ± 4.14	11.0	5.2	18.8

The mean calculus size in the study population was 11.46 ± 4.14 mm, ranged from 5.2 mm to 18.8 mm.

Table 6: Descriptive analysis of calculus related parameters in the study population (N=45)

Parameter	Mean ± SD	Median	Minimum	Maximum
Hounsfield units Value	824.36 ± 315.47	907.0	274.0	1338.0
Hounsfield Density (HU/mm)	81.04 ± 38.65	75.3	11.6	167.3
Skin-Stone Distance (in cm)	8.63 ± 2.97	8.3	4.5	24.8

The mean Hounsfield units in the study population were 824.36 ± 315.47 units, ranged from 274 units to 1338 units. The mean Hounsfield density in the study population was 81.04 ± 38.65 HU/mm, ranged from 11.6 HU/mm to 167.3 HU/mm. The mean skin to stone distance in the study population was 8.63 ± 2.97 cm, ranged from 4.5 cm to 24.8 cm.

Table 7: Descriptive analysis of clearance in the study population (N=45)

Clearance	Frequency	Percentages
Yes	36	80.00%
No	9	20.00%

Among the study population, 36 (80.00%) participants had clearance.

Table 8: Descriptive analysis of sessions in the study population (N=45)

Sessions	Frequency	Percentages
1.00	33	73.33%
2.00	9	20.00%
3.00	3	6.67%

The number of sessions was 1 for 33 (73.33%) participants, 2 for 9 (20.00%) participants and 3 for 3 (6.67%) participants.

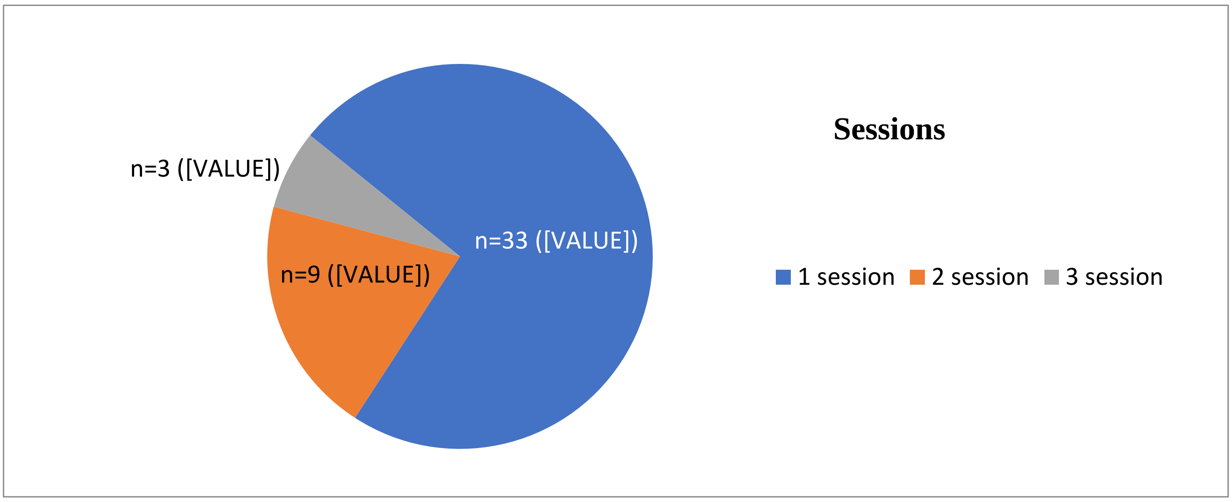


Figure 20: Bar chart for sessions

Table 9: Descriptive analysis of result in the study population (N=45)

Result	Frequency	Percentages
Success	42	93.33%
Failure	3	6.67%

Among the study population, the result was success for 42 (93.33%) participants and failure for 3 (6.67%) participants.

Figure 21: Bar chart for ESWL result

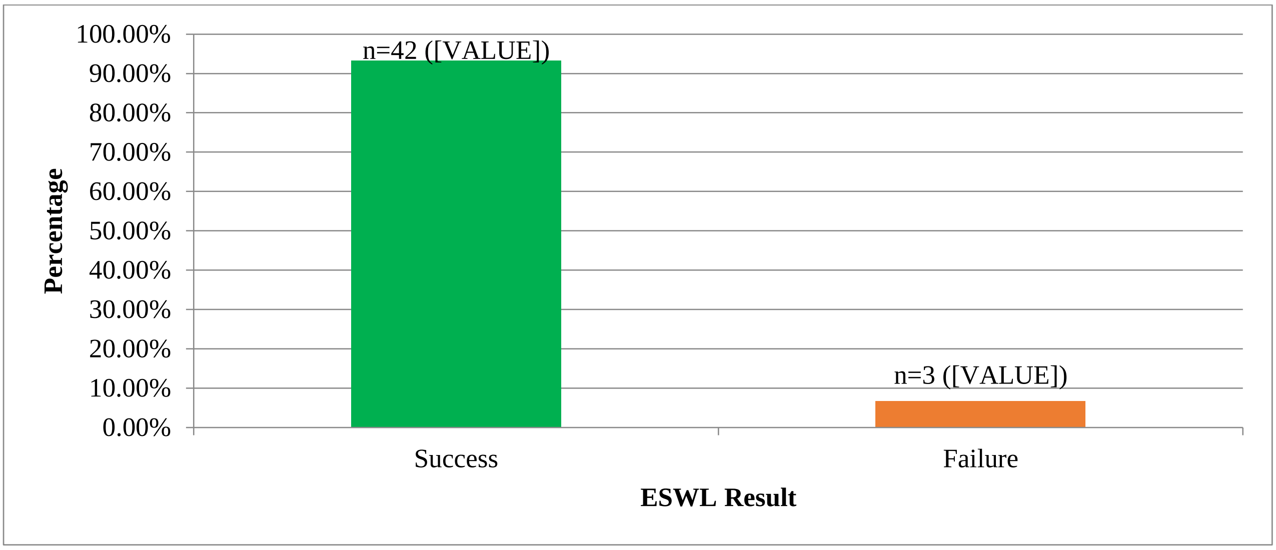


Table 10: Comparison of Hounsfield Density between study group (N=45)

Hounsfield Density	Result		Chi square	P value
	Success (N=42)	Failure (N=3)		
<89.65	27 (64.29%)	1 (33.33%)	1.141	**0.285**
>=89.65	15 (35.71%)	2 (66.67%)		

Out of 42 participants having success as result, the Hounsfield density was <89.65 for 27 (64.29%) participants and >=89.65 for 15 (35.71%) participants. Out of 3 participants having failure as result, the Hounsfield density was <89.65 for 1 (33.33%) participant and >=89.65 for 2 (66.67%) participants. No statistically significant difference was observed in Hounsfield density between result (P Value>0.05).

Table 11: Predictive validity of Hounsfield Density in predicting success (N=45)

Parameter	Value	95% CI	
		Lower	Upper
Sensitivity	64.29%	48.03%	78.45%
Specificity	66.67%	9.43%	99.16%
False positive rate	33.33%	0.84%	90.57%
False negative rate	35.71%	21.55%	51.97%
Positive predictive value	96.43%	81.65%	99.91%
Negative predictive value	11.76%	1.46%	36.44%
Diagnostic accuracy	64.44%	48.78%	78.13%

The Hounsfield Density of 89.65 and above had sensitivity of 64.29% (95% CI 48.03% to 78.45%) in predicting success. Specificity was 66.67% (95% CI 9.43% to 99.16%), false positive rate was 33.33% (95% CI 0.84% to 90.57%), false negative rate was 35.71% (95% CI 21.55% to 51.97%), positive predictive value was 96.43% (95% CI 81.65% to 99.91%), negative predictive value was 11.76% (95% CI 1.46% to 36.44%), and the total diagnostic accuracy was 64.44% (95% CI 48.78% to 78.13%).

Table 12: Comparison of Calculus size between study group (N=45)

Calculus size	Result		Chi square	P value
	Success (N=42)	**Failure (N=3)**		
<13.30 mm	28 (66.67%)	1 (33.33%)	1.358	**0.244**
>=13.30 mm	14 (33.33%)	2 (66.67%)		

Out of 42 participants having success as result, the calculus size was <13.30 mm for 28 (66.67%) participants and >=13.30 mm for 14 (33.33%) participants. Out of 3 participants having failure as result, the calculus size was <13.30 mm for 1 (33.33%) participants and >=13.30 mm for 2 (66.67%) participants. No statistically significant difference was observed in calculus size between result (P Value>0.05).

Table 13: Predictive validity of Calculus size in predicting success (N=45)

Parameter	Value	95% CI	
		Lower	Upper
Sensitivity	66.67%	50.45%	80.43%
Specificity	66.67%	9.43%	99.16%
False positive rate	33.33%	0.84%	90.57%
False negative rate	33.33%	19.57%	49.55%
Positive predictive value	96.55%	82.24%	99.91%
Negative predictive value	12.50%	1.55%	38.35%
Diagnostic accuracy	66.67%	51.05%	80.00%

The calculus size of 13.30 mm and above had sensitivity of 66.67% (95% CI 50.45% to 80.43%) in predicting success. Specificity was 66.67% (95% CI 9.43% to 99.16%), false positive rate was 33.33% (95% CI 0.84% to 90.57%), false negative rate was 33.33% (95% CI 19.57% to 49.55%), positive predictive value was 96.55% (95% CI 82.24% to 99.91%), negative predictive value was 12.50% (95% CI 1.55% to 38.35%), and the total diagnostic accuracy was 66.67% (95% CI 51.05% to 80.00%).

Table 14: Comparison of Hounsfield units between study group (N=45)

Hounsfield units	Result		Chi square	P value
	Success (N=42)	Failure (N=3)		
<1179.50	41 (97.62%)	0 (0%)	32.946	**<0.001**
>=1179.50	1 (2.38%)	3 (100%)		

Out of 42 participants having success as result, the Hounsfield units was <1179.50 for 41 (97.62%) participants and >=1179.50 for 1 (2.38%) participant. Out of 3 participants having failure as result, the Hounsfield units was <1179.50 for no participant and >=1179.50 for 3 (100%) participant. A statistically significant difference was observed in Hounsfield units between result (P Value>0.05).

