

Radiological investigations in nephrolithiasis and: a narrative review.

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Abstract

Nephrolithiasis and ureterolithiasis are increasing in incidence and prevalence worldwide, which are significant clinical challenges in management. Radiological assessments are vital in early diagnosis and effective management to decrease morbidity and healthcare costs. This narrative review explores the role of various radiological investigations in nephrolithiasis and ureterolithiasis, focusing on their clinical implications and limitations. Plain X-ray of the kidney, ureter, and bladder (X-ray KUB) is a widely available, relatively inexpensive modality with limited sensitivity, mainly for smaller stones. However, it is most beneficial when assessing follow-up patients diagnosed with renal or ureteric calculi, but it is less effective in acute ureteric colic. Intravenous Urogram/Intravenous Pyelography (IVU/IVP) is an obsolete investigation and has largely been replaced by newer modalities due to numerous drawbacks. Ultrasonography (USG) is a widely available, relatively low-cost, non-invasive radiological modality without ionising radiation, considered first-line for children and pregnant patients. However, its sensitivity and specificity are traditionally lower than computed tomography and largely depend on the operator and patient factors. Computed tomography kidney, ureter, and bladder (CT-KUB) is the gold standard for diagnosing urolithiasis. It offers high sensitivity, specificity, and the ability to calculate the exact size and stone composition, but it comes with substantial radiation exposure. However, low-dose and ultralow-dose CT (LDCT-KUB) protocols reduce radiation to the patient significantly, compromising image clarity. Magnetic Resonance Urography (MRU) is a second-line investigation in obstructive uropathy, particularly in pregnancy and children. It provides vital anatomical and functional information without ionising radiation. Urology and radiology

professionals should collaborate to identify individualised and optimal radiological investigations, considering the risks and benefits associated with each modality.

Introduction

Urinary calculi are a significant global health concern with a gradual incline in incidence and prevalence during the last few decades [1]. Clinical diagnosis of urinary calculi is achievable when symptomatic with classic clinical features. Large intrarenal calculi may be symptomatic and patients may seek medical advice due to haematuria or renal colic. Most ureteral stones are also symptomatic, leading to quick medical attention and diagnosis. However, the clinical suspicion is confirmed by imaging. Still, about 10% of urinary calculi are asymptomatic and found incidentally in imaging, probably due to the frequent use of high-resolution imaging modalities [1]. It must be noted that both symptomatic and asymptomatic calculi have a substantial potential to cause chronic kidney disease (CKD) and end-stage renal disease (ESRD). Hence, in addition to the clinical and biochemical clues, early radiological assessments are mandatory in managing urolithiasis to minimise morbidity, mortality, and healthcare budget.


In current clinical practice, many radiological investigations are available to diagnose urolithiasis. The test of choice depends on its cost, availability, relative advantages and disadvantages, and disease burden. [2]. However, the radiological investigation should describe adequate information to narrow down differential diagnoses with minimal hazard to the patient. Besides, the test should be able to monitor the response to treatment. Radiological investigations in urolithiasis include X-ray kidney-ureter-bladder (X-ray KUB), intravenous urogram/intravenous pyelogram (IVU/IVP), ultrasonography (USG), non-contrast computed tomography of kidney-ureter-bladder (CT-KUB), CT intravenous urogram (CT-IVU), and magnetic resonance urogram (MRU). This review will discuss such radiological modalities with their clinical implications.

Plain radiograph of the kidney, ureter, and bladder

Like all other X-rays, plain X-ray KUB uses a single energy

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source to produce electromagnetic radiation to capture images of abdominal organs. The region imaged in the X-ray-KUB includes the area between the upper poles of kidneys to the inferior pubic rami.

Plain X-ray KUB is a readily available, relatively less expensive (~10% of the cost of CT-KUB) and simple radiological investigation. It utilises a significantly low radiation dose to the patient (about 0.5 mSv) compared to the radiation used in CT-KUB, in which the radiation dose is about 10-20 times higher than X-ray KUB [2]. X-ray KUB helps to detect radiopaque calculi in the urinary system. Approximately 80% of renal calculi are radiopaque, while 20% remain invisible in plain radiographs due to the inherent radiolucency of certain stones like uric acid and matrix stones [2]. Therefore, the location and growth of radiopaque calculi are monitored using a plain X-ray during follow-up. Further, X-ray KUB has a specificity of 99.1% in diagnosing urolithiasis [3].