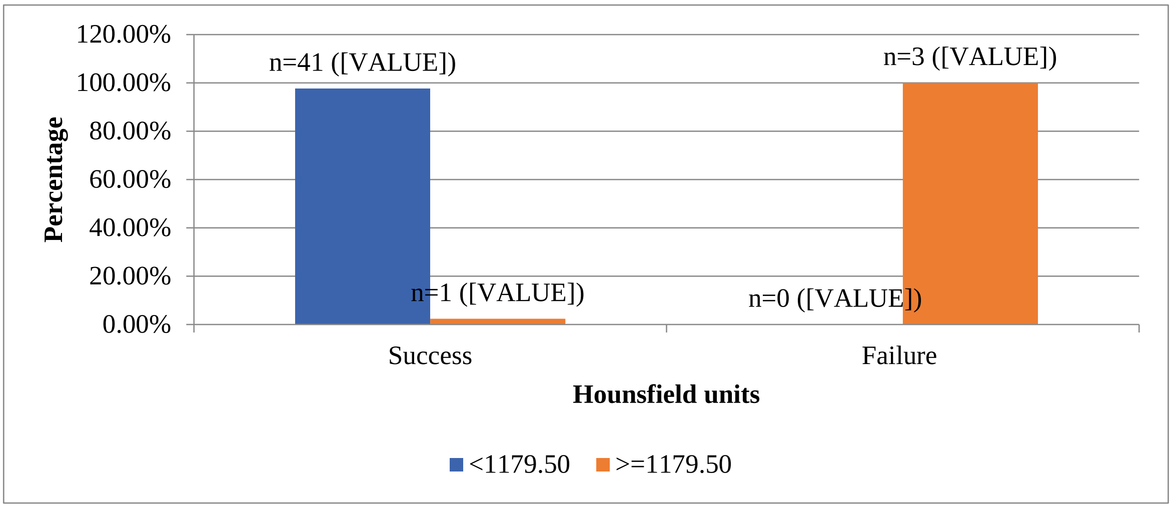


Figure 22: Clustered bar chart for comparison of Hounsfield unit between results.

Table 15: Predictive validity of Hounsfield units in predicting success (N=45)

Parameter	Value	95% CI	
		Lower	Upper
Sensitivity	97.62%	87.43%	99.94%
Specificity	100.00%	29.24%	100.00%
False positive rate	0.00%	-	-
False negative rate	2.38%	0.06%	12.57%
Positive predictive value	100.00%	91.40%	100.00%
Negative predictive value	75.00%	19.41%	99.37%

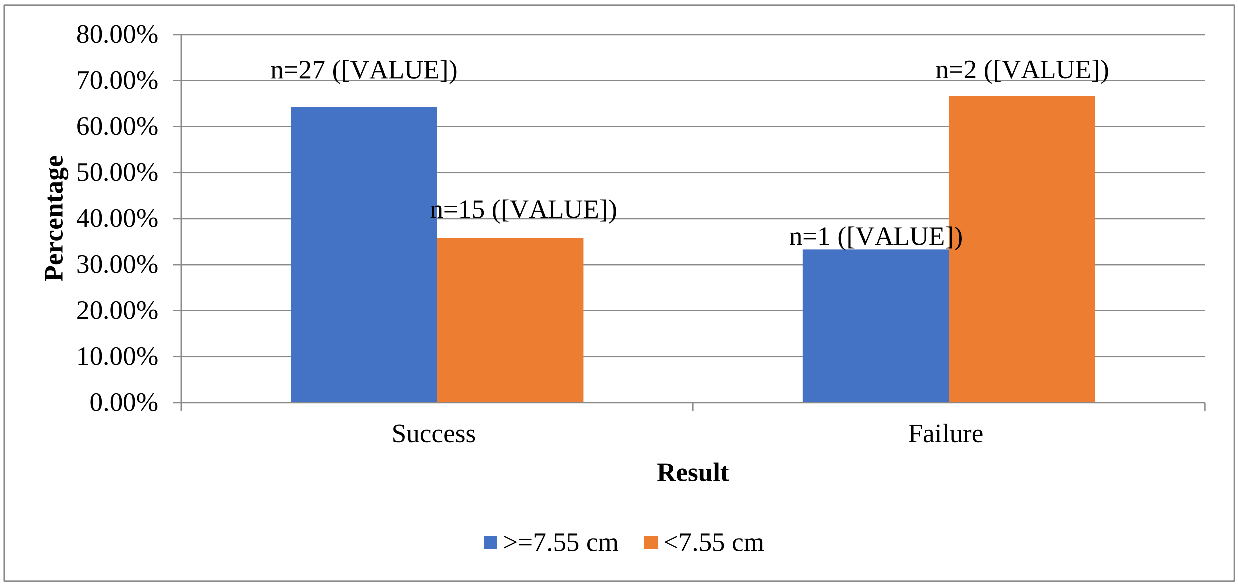
Diagnostic accuracy	97.78%	88.23%	99.94%

The Hounsfield units of 1179.50 and below had sensitivity of 97.62% (95% CI 87.43% to 99.94%) in predicting success. Specificity was 100.00% (95% CI 29.24% to 100%), false positive rate was 0.00, false negative rate was 2.38% (95% CI 0.06% to 12.57%), positive predictive value was 100.00% (95% CI 91.40% to 100.00%), negative predictive value was 75.00% (95% CI 19.41% to 99.37%), and the total diagnostic accuracy was 97.78% (95% CI 88.23% to 99.94%).

Table 16: Comparison of skin to stone distance between study group (N=45)

Skin to stone distance	**Result**		**Chi square**	**P value**
	Success (N=42)	**Failure (N=3)**		
>=7.55 cm	27 (64.29%)	1 (33.33%)	1.141	**0.285**
<7.55 cm	15 (35.71%)	2 (66.67%)		

Out of 42 participants having success as result, the skin to stone distance was >=7.55 cm for 27 (64.29%) participants and <7.55 cm for 15 (35.71%) participants. Out of 3 participants having failure as result, the skin to stone distance was >=7.55 cm for 1 (33.33%) participant and <7.55 cm for 2 (66.67%) participant. No statistically significant difference was observed in skin to stone distance between result (P



Value>0.05).

Figure 23: Clustered bar chart for comparison of skin to stone distance between results.

Table 17: Predictive validity of Skin to stone distance in predicting success (N=45)

Parameter	Value	95% CI	
		Lower	Upper
Sensitivity	64.29%	48.03%	78.45%

Specificity	66.67%	9.43%	99.16%
False positive rate	33.33%	0.84%	90.57%
False negative rate	35.71%	21.55%	51.97%
Positive predictive value	96.43%	81.65%	99.91%
Negative predictive value	11.76%	1.46%	36.44%
Diagnostic accuracy	64.44%	48.78%	78.13%

SSD of 7.55 cm and above had sensitivity of 64.29% (95% CI 48.03% to 78.45%) in predicting success. Specificity was 66.67% (95% CI 9.43% to 99.16%), false positive rate was 33.33% (95% CI 0.84% to 90.57%), false negative rate was 35.71% (95% CI 21.55% to 51.97%), positive predictive value was 96.43% (95% CI 81.65% to 99.91%), negative predictive value was 11.76% (95% CI 1.46% to 36.44%), and the total diagnostic accuracy was 64.44% (95% CI 48.78% to 78.13%).

<u>IMAGES</u>

Figure 24: NCCT-KUB (bone window) shows a calculus in the renal pelvis with a mean/average HU value of 1006.8

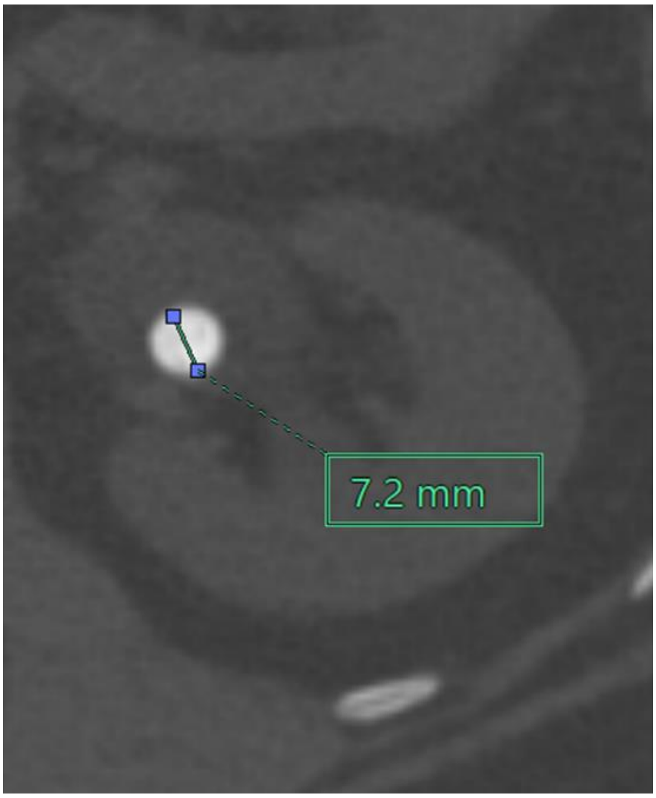


Figure 25: NCCT-KUB axial section shows a 7.2 mm calculus in the renal pelvis.

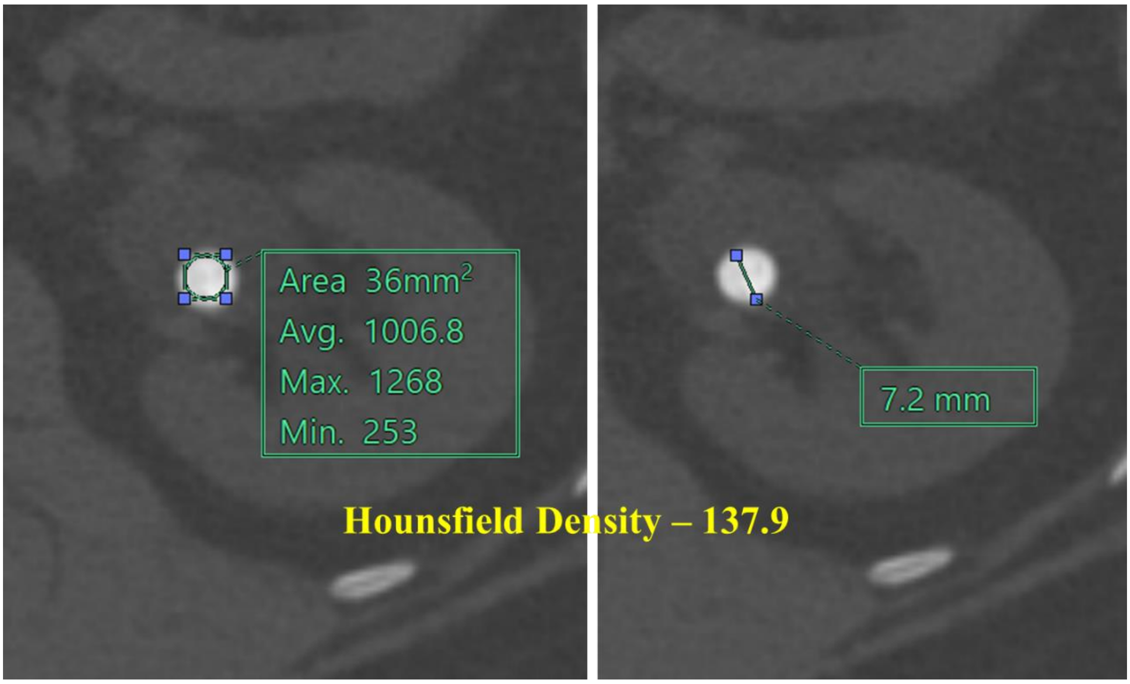


Figure 26: NCCT-KUB (bone window) shows calculus of 1006.8 HU and 7.2 mm size. The calculated Hounsfield density was 137.9 HU/mm.

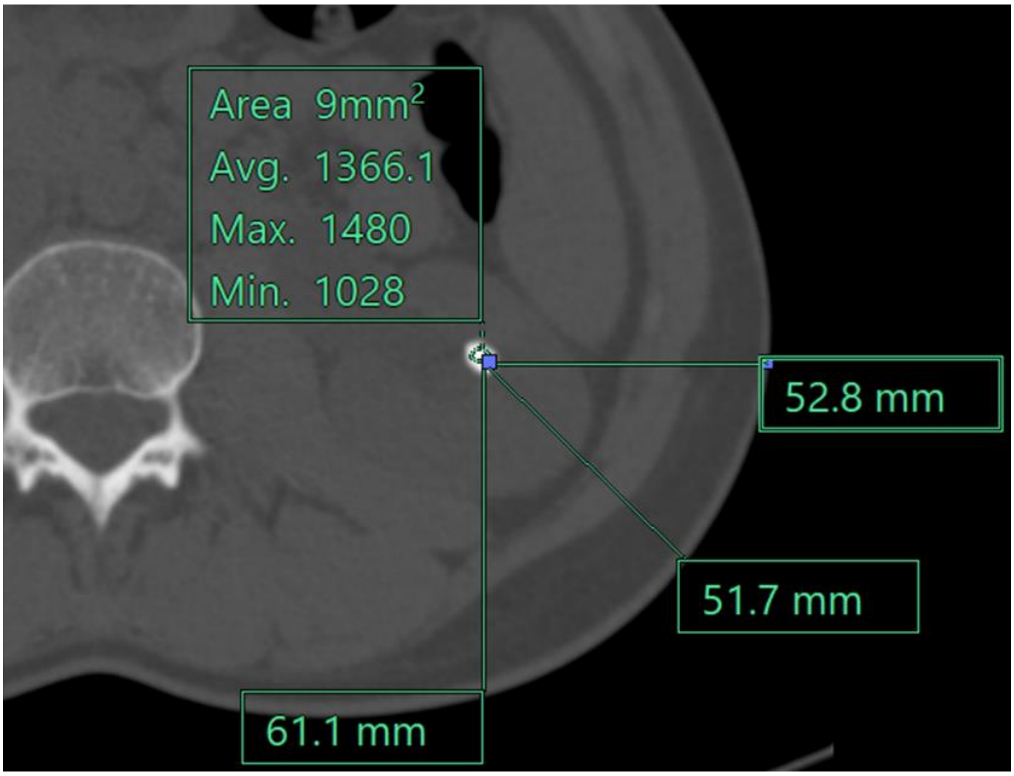
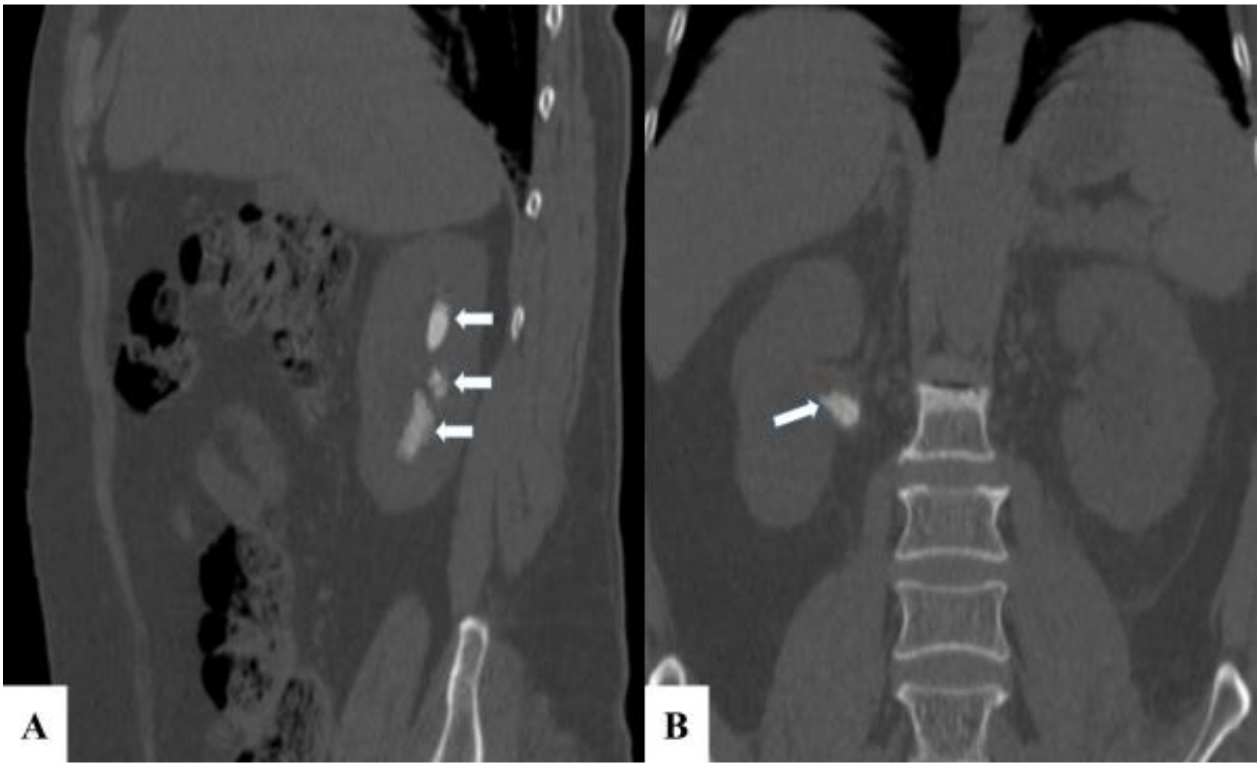
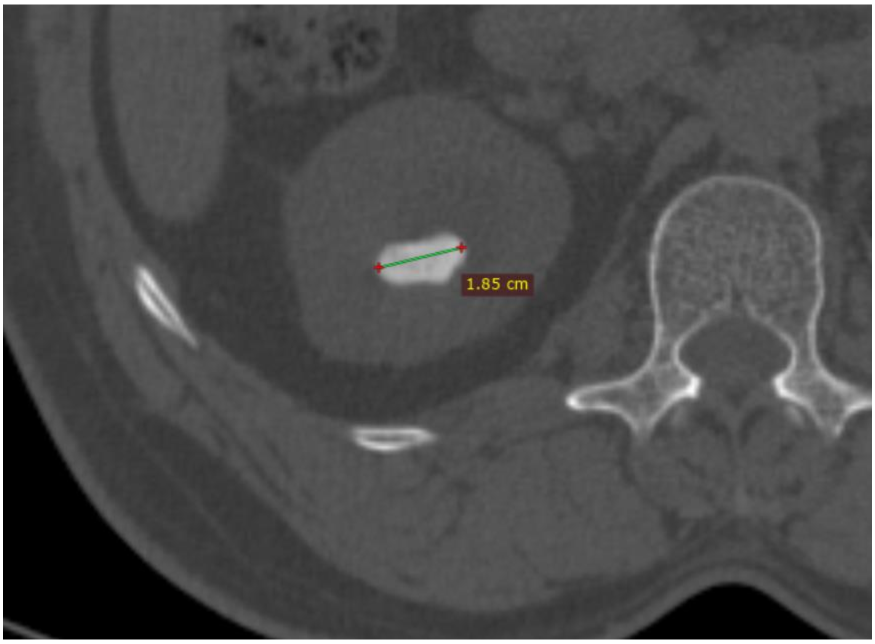


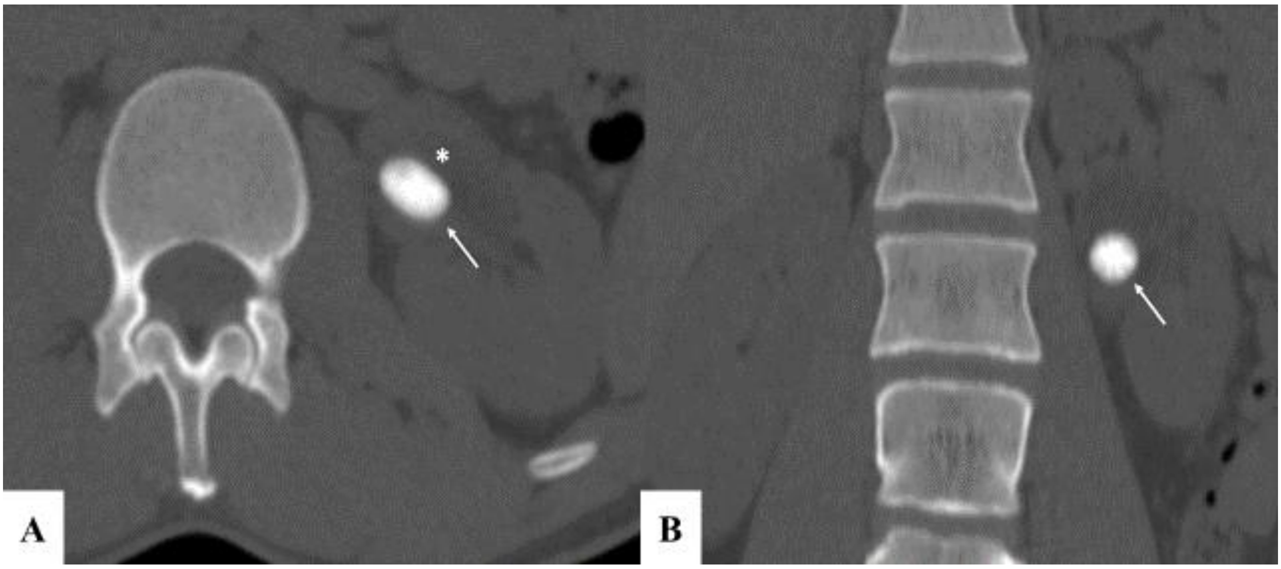
Figure 27: NCCT-KUB showing SSD. Three lines are drawn from the skin surface – horizontal (5.2 cm), vertical – 6.1 cm and line making 45° angle with both – 5.1 cm. Mean SSD is 5.4 cm.