However, X-ray KUB has several downsides. The overall sensitivity of X-ray KUB is about 49.1% in detecting renal calculi, and it has minimal value for diagnosing calculi < 5mm [3]. About 63% of ureteric calculi < 5 mm and 21% of calculi > 5 mm are not visible in plain radiography [3]. This is due to various factors, such as overlying bowel gas, colonic faecal shadows, soft tissues, and osseous structures, which obscure renal or ureteral calculi visualisation. In addition, pelvic venous wall calcification (phleboliths) and calcified lymph nodes are mistakenly detected as ureteric stones, particularly in approximation with the vesicoureteric junction [3]. The plain radiological appearance of phleboliths is traditionally described as rounded opacities with central lucency [3]. As per recent guidelines, the sensitivity and specificity of X-ray KUB are increased when plain radiography is combined with ultrasonography (USG), especially when the stone diameter is > 5mm [3].

Intravenous Urography/Intravenous Pyelography

IVP is a minimally invasive investigation to image the urinary tract using serial plain X-rays after intravenous administration of non-ionic contrast media. It offers additional information compared to plain radiographs, including anatomy and pathology visualisation of the pelvicalyceal system, ureter, and bladder. Additionally, it demonstrates the relationship of calculi to each part of the urinary system and provides evidence of the functional status of the kidneys [4]. When performing percutaneous nephrolithotomy (PCNL) to remove complex renal and upper ureteric stones from the upper pole of the kidney, the success rates and possible complications are assessed using Guy's

Stone Score (GSS). Hence, GSS, based on IVP interpretation, is a reliable and simple tool for predicting the outcome, assisting in pre-operative planning, and counselling the patient [5].

However, many disadvantages of IVP have limited its use. One of the traditional concerns is that the use of an intravenous iodinated contrast medium has the potential to cause hypersensitivity (HST) reactions (incidence of mild HST <3%, moderate to severe <0.04%) against the contrast medium [6]. Another limitation of its use is the occurrence of contrast-induced nephropathy (CIN), particularly in pre-existing renal impairment and diabetes [6]. Small intrarenal non-obstructing calculi may not be visualised in IVP films, especially in inadequate bowel preparation and when the gas-filled bowel shadow obstructs the renal area. The IVU inadequately differentiates renal changes due to acute obstruction from residual changes in chronic ureteric obstruction [6]. Moreover, IVU has a moderate radiation dose (effective radiation dose is about 3mSv). Therefore, owing to many limitations, IVP has largely been replaced by newer radiological modalities such as real-time USG, CT, and MRU.

Ultrasonography

USG is a commonly used non-invasive radiological modality that does not use ionising radiation. Ultrasound transducers generate and send high-frequency sound waves into the body tissue and then receive the echoes back to generate an image.

USG is a versatile investigation for diagnosing urolithiasis. Its wide availability, relatively low cost, safe bedside nature, and repeatability, especially in the follow-up of ureteric calculi, make it a valuable test for most urolithiasis cases. Besides, sonography has a significant advantage in detecting extrarenal pathologies that mimic acute urolithiasis. Major such pathologies as acute appendicitis, ectopic pregnancy, ovarian torsion, acute pyelonephritis, haemorrhage into an ovarian cyst, endometriomas, and aortic dissection

The non-ionisation property of USG makes it the first-line investigation in urolithiasis in children and pregnancy [6]. Doppler USG has a relative advantage in differentiating the obstructive ureteric system from the non-obstructive system due to ureteric calculi, especially with a short duration (6-24 hours) of symptoms [7]. Acute unilateral ureteric obstruction is suspected when the intrarenal resistive index (RI) is ≥ 0.7 , and the difference in mean RI (Delta RI) between obstructed kidney and non-obstructed contralateral kidney is ≥ 0.06 . (RI >7 and <7). Delta RI is more sensitive and specific than RI in acute ureteric obstruction [7]. However, these results can change based on the patient's age, body habitus, current NSAID usage, and comorbidities like diabetes, hypertension,

and heart disease [7]. The absence of ureterovesical jet dynamics in colour Doppler examination in an obstructed ureter is adjunct to greyscale sonography as a secondary finding to improve diagnostic accuracy [6]. (Figure 1) However, a ureteric jet does not entirely rule out the ureteric obstruction because a partial obstruction still shows a colour change with low frequency and velocity [6].

In USG, the posterior acoustic shadow is frequently seen behind the echogenic calculus, and it is an essential secondary sign in doubtful cases of urolithiasis (Figure 2A). When this sign is not visible due to the small size of the calculus and surrounding renal sinus fat, a colour Doppler twinkling artefact (A rapidly changing mixture of red and blue colours behind a strongly reflecting structure in colour Doppler) has shown an excellent secondary sign to locate the calculus (Figure 2B). It has been noted that the overall sensitivity and specificity of twinkling artefacts are 99.6% and 100%, respectively, in colour Doppler [8]. Furthermore, Point-of-care ultrasound (PoCUS) has received significant attention in managing acute urolithiasis in past decades. An emergency care physician performs the PoCUS to assess the degree of hydronephrosis as an indirect sign of suspected renal colic (Figure 3A). This moderately sensitive test significantly reduces the length of stay in an emergency room and medical costs [9]. Further, in PoCUS, ureterovesical calculi are easily detected when the urinary bladder is adequately filled (Figure 3B).

Despite its utility, USG has certain inherited limitations, particularly in detecting urolithiasis. The sensitivity and specificity of USG depend on factors such as ultrasound machine settings, techniques used, patients' body habits, and operator expertise. According to Toru Kanno et al., the sensitivity and specificity in identifying calyceal calculi are

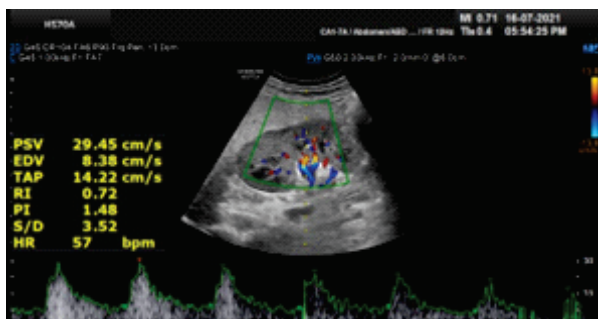


Figure 1. A patient with a suspected right-side ureteric calculus presents mild hydronephrosis and proximal hydroureter on ultrasound without a visible obstructing calculus. Duplex ultrasonography reveals the resistive index (RI) to be just above 0.7, indicating suspicion of a ureteric calculus.

78.9% and 83.7%, respectively, whereas for ureteric calculi, the sensitivity is 57.3%, and the specificity is 97.5% [10]. Moreover, mid-ureter calculi may not be readily visible, especially in obese patients, due to overlying bowel shadows and fat pads. The limited visibility of ureteric calculi < 5 mm further hinders accurate diagnoses, mainly due to the partial volume effect and lack of posterior acoustic shadowing [10]. Another drawback of USG is its tendency to overestimate the length of stones, particularly those < 5 mm, which can affect management decisions [10]. Additionally, USG may mistakenly detect vascular or parenchymal calcifications and renal fat as intrarenal calculi, leading to unnecessary interventions [10]. Furthermore, its sensitivity for detecting ureteric calculi in pregnant women is considerably low, ranging from 34% to 69% [11]. However, secondary signs like proximal hydronephrosis, hydroureter, ureteric jet sign, and RI values can improve diagnostic sensitivity. Still,

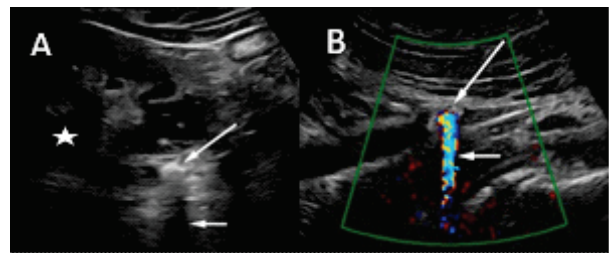


Figure 2A: A patient with right side upper ureteric calculus (long arrow) with posterior acoustic shadowing (short arrow). Note: Mild to moderate hydronephrosis and proximal hydroureter (asterisk)

Figure 2B: A patient with right side mid ureteric calculus (long arrow) with twinkling artefact posterior to the calculus (short arrow) in Doppler mode of ultrasound.

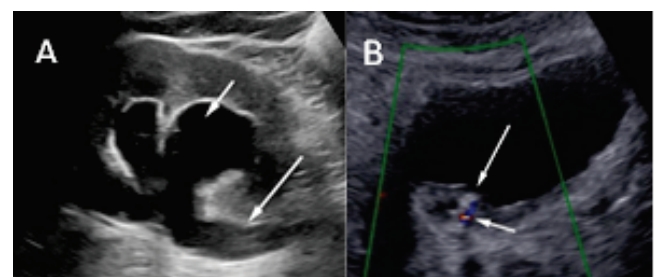


Figure 3A: A patient with acute left-side loin pain. Emergency ultrasound shows moderate hydronephrosis (short arrow) and proximal hydroureter (long arrow).