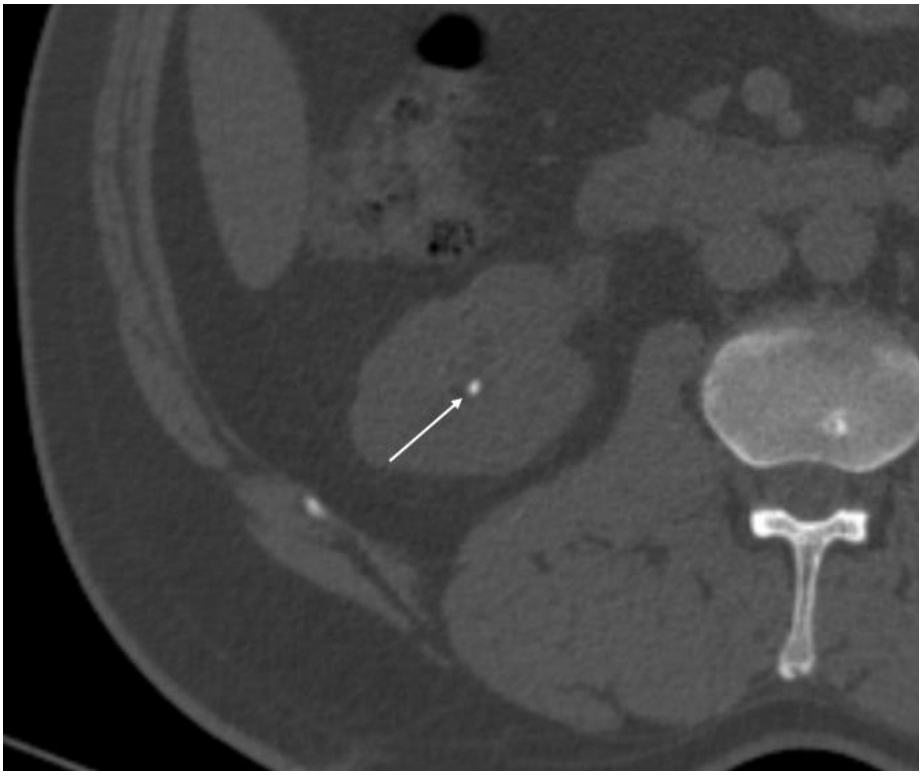
<u>Figure 28</u>: NCCT-KUB (A) sagittal & (B) coronal reformatted image in bone window of a 54 years old male patient with 4 calculi involving all locations (upper, inter & lower pole and pelvis) in right kidney (arrows).



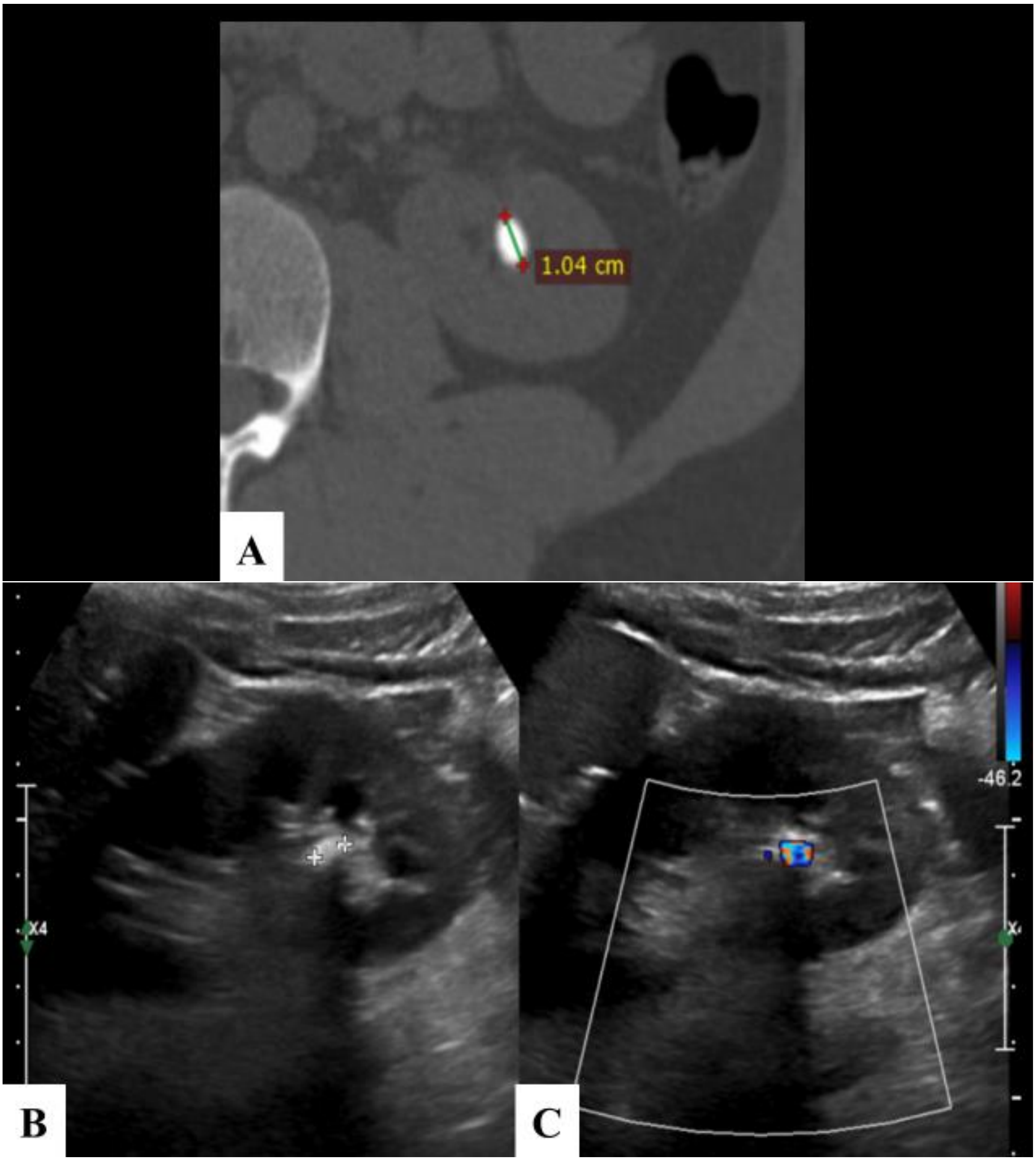
<u>Figure 29</u>: NCCT KUB axial section shows a large 18.5 mm calculus in the upper pole with a mean HU value of 530.



<u>Figure 30</u>: NCCT KUB axial and coronal reformatted images showing a calculus (arrow) in the renal pelvis with hydronephrosis (asterisk).



<u>Figure 31</u>: NCCT-KUB (axial section) of 38 years old male with a 2.8 mm residual fragment (arrow) after 2 sessions of ESWL.



<u>Figure 32</u>: (A) Pre-ESWL CT-KUB and (B,C) post-ESWL ultrasound grey scale images of 45 years old male who had a 10.4 mm calculus in lower pole of left kidney with mean HU of 1189. Ultrasound grey scale image shows a 5.7 mm residual calculus as ESWL failed after 3 sessions.

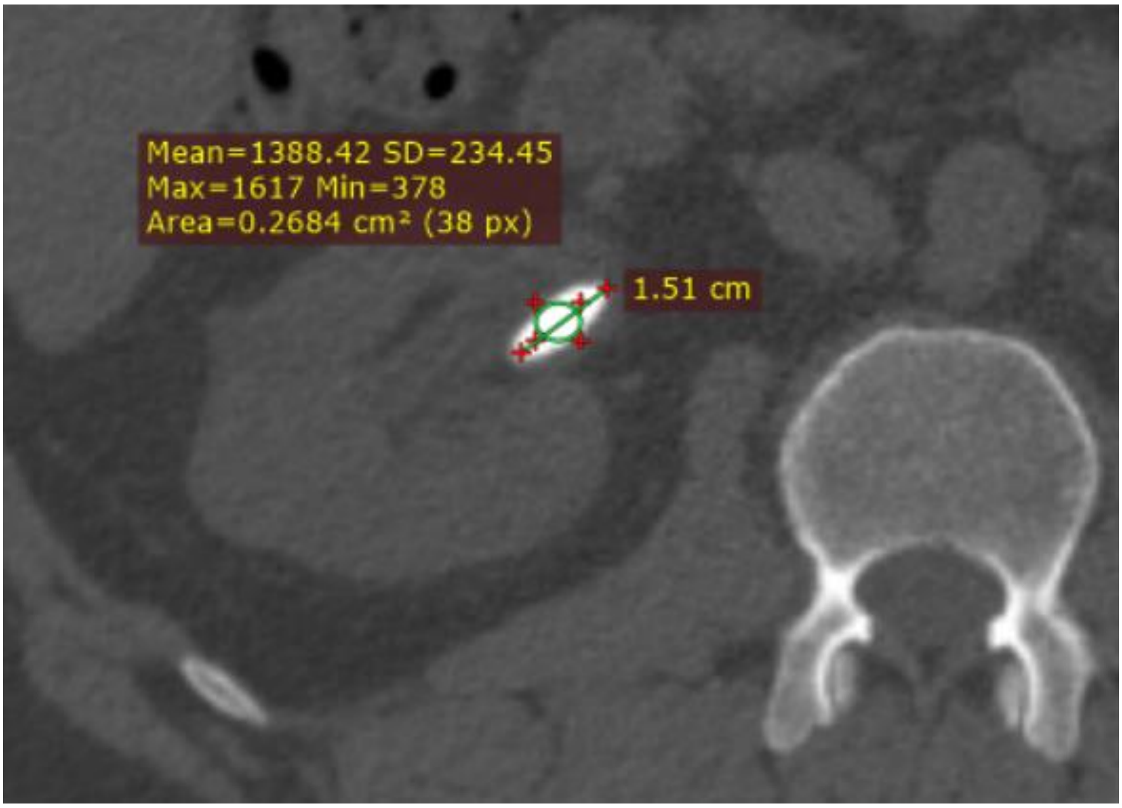


Figure 33: NCCT-KUB axial section (bone window) in a 39 years old male with a 15.1 mm calculus in the renal pelvis and a high mean HU value of 1388. Despite large size and high HU value, ESWL proved to be successful in this case as clearance rates are higher for renal pelvic calculus. In our study, 100% success rate for ESWL was observed for calculi in renal pelvis.

DISCUSSION

Nephrolithiasis causes significant morbidity and health burden. It has significant influence on the quality of life[3]. ESWL is the 1st choice for renal stones <2 cm size. However, there is variation in results of different studies. The results of ESWL can be optimized by using certain principles and proper selection of cases[23, 24]. Non Contrast CT (NCCT) KUB has been revolutionary for evaluation and management of nephrolithiasis[16-18]. We wished to determine the diagnostic accuracy of different Multi-Detector CT indices in predicting successful ESWL outcome.

Our present cross-sectional study had 45 subjects with nephrolithiasis for final analysis. The methodology was similar to that of studies done by Massoud AM al (2014), Sengupta S et al (2021), Ullah S et al (2021), Waqas M et al (2017), El Mahdy AM et al (2016), Nasef A et al (2015), Sheikh AH et al (2020), Saygin H et al (2020) and Park BH et al (2012). The objectives of these studies were similar to our present study as they also evaluated different CT indices in predicting the outcome of ESWL.

Socio-demographic characteristics:

Approximately 7-10 % of people will suffer from renal calculi at least once during their lifetime[4, 5]. The mean age was 41.62 ± 15.25 years in the present study. The youngest subject was 18 years while the oldest was 85 years. In case of multiple recurrent calculi, first episode usually occurs in the second or third decade of life. The mean age of the study population was similar to that of studies done by other authors like Massoud AM al (2014), Sengupta S et al (2021) and Waqas M et al (2017).

It occurs more commonly in men than women[40, 41]. There was a fairly equal distribution of males (53.33%) and females (46.67%) in the present study with a slight preponderance in males as reported by other authors[30, 34, 76, 83]. This could be due to increased reporting in male subjects compared to female subjects.

Table 18: Comparison of stone characteristics and predictors of successful ESWL across studies:

Study	Calculus parameters	Predictors of successful ESWL
Present study	**1. Mean SAV** = 824.36 ± 315.47 HU **2. Calculus location** - pelvis (31.11%), upper pole (26.67%), lower pole, (26.67%) interpole (15.56%) **3. Mean calculus size=** 11.46 ± 4.14 mm **4. Hounsfield density**= 81.04 ± 38.65 HU/mm **5. SSD**= 8.63 ± 2.97 cm	HU value and location of calculus are significant predictors of outcome of ESWL. HU <1179 and in renal pelvis are good prognostic factors for ESWL.
Sengupta S et al	**1. Mean CT attenuation** – (SAV) - 769.42 ± 200.76 HU **2. Mean SSD** = 11.59 ± 0.9 cm **3. Stone volume** = 396.12 ± 195.37 mm^3	Calculus dimension, density and SSD were positive predictors of ESWL success.
Ullah S et al	**1. Mean Density**=772.63±22.2 HU **2. Mean calculus size**= 1.51 ± 0.5 cm	They concluded ESWL for high-density renal stone with size < 10 mm on NCCT was satisfactory.

Waqas M et al	**1. HU density (mean)** = 70.87±35.12 HU/mm **2. Mean HU** = 625.97±275.43 HU **3. Mean calculus size**= 9.64±3.42 mm **4. Mean Skin to stone distance** = 121.78±17.40 mm	BMI, SSD, HU and HD can predict success for ureteric calculi.
El Mahdy AM et al	**1. Stone density**: 56% - 500 to 1000 HU 28% - <500 HU **2. SSD**: 61% ≤ 10 cm **3. Calculus location** – mainly lower pole	A combination of SSD and other factors may be useful for influencing ESWL result.
Massoud AM al	**1. SAV** = 770 ± 311 HU 2**. Location** – pelvis (38%), lower calyx (24%). **3. Size** - 19.1 ± 4.5 mm.	On a multivariate logistic regression analysis in all patients, only a high BMI (>30) and higher SAV (>1000) were predictors of failure ($P < 0.001$)
Park BH et al	**1. Mean SAV -** Success group (784.12±306.35) and failure group (837.50±391.45). **2. Mean SSD -** 7.8 ± 1.2 cm in success group and 9.2 ± 1.4 mm in failure group. **3. Location** – lower pole(n=19), pelvis(n=13), interpole(n=8), upper pole(n=3). **4. Mean calculus size**= 11.09±4.23 mm.	Only SSD was a factor influencing success: the success group clearly had a shorter SSD (78.25±12.15 mm) than did the failure group (92.03±14.51 mm). The results showed SSD as the only single important index for ESWL.

Characteristics of calculus as on Non-Contrast CT (NCCT) KUB:

In our study analysis, 57.78% of the subjects had involvement of right kidney. The major location of calculus was pelvis (31.11%) followed by upper pole (26.67%) and lower pole (26.67%). Ullah S et al reported that calculi in kidney and ureter were observed in 69.7% and 30.3% of patients respectively.

1. **Mean calculus size:**

The mean calculus size in the study population was 11.46 ± 4.14 mm, ranged from 5.2 mm to 18.8 mm. Kidney stones less than 20 mm and ureteric stones less than 10 mm in size are more suitable for ESWL and yield good results[76]. Waqas M et al reported a Mean Maximum calculus size as 9.64±3.42 mm while Ullah S et al reported a Mean stone size (15.1 ± 5 mm) similar to the present study. Stone size (≤ 10 mm) and increasing age had a significant correlation with a satisfactory outcome in the study by Ullah S et al[83].

2. **Stone attenuation value / HU and HD (HU/mm):**

HU gives significant information about the density of renal calculi. The mean Hounsfield units of calculi in this study was 824.36 ± 315.47 units, ranged from 274 units to 1338 units.

Hounsfield Density is another new parameter that can be used to prognosticate ESWL outcome. It is defined as HU value divided by the largest transverse diameter of the calculus. The mean Hounsfield density was 81.04 ± 38.65 HU/mm, ranged from 11.6 HU/mm to 167.3 HU/mm in the present study. As reported in the study by El Mahdy AM et al, smaller density calculi will enhance the ESWL success[76].

3. **Skin-to-stone distance (SSD):**

The mean SSD was 8.63 ± 2.97 cm, ranged from 4.5 cm to 24.8 cm. SSD <10 cm is considered favorable for ESWL[27, 31]. In obese patients with higher BMI, skin-stone distance increases which decreases the chances of success[31]. El Mahdy AM et al observed that SSD in majority (61%) of subjects was ≤ 10 cm. Park BH et al in their study observed that only SSD was a factor influencing success: the success group clearly had a shorter SSD (78.25±12.15 mm) than did the failure group (92.03±14.51 mm). The results showed SSD the sole index that influences ESWL results.

Diagnostic accuracy of different Multi-Detector CT indices in predicting successful outcome of ESWL:

Factors identified by NCCT can predict ESWL success such as stone-to-skin distance and calculus density[95-97]. The composition and calculus density vary which affects the fragility of a calculus, inevitably affecting clinical outcome in ESWL.

80% of subjects had complete clearance of the calculus after ESWL in the present study. 73.33% required only one session while 20% required 2 sessions. ESWL was successful for 93.33% of subjects. In 6.67%, it was a failure. El Mahdy AM et al in their study observed that a high rate of ESWL success after a second session of ESWL (48.1%). Ullah S et al reported that 21.3% of patients showed stone clearance after two ESWL sessions, 27% of patients after three ESWL sessions, and 51.6% of patients after four ESWL sessions. Stone clearance was found in 58.2% of patients and a satisfactory result was observed in 42.6% of patients in their study. Waqas M et al in their study observed the success percentage to be 78%.

In the present study, the Hounsfield units had excellent predictive validity with AUC of 0.984 (P value <0.006). The Hounsfield density had average predictive validity AUC of 0.548. The SSD had fair predictive validity AUC of 0.540. The calculus size had fair predictive validity AUC of 0.687. The only statistically significant predictor was Hounsfield unit. HU of 1179.50 and below had Sensitivity of 97.62%, Specificity of 100%, Positive predictive value of 100%, Negative predictive value of 75% and Total diagnostic accuracy of 97.78%.

Sengupta S et al in their study observed that the ROC curve analysis revealed a low AUC (0.598) of Triple-D score for SFR prediction[34]. Similar to the present study, Massoud AM al put forward that a SAV ⩽956.5 HU would predict success with 98% specificity and 83% sensitivity. So, for 1-2 cm size, calculus and anatomical factors must be carefully studied when considering ESWL as a treatment modality[30].

Park BH et al in their study observed that SSD can be readily measured by CT scan; the ESWL stone-free rate was inversely proportional to SSD in renal calculus patients. SSD may therefore be a useful clinical predictive factor of ESWL success [27].

El Mahdy AM et al in their study observed that smaller size and density of urinary calculi will increase the success rate of ESWL. They observed that the low densities corresponded to the higher success, whereas the larger the density of urinary calculi, the greater the hardness of the stone, thus requiring more ESWL sessions and even resulting in ESWL failure; the suitable stone density for ESWL was usually below 1000 HU. They concluded that renal calculi less than 2 cm in size are more suitable for ESWL[76].

Ullah S et al reported that there was a satisfactory outcome of ESWL for high-density renal stone on non-contrast computed tomography. Increasing age and stone size had a significant correlation with a satisfactory outcome[83].

In this study, the mean age was 41.62 ± 15.25 years in the present study. There was a fairly equal distribution of males (53.33%) and females (46.67%). 57.78% of the subjects had involvement of right kidney. The major location of calculus was pelvis (31.11%) followed by upper pole (26.67%) and lower pole (26.67%). The mean calculus size in the study population was 11.46 ± 4.14 mm, ranged from 5.2 mm to 18.8 mm. The mean Hounsfield unit of calculi was 824.36 ± 315.47 units, ranged from 274 to 1338. The mean Hounsfield density was 81.04 ± 38.65 HU/mm, ranged from 11.6 HU/mm to 167.3 HU/mm. The mean SSD was 8.63 ± 2.97 cm, ranged from 4.5 cm to 24.8 cm. 80% of subjects had clearance of the stone after ESWL in the present study. 73.33% required only one session while 20% required 2 sessions. ESWL was successful for 93.33% of subjects and in 6.67%, it was failure.

In this study, the Hounsfield units had excellent predictive role for ESWL success (p value <0.006). HU of 1179.50 and below had sensitivity of 97.62%, Specificity of 100%, Positive predictive value of 100%, Negative predictive value of 75% and Total diagnostic accuracy of 97.78%.

The location of calculus was renal pelvis for 14 (31.11%), upper pole for 12 (26.67%), lower pole for 12 (26.67%) and interpole for 7 (15.56%) participants.

ESWL showed 100% success rate for renal pelvic stones while there was 1 case of failure each in upper, inter and lower pole. Hence, calculus in renal pelvis is a good prognostic factor for ESWL.

Out of 42 cases with successful ESWL, the Hounsfield density was <89.65 for 27 (64.29%) and >=89.65 for 15 (35.71%) participants. Out of 3 participants having failure as result, the Hounsfield density was <89.65 for 1 (33.33%) and >=89.65 for 2 (66.67%). The total diagnostic accuracy of predicting ESWL success with Hounsfield density was 64.4% and no statistically significant difference was observed in Hounsfield density between result (P Value>0.05).