Figure 3B: A patient with suspected right-side ureteric calculus. Bedside ultrasound shows a calculus at the right ureterovesical junction (long arrow). Note: twinkling artefact posterior to the calculus (short arrow).

differentiating pathological hydroureter from physiological hydroureter may be challenging in the second trimester of pregnancy [11]. It is important to note that the physiological hydroureter may not extend beyond the internal iliac vessels, and the renal pelvic diameter typically does not dilate > 17mm [11]. However, when the initial ultrasound findings are inconclusive in pregnancy, a transvaginal ultrasound scan enhances the stone detection in the distal ureter with a sensitivity of 94% compared to 29 % in transabdominal USG [12].

Non-contrast computed tomography of the kidney, ureter and bladder.

Computed tomography (CT) uses a rotating narrow beam X-ray generator to create cross-sectional images of the site of interest from different angles, and results are reformatted into multiple planes using computerised algorithms.

CT of the kidney ureter and bladder (CT-KUB) is performed without introducing intravenous contrast material. It has become the gold standard for assessing renal and ureteric calculi, surpassing other imaging techniques with high sensitivity and specificity of up to 98% and 96-100%, respectively [13]. The introduction of multidetector CT (MDCT) further enhances its capabilities, allowing the rapid detection of stones without requiring an intravenous contrast medium. In addition, The 3-dimensional reconstruction feature assists in precise localisation and size measurement of uroliths. Moreover, CT attenuation values of the stone provide the composition of the stone, which immensely helps the clinician to plan future management. These values, measured in Hounsfield units (HU), fall within specific ranges for different urinary calculi: Calcium oxalate monohydrate/dihydrate and brushite (1700-2800 HU), hydroxyapatite (calcium phosphate) (1200-1600 HU), cystine (600-1100 HU), struvite (600-900 HU), and uric acid (200-450 HU) [14]. (Figure 4A and Figure 4B). However, due to their radiolucent nature, CT-KUB may still face challenges in identifying certain rare calculi, such as protease inhibitor (indinavir)-induced stones and matrix stones [15]. Conventional single-energy CT-KUB has drawbacks in evaluating the density of stones since a substantial proportion of renal calculi contain mixed chemical materials [16]. Therefore, a single energy CT-KUB may not represent the actual density of the calculus. Additionally, density measurements of small stones can be inaccurate due to partial volume effects. DECT-KUB uses two different voltages (140kV and 80-100kV) and two separate detectors to quantify the chemical composition precisely, distinguishing uric acid and non-uric acid proportions in mixed stones [16]. DECT-KUB helps assess the stone site, size, and internal composition to manage urolithiasis. Kambadakone AR et al.



Figure 4A: Coronal view of non-contrast CT KUB shows a Staghorn calculus at the left renal pelvis. The density of the calculus is about 1296 HU.

Figure 4B: Coronal view of a non-contrast CT KUB shows bilateral ureteric calculi with proximal obstruction. The density of the right ureteric calculus is about 1163 HU, and that of the left ureteric calculus is about 1184 HU.

demonstrated that oral dissolution therapy can treat uric acid stones (< 400HU) while cystine stones (600-1100HU) are best managed with ureteroscopy or PCNL due to their hardness and resistance to shock wave lithotripsy (SWL) [14]. They further explained that non-uric acid, non-cystine stones <1 cm in diameter (500 HU-1000HU) can be treated with SWL or ureteroscopy, whereas large cystine stones (>1cm) with high density (>1000HU) in the lower poles of kidneys are treated with ureteroscopy or PCNL [14]. Therefore, knowing the chemical composition of the stone helps to plan the management option, avoiding unnecessary surgical interventions and treatment failures. Furthermore, CT-KUB is important in planning SWL to measure stone-to-skin distance (SSD). A distance > 10 cm from the centre of the stone to the skin surface indicates a high chance of failure [17]. Prior to PCNL for staghorn calculi removal, evaluating CT-KUB and multidetector computed tomographic urography (CTU) with intravenous contrast material is important to achieve success with minimal procedural complications.

These investigations accurately assess the orientation of the pelvicalyceal system (PCS), the exact location of the stone in the PCS, the position of the kidney, anatomical variations, and the relationship of the kidney to other surrounding organs like the spleen, liver, and colon specially retro-renal colon [18]. In addition, three-dimensional (3-D) coronal reformatted reconstruction and multiplanar assessments are beneficial to guide instruments in interventional procedures [18]. CT-KUB significantly