Out of 42 participants having success as result, the calculus size was <13.30 mm for 28 (66.67%) and >=13.30 mm for 14 (33.33%) participants. Out of 3 with failed ESWL, the calculus size was <13.30 mm for 1 (33.33%) and >=13.30 mm for 2 (66.67%) participants. Total diagnostic accuracy was 66.6%. No statistically significant difference was observed in calculus size between result (P Value>0.05).

Similarly, among successful cases, the SSD was >=7.55 cm for 27 (64.29%) and <7.55 cm for 15 (35.71%) participants. Out of 3 ESWL failure, the SSD was >=7.55 cm for 1 (33.33%) and <7.55 cm for 2 (66.67%) participants. Diagnostic accuracy was No statistically significant difference was observed in SSD between result (P Value>0.05).

CONCLUSION

Nephrolithiasis causes significant morbidity and health burden. It has greatly influences on quality of life. Extracorporeal shockwave lithotripsy (ESWL) is the 1st choice for calculi <2 cm. The results of ESWL can be optimized by using certain principles and proper selection of cases. Non Contrast CT (NCCT) KUB has played a revolutionary role in evaluation and management of nephrolithiasis. The present study was carried out to determine the diagnostic accuracy of different Multi-Detector CT indices in predicting successful outcome of ESWL.

In our study, HU value turned out to be a statistically significant predictor of ESWL success ($p<0.006$) while renal pelvis also proved to be a good prognostic indicator for ESWL success. HU of 1179.50 and below had sensitivity of 97.62%, Specificity of 100%, Positive predictive value of 100%, Negative predictive value of 75% and Total diagnostic accuracy of 97.78%. The cut-off value of <1179 HU favored successful outcome of ESWL while >1179 HU, ESWL is likely to fail. Hence, successful outcome of ESWL is inversely proportional to the HU value. Renal pelvic calculi (n=14) showed 100% success rate, which was better than all other locations. However, cut-off values for other parameters could not be derived which is a limitation of the study that may resolve with a larger study population.

Therefore, NCCT-KUB will help in the selection of patients with a favorable prognosis for ESWL, thereby preventing unnecessary procedures and interventions.

LIMITATIONS:

1. The cross-sectional nature of the study limits the causality of the results. The small sample size of 45 subjects and the consecutive sampling method questions the accuracy of the results and the external validity. Practical constraints restricted the conduct of study on a large scale involving multiple centers. Generalization of the present study findings is questionable.
2. Cut-off values for all calculus parameters could not be derived.
3. Chemical analysis of the calculi was not done in our study.

SUMMARY

Nephrolithiasis is a routinely encountered urological pathology which causes great pain and impacts quality of life. The incidence has been found out to be 10.6% in males and 7.1% in females. Radiological imaging is crucial in diagnosing renal calculi. NCCT (non-contrast computed tomography) is the investigation of choice for urolithiasis. Based on indices such as calculus size, location, HU value, skin to stone distance and HD (Hounsfield density), CT helps in deciding treatment for urolithiasis which can be non-invasive such as ESWL or invasive such as PCNL, RIRS, etc.

The aims and objectives of this study were to perform NCCT-KUB and evaluate Hounsfield unit, Hounsfield density, size, location and SSD of renal calculi; to derive cut off values for the aforementioned indices in predicting successful outcome of ESWL.

This was a cross-sectional analytical study which was conducted for over a period of 18 months from on 45 study subjects who were referred for NCCT-KUB to the department of Radiodiagnosis, R.L. Jalappa Hospital & Research Centre attached to Sri Devaraj Urs Medical College, Tamaka, Kolar in view of clinically/sonographically suspected nephrolithiasis. Informed and written consents were taken from the patients. The inclusion criteria was patients with age of 18 years and above with calculus between from 5 mm to 20 mm. Patients who were pregnant or were suffering from coagulopathy and severe untreated hypertension were not a part of this study.

Structured pre-prepared Performa containing the patient details, significant clinical and past history were taken. NCCT was performed on SIEMENS® SOMATOM EMOTION 16 slice CT machine. After the scan, CT indices of the

calculus were evaluated. Patients meeting the inclusion criteria further underwent ESWL which was performed with SIEMENS SIGMA® ORILITHO-CAL, equipped with C-arm & ultrasound (SIEMENS ACUSON X300). Patients underwent ESWL upto a maximum of 3 sessions depending. The parameters of the lithotripter were set at 60 shockwaves/min for 45 minutes at an energy of 20 kV. Follow up ultrasound was performed to see for absence of calculus or fragmented calculus measuring 4 mm or less (which is considered successful treatment).

CT indices for our study were HU value of calculus, calculus size & location, SSD and HD (Hounsfield density). HU value provides information about the hardness of calculus which is an important deciding factor for treatment of nephrolithiasis. Hounsfield density is derived from HU value which is calculated as the ratio of Hounsfield unit to greatest diameter of the calculus. Calculus size also plays an important role as according to EAU guidelines, calculus <20 mm should be considered for ESWL. The locations of calculus include upper, inter & lower poles and renal pelvis. SSD is a parameter which is calculated as a mean of 3 distances measured from skin to calculus in axial CT section including horizontal distance, vertical distance and

Result (Success v/s failure) was considered as primary outcome variable. Hounsfield units, Hounsfield density, calculus size, location and skin to skin distance etc., were considered as secondary outcome variables. Descriptive analysis was carried out by mean and standard deviation for quantitative variables, frequency and proportion for categorical variables. Data was also represented using pie charts, bar charts and clustered bar charts. Cross tabulation was performed to determine the relation between categorical outcome parameters. P value <0.05 taken as a statistically significant difference. IBM SPSS was used for statistical analysis

45 patients were analyzed, aging between 18 to 85 years with a mean age of 41.62 ± 15.25. Among the 45 patients, 53.3% of the subjects were males and 46.6% were females. 26 patients had calculus in the right kidney while 19 had calculus in left kidney. The most common calculus location was renal pelvis (31.1%) followed by upper pole (26.6%), lower pole (26.6%) and interpole (15.5%).

On evaluation of the CT indices it was found that the mean calculus size was 11.46 ± 4.14 mm (5.2-18.8 mm). Mean HU value was 824.36 ± 315.47 (274-1338). The Hounsfield density ranged from 11.6-167.3 HU/mm. Lastly, SSD showed a mean value of 8.63 ± 2.97 cm. 80% of subjects had clearance of the stone after ESWL in the present study. 73.33% required only one session while 20% required 2 sessions. ESWL was successful for 93.33% of subjects. In 6.67%, it was a failure. Out of all the indices, only HU value emerged as a statically significant index for prognosticating the outcome of ESWL. Out of 42 participants with a successful outcome, the Hounsfield unit was <1179.50 for 41 (97.62%) and >=1179.50 for 1 (2.38%) participant. Out of 3 failure cases, the Hounsfield units was <1179.50 for none and >=1179.50 for 3 (100%) participants. A statistically significant difference was observed in Hounsfield units between result (P Value<0.05) with a sensitivity of 97.62%, specificity of 100%, positive predictive value of 100% , negative predictive value of 75% and total diagnostic accuracy of 97.78%. ESWL showed 100% success rate for calculi in the renal pelvis while there was 1 case of failure each in upper, inter and lower pole. Hence, calculus in renal pelvis is a good prognostic factor for ESWL. For Hounsfield density, out of 3 failed cases, the HD was <89.65 for 1 (33.33%) and

>=89.65 for 2 (66.67%) participants. The total diagnostic accuracy of predicting ESWL success with Hounsfield density was 64.4% and no statistically significant difference was observed in Hounsfield density between result (P Value>0.05). When it came to calculus size, out of 3 failed cases, the calculus size was <13.30 mm for 1 (33.33%) and >=13.30 mm for 2 (66.67%) participants. Total diagnostic accuracy was 66.6% and no statistically significant difference was observed in calculus size between result (P Value>0.05). Similarly, among successful cases, the SSD was >=7.55 cm for 27 (64.29%) and <7.55 cm for 15 (35.71%) cases. Out of 3 failed cases, the SSD was >=7.55 cm for 1 (33.33%) and <7.55 cm for 2 (66.67%) cases. Diagnostic accuracy was No statistically significant difference was observed in skin to stone distance between result (P Value>0.05).

We concluded the MDCT evaluation of nephrolithiasis can successfully predict the outcome of ESWL. Out of the all the indices HU value plays the most significant role as an independent predictor while other indices do not significantly impact the ESWL outcome. The cut-off value of <1179 HU was found to be favoring successful outcome of ESWL while >1179 HU, ESWL is likely to fail. Also, as 100% success rate was observed for calculi in the renal pelvis indicative of good prognostic outcome. Since other indices did not show any statistically significant correlation with the ESWL success, cut-off values could not be derived for Hounsfield density, calculus size and skin to stone distance. This is a limitation of this study which may resolve with a larger study population. Therefore, NCCT-KUB can be used to select patients with a favorable prognosis which further helps in choosing from the treatment options, especially non-invasive v/s interventional procedures. However, the study has its limitations as the small sample size of 45 subjects and the consecutive sampling method question the accuracy of the results and the external validity.

BIBLIOGRAPHY

1. López M, Hoppe B. History, epidemiology and regional diversities of urolithiasis. Pediatr Nephrol 2010;25:49-59.

2. Rule AD, Bergstralh EJ, Melton LJ, Li X, Weaver AL, Lieske JC. Kidney stones and the risk for chronic kidney disease. Clin J Am Soc Nephrol 2009;4:804-11.

3. Patel N, Brown RD, Sarkissian C, De S, Monga M. Quality of life and urolithiasis: the patient - reported outcomes measurement information system (PROMIS). Int Braz J Urol 2017;43:880-6.

4. Rule AD, Roger VL, Melton LJ 3rd, et al. Kidney stones associate with increased risk for myocardial infarction. J Am Soc Nephrol 2010;21:1641-4.

5. Knoll T. Epidemiology, pathogenesis and pathophysiology of urolithiasis. Eur Urol Suppl 2010;9:802–6.

6. Sofia HN, Manickavasakam K, Walter TM. Prevalence And Risk Factors Of Kidney Stone. Glob J Res Anal 2016;5:183-7.

7. Ferraro PM, Bargagli M, Trinchieri A, Gambaro G. Risk of Kidney Stones: Influence of Dietary Factors, Dietary Patterns, and Vegetarian-Vegan Diets. Nutrients 2020;12:779.

8. Sohgaura A, Bigoniya P. A Review on Epidemiology and Etiology of Renal Stone. Am J Drug Discov Dev 2017;7:54-62.

9. Ansari MS, Gupta NP, Hemal AK, Dogra PN, Seth A, Aron M, Singh TP. Spectrum of stone composition: structural analysis of 1050 upper urinary tract calculi from northern India. Int J Urol 2005;12:12-6.

10. Sharma AP, Filler G. Epidemiology of pediatric urolithiasis. Indian J Urol 2010;26:516-22.

11. York NE, Zheng M, Elmansy HM, Rivera ME, Krambeck AE, Lingeman JE. Stone-free Outcomes of Flexible Ureteroscopy for Renal Calculi Utilizing Computed Tomography Imaging. Urol J 2019;124:52-6.

12. Ratkalkar VN, Kleinman JG. Mechanisms of Stone Formation. Clin Rev Bone Miner Metab 2011;9:187-97.

13. Kittanamongkolchai W, Vaughan LE, Enders FT, Dhondup T, Mehta RA, Krambeck AE, et al. The Changing Incidence and Presentation of Urinary Stones Over 3 Decades. Mayo Clin Proc 2018;93:291–9.

14. Riddell J, Case A, Wopat R, Beckham S, Lucas M, McClung CD et al. Sensitivity of emergency bedside ultrasound to detect hydronephrosis in patients with computed tomography-proven stones. West J Emerg Med 2014;15:96-100.

15. Brisbane W, Bailey MR, Sorensen MD. An overview of kidney stone imaging techniques. Nat Rev Urol 2016;13:654-62.

16. Batura D, Hashemzehi T, Gayed W. Should contrast CT urography replace non-contrast CT as an investigation for ureteric colic in the emergency department in those aged 65 and over? Emerg Radiol 2018;25:621-6.

17. Rodger F, Roditi G, Aboumarzouk OM. Diagnostic Accuracy of Low and Ultra-Low Dose CT for Identification of Urinary Tract Stones: A Systematic Review. Urol Int 2018;100:375-85.

18. Kennish SJ, Wah TM, Irving HC. Unenhanced CT for the evaluation of acute ureteric colic: the essential pictorial guide. Postgrad Med J 2010;86:428-36.

19. Chaussy C, Brendel W, Schmiedt E. Extracorporeally induced destruction of kidney stones by shock waves. Lancet 1980;2:1265-8.

20. Albala DM, Assimos DG, Clayman RV, Denstedt JD, Grasso M, Gutierrez-Aceves J et al. Lower pole I: a prospective randomized trial of extracorporeal shock wave lithotripsy and percutaneous nephrostolithotomy for lower pole nephrolithiasis-initial results. Urol J 2001;166:2072-80.

21. Coz F, Orvieto M, Bustos M, Lyng R, Stein C, Hinrichs A et al. Extracorporeal shockwave lithotripsy of 2000 urinary calculi with the modulith SL-20: success and failure according to size and location of stones. J Endourol 2000;14:239-46.

22. Pace KT, Ghiculete D, Harju M, Honey RJ. University of Toronto Lithotripsy Associates. Shock wave lithotripsy at 60 or 120 shocks per minute: a randomized, double-blind trial. J Urol 2005;174:595-9.

23. Torricelli FC, Danilovic A, Vicentini FC, Marchini GS, Srougi M, Mazzucchi E. Extracorporeal shock wave lithotripsy in the treatment of renal and ureteral stones. Rev Assoc Med Bras 2015;61:65-71.

24. Chaussy C, Schüller J, Schmiedt E, Brandl H, Jocham D, Liedl B. Extracorporeal shock-wave lithotripsy (ESWL) for treatment of urolithiasis. Urol J 1984;23:59-66.

25. Shah K, Kurien A, Mishra S, Ganpule A, Muthu V, Sabnis RB et al. Predicting effectiveness of extracorporeal shockwave lithotripsy by stone attenuation value. J Endourol 2010;24:1169-73.

26. Kim SC, Burns EK, Lingeman JE, Paterson RF, McAteer JA, Williams JC. Cystine calculi: correlation of CT-visible structure, CT number, and stone morphology with fragmentation by shock wave lithotripsy. Urol Res 2007;35:319-24.

27. Park BH, Choi H, Kim JB, Chang YS. Analyzing the effect of distance from skin to stone by computed tomography scan on the extracorporeal shock wave lithotripsy stone-free rate of renal stones. Korean J Urol 2012;53:40-3.

28. Zou D, Li W, Deng C, Du G, Xu N. The use of CT Hounsfield unit values to identify the undiagnosed spinal osteoporosis in patients with lumbar degenerative diseases. Eur Spine J 2019;28:1758-66.

29. Nasef A, El-Feky M, El-Shorbagy M, Tarek M, Farouk I. The relationship between renal stone radio-density, chemical composition and fragmentation by Extracorporeal Shockwave Lithotripsy. Al-Azhar Assiut Med J 2015;13:63-7.

30. Massoud AM, Abdelbary AM, Al-Dessoukey AA, Moussa AS, Zayed AS, Mahmmoud O. The success of extracorporeal shock-wave lithotripsy based on the stone-attenuation value from non-contrast computed tomography. Arab J Urol 2014;12:155-61.

31. Cho KS, Jung HD, Ham WS, Chung DY, Kang YJ, Jang WS et al. Optimal Skin-to-Stone Distance Is a Positive Predictor for Successful Outcomes in Upper Ureter Calculi following Extracorporeal Shock Wave Lithotripsy: A Bayesian Model Averaging Approach. PLoS One 2015;10:e0144912.

32. Kim BS. How to determine the treatment options for lower-pole renal stones. Ann Transl Med 2016;4:317.

33. Junuzovic D, Prstojevic JK, Hasanbegovic M, Lepara Z. Evaluation of Extracorporeal Shock Wave Lithotripsy (ESWL): Efficacy in Treatment of Urinary System Stones. Acta Inform Med 2014:309-14.

34. Sengupta S, Basu S, Ghosh K, Sengupta S. An observational study on the predictability of the Triple-D score in the success rate of extracorporeal shock wave lithotripsy in renal stones 1 – 2 cm in diameter: Triple D score predicts SFR after ESWL successfully. Med Res Chronicles 2021;8:55-63.

35. Nakasato T, Morita J, Ogawa Y. Evaluation of Hounsfield Units as a predictive factor for the outcome of extracorporeal shock wave lithotripsy and stone composition. Urolithiasis 2015;43:69-75.

36. Nagata M. Glomerulogenesis and the role of endothelium. Curr Opin Nephrol Hypertens 2018;27:159-64.

37. Ludwig KS, Landmann L. Early development of the human mesonephros. Anat Embryol 2005;209:439-47.

38. Chromek M, Brauner A. Antimicrobial mechanisms of the urinary tract. J Mol Med 2008;86:37-47.

39. Skolarikos A, Straub M, Knoll T, Sarica K, Seitz C, Petřík A et al. Metabolic evaluation and recurrence prevention for urinary stone patients: EAU guidelines. Eur Urol 2015;67:750-63.

40. Edvardsson VO, Indridason OS, Haraldsson G, Kjartansson O, Palsson R. Temporal trends in the incidence of kidney stone disease. Kidney Int 2013;83:146-52.

41. Strope SA, Wolf JS Jr, Hollenbeck BK. Changes in gender distribution of urinary stone disease. Urol J 2010;75:543-6.

42. Moe OW. Kidney stones: pathophysiology and medical management. Lancet 2006;367:333-44.

43. Ziemba JB, Matlaga BR. Epidemiology and economics of nephrolithiasis. Investig Clin Urol 2017;58:299-306.

44. Parmar MS. Kidney stones. BMJ 2004;328:1420-4.

45. Zuckerman JM, Assimos DG. Hypocitraturia: pathophysiology and medical management. Rev Urol 2009;11:134-44.

46. Aune D, Mahamat-Saleh Y, Norat T, Riboli E. Body fatness, diabetes, physical activity and risk of kidney stones: a systematic review and meta-analysis of cohort studies. Eur J Epidemiol 2018;33:1033-47.

47. Letavernier E, Daudon M. Vitamin D, Hypercalciuria and Kidney Stones. Nutrients 2018;10:366.

48. Kohjimoto Y, Sasaki Y, Iguchi M, Matsumura N, Inagaki T, Hara I. Association of metabolic syndrome traits and severity of kidney stones: results from a nationwide survey on urolithiasis in Japan. Am J Kidney Dis 2013;61:923-9.

49. Khan SR, Pearle MS, Robertson WG, Gambaro G, Canales BK, Doizi S et al. Kidney stones. Nat Rev Dis Primers. 2016;25;2:16008.

50. Bhat A, Singh V, Bhat M, Kumar V, Bhat A. Spectrum of urinary stone composition in Northwestern Rajasthan using Fourier transform infrared spectroscopy. Indian J Urol 2018;34:144-8.

51. Hussain F, Billimoria FR, Singh PP. Urolithiasis in northeast Bombay: seasonal prevalence and chemical composition of stones. Int Urol Nephrol 1990;22:119-24.

52. Singh PP, Singh LB, Prasad SN, Singh MG. Urolithiasis in Manipur (north eastern region of India). Incidence and chemical composition of stones. Am J Clin Nutr 1978;31:1519-25.

53. Sandhu MS, Gulati A, Saritha J, Nayak B. Urolithiasis: Comparison of diagnostic performance of digital tomosynthesis and ultrasound. Which one to choose and when? Eur J Radiol 2018;105:25-31.

54. Erbay G, Yalcın A, Gultekin MH. Predictor Role of Pretreatment Resistive and Pulsatile Indexes in the Success of Medical Expulsive Therapy of Ureteral Stones. Urol J 2018;118:47-51.

55. Goldman LW. Principles of CT and CT technology. J Nucl Med Technol 2007;35:115-28.

56. Cocchi MN, Lucas JM, Salciccioli J, Carney E, Herman S, Zimetbaum P et al. The role of cranial computed tomography in the immediate post-cardiac arrest period. Intern Emerg Med 2010;5:533-8.

57. Hathcock JT, Stickle RL. Principles and concepts of computed tomography. Vet Clin North Am Small Anim Pract 1993;23:399-415.

58. Primiano A, Persichilli S, Gambaro G, Ferraro PM, D'Addessi A, Cocci A et al. FT-IR analysis of urinary stones: a helpful tool for clinician comparison with the chemical spot test. Dis Markers 2014;2014:176165.

59. Holdgate A, Pollock T. Nonsteroidal anti-inflammatory drugs (NSAIDs) versus opioids for acute renal colic. Cochrane Database Syst Rev 2005;2004:CD004137.

60. Picozzi SC, Marenghi C, Casellato S, Ricci C, Gaeta M, Carmignani L. Management of ureteral calculi and medical expulsive therapy in emergency departments. J Emerg Trauma Shock 2011;4:70-6.

61. Trinchieri A, Esposito N, Castelnuovo C. Dissolution of radiolucent renal stones by oral alkalinization with potassium citrate/potassium bicarbonate. Arch Ital Urol Androl 2009;81:188–91.

62. Lazaros T, ChristianT, Andreas S. European Association of Urology Urolithiasis Guidelines: Where Are We Going?. Eur Urol Focus 2021;7:34-8.

63. Prstojevic JK, Junuzovic D, Hasanbegovic M, Lepara Z, Selimovic M. Characteristics of calculi in the urinary tract. Mater Sociomed 2014;26:297-302.

64. Lingeman JE, Newman D, Mertz JH, Mosbaugh PG, Steele RE, Kahnoski RJ et al. Extracorporeal shock wave lithotripsy: the Methodist Hospital of Indiana experience. Urol J 1986;135:1134-7.

65. Newman RC, Bezirdjian L, Steinbock G, Finlayson B. Complications of extracorporeal shock wave lithotripsy: prevention and treatment. Semin Urol 1986;4:170-4.

66. Sofras F, Karayannis A, Kostakopoulos A, Delakas D, Kastriotis J, Dimopoulos C. Methodology, results and complications in 2000 extracorporeal shock wave lithotripsy procedures. BJU Int 1988;61:9-13.

67. Dretler SP, Spencer BA. CT and stone fragility. J Endourol 2001;15:31-6.

68. Dixon AK. Abdominal fat assessed by computed tomography: sex difference in distribution. Clin Radiol 1983;34:189-91.

69. Geng JH, Tu HP, Shih PM, Shen JT, Jang MY, Wu WJ et al. Noncontrast computed tomography can predict the outcome of shockwave lithotripsy via accurate stone measurement and abdominal fat distribution determination. Kaohsiung J Med Sci 2015;31:34-41.

70. Coursey CA, Casalino DD, Remer EM, Arellano RS, Bishoff JT, Dighe M et al. ACR Appropriateness Criteria® acute onset flank pain--suspicion of stone disease. Ultrasound Q 2012;28:227-33.

71. Memarsadeghi M, Heinz-Peer G, Helbich TH, Schaefer-Prokop C, Kramer G, Scharitzer M et al. Unenhanced multi-detector row CT in patients suspected of

having urinary stone disease: effect of section width on diagnosis. Radiology 2005;235:530-6.

72. Schwartz BF, Schenkman N, Armenakas NA, Stoller ML. Imaging characteristics of indinavir calculi. Urol J 1999;161:1085-7.

73. Gücük A, Uyetürk U. Usefulness of hounsfield unit and density in the assessment and treatment of urinary stones. World J Nephrol 2014;3:282-6.

74. Nakada SY, Hoff DG, Attai S, Heisey D, Blankenbaker D, Pozniak M. Determination of stone composition by noncontrast spiral computed tomography in the clinical setting. Urol J 2000;55:816-9.

75. Gücük A, Uyetürk U, Oztürk U, Kemahli E, Yildiz M, Metin A. Does the Hounsfield unit value determined by computed tomography predict the outcome of percutaneous nephrolithotomy? J Endourol 2012;26:792-6.

76. El Mahdy AM, El Sayed EE. Role of multidetector computed tomography without contrast enhancement in predicting the outcome of extracorporeal shock wave lithotripsy for urinary calculi. Menoufia Med J 2016;29:297-302.

77. Duan X, Qu M, Wang J, Trevathan J, Vrtiska T, Williams JC et al. Differentiation of calcium oxalate monohydrate and calcium oxalate dihydrate stones using quantitative morphological information from micro-computerized and clinical computerized tomography. Urol J 2013;189:2350-6.

78. Primak AN, Fletcher JG, Vrtiska TJ, Dzyubak OP, Lieske JC, Jackson ME et al. Noninvasive differentiation of uric acid versus non-uric acid kidney stones using dual-energy CT. Acad Radiol 2007;14:1441-7.

79. Fulgham PF, Assimos DG, Pearle MS, Preminger GM. Clinical effectiveness protocols for imaging in the management of ureteral calculous disease: AUA technology assessment. Urol J 2013;189:1203-13.

80. Jellison FC, Smith JC, Heldt JP, Spengler NM, Nicolay LI, Ruckle HC et al. Effect of low dose radiation computerized tomography protocols on distal ureteral calculus detection. Urol J 2009;182:2762-7.

81. Niemann T, Kollmann T, Bongartz G. Diagnostic performance of low-dose CT for the detection of urolithiasis: a meta-analysis. Am J Roentgenol 2008;191:396-401.

82. Alsyouf M, Smith DL, Olgin G, Heldt JP, Lightfoot M, Li R et al. Comparing stone attenuation in low- and conventional-dose noncontrast computed tomography. J Endourol 2014;28:704-7.

83. Ullah S, Muhammad SR, Farooque R, Farooque U, Farukhuddin F, Bin Zafar MD et al. The Outcomes of Extracorporeal Shock Wave Lithotripsy for High-Density Renal Stone on Non-Contrast Computed Tomography. Cureus 2021;13:e13271.

84. Sheikh AH, Ali SI, Mughal A, Iqbal N, Nazar A, Hassan MH, et al. Outcome of Extracorporeal Shockwave Lithotripsy (ESWL) in Cases with Renal Calculi in a Local Community. Clin Med 2020;2:1017.

85. Saygın H, Gökce G, Korğalı E. The evaluations of ESWL, RIRS and m-PCNL treatments in kidney stones smaller than two centimeters. Med Sci Discov 2020;7:450-4.

86. Chung DY, Kang DH, Cho KS, Jeong WS, Jung HD, Kwon JK et al. Comparison of stone-free rates following shock wave lithotripsy, percutaneous nephrolithotomy, and retrograde intrarenal surgery for treatment of renal stones: A systematic review and network meta-analysis. PLoS One 2019;14:e0211316.

87. Waqas M, Saqib IU, Imran Jamil M, Ayaz Khan M, Akhter S. Evaluating the importance of different computed tomography scan-based factors in predicting the outcome of extracorporeal shock wave lithotripsy for renal stones. Investig Clin Urol 2018;59:25-31.

88. Yamashita S, Kohjimoto Y, Iwahashi Y, Iguchi T, Nishizawa S, Kikkawa K et al. Noncontrast Computed Tomography Parameters for Predicting Shock Wave Lithotripsy Outcome in Upper Urinary Tract Stone Cases. Biomed Res Int 2018;2018:1-6.

89. Waqas M, Ayaz Khan M, Waqas Iqbal M, Akbar MK, Saqib IU, Akhter S. Non-Contrast Computed Tomography Scan Based Parameters of Ureteric Stones Affecting the Outcome of Extracorporeal Shock Wave Lithotripsy. Cureus 2017;9:e1227.

90. Gallioli, A., De Lorenzis, E., Boeri, L. et al. Clinical utility of computed tomography Hounsfield characterization for percutaneous nephrolithotomy: a cross-sectional study. BMC Urol 2017;17:104.

91. Yazici O, Tuncer M, Sahin C, Demirkol MK, Kafkasli A, Sarica K. Shock Wave Lithotripsy in Ureteral Stones: Evaluation of Patient and Stone Related Predictive Factors. Int Braz J Urol 2015;41:676-82.

92. Elkholy MM, Ismail H, Abdelkhalek MA, Badr MM, Elfeky MM. Efficacy of extracorporeal shockwave lithotripsy using Dornier SII in different levels of ureteral stones. Urol Ann 2014;6:346-51.

93. Tanaka M, Yokota E, Toyonaga Y et al. Stone attenuation value and cross-sectional area on computed tomography predict the success of shock wave lithotripsy. Korean J Urol 2013;54:454-9.

94. Abdelghany M, Zaher T, El Halaby R, et al. Extracorporeal shock wave lithotripsy of lower ureteric stones: outcome and criteria for success. Arab J Urol 2011;9:35-9.

95. Yang SW, Hyon YK, Na HS, Jin L, Lee JG, Park JM et al. Machine learning prediction of stone-free success in patients with urinary stone after treatment of shock wave lithotripsy. BMC Urol 2020;20:88.

96. El-Nahas AR, El-Assmy AM, Mansour O, Sheir KZ. A prospective multivariate analysis of factors predicting stone disintegration by extracorporeal shock wave lithotripsy: the value of high-resolution noncontrast computed tomography. Eur Urol 2007;51:1688-93.

97. Perks AE, Schuler TD, Lee J, Ghiculete D, Chung D-G, D'A Honey RJ et al. Stone attenuation and skin-to-stone distance on computed tomography predicts for stone fragmentation by shock wave lithotripsy. Urol J 2008;72:765-9.

ANNEXURES

PROFORMA

Demographic details:

Name:

Age:

Gender:

Address:

Clinical History:

General examination

Local Examination:

CT Examination:

	Right Kidney	Left Kidney
Location of calculus		
Size & number of calculi		
HU value		
Hounsfield Density		
Skin to stone distance		
Hydronephrosis		

ESWL outcome:

USG follow-up:

CONSENT FORM

Participant's name: Age: Sex:

Address:

Title of the study: ROLE OF MULTI-DETECTOR COMPUTED TOMOGRAPHY INDICES IN PREDICTING EXTRACORPOREAL SHOCKWAVE LITHOTRIPSY OUTCOME IN PATIENTS WITH NEPHROLITHIASIS.

The details of the study have been provided to me in writing and explained to me/us in my/our own language. I/we confirm that I have understood the above study and had the opportunity to ask questions. I/we understand that my participation in the study is voluntary and that I/we am free to withdraw at any time, without giving any reason, without the medical care that will normally be provided by the hospital being affected. I/we have been given an information sheet giving details of the study. I/we fully consent for detailed examination, investigations and to participate in the above study.

Signature of the participant/ next of kin: ______________________ Date: _____________

Signature of the witness ______________________ Date: _____________

Patient Information Sheet

Principal Investigator: Dr. AASHISH / Dr. ANIL KUMAR SAKALECHA

I, Dr. Aashish**,** post-graduate student in Department of Radio-Diagnosis at Sri Devaraj Urs Medical College. I will be conducting a study titled "Role of Multi-Detector Computed Tomography indices in predicting Extracorporeal Shock Wave Lithotripsy outcome in patients with nephrolithiasis" for my dissertation under the guidance of Dr. Anil Kumar Sakalecha, Professor, Department of Radio-Diagnosis. In this study, we will assess the role of CT indices to predict the outcome and efficacy of ESWL. You would have to undergo CT urogram and ESWL to be a part of the study. You will not be paid any financial compensation for participating in this research project.

All of your personal data will be kept confidential and will be used only for research purpose by this institution. You are free to participate in the study. You can also withdraw from the study at any point of time without giving any reasons whatsoever. Your refusal to participate will not prejudice you to any present or future care at this institution.

Name and Signature of the Principal Investigator

Date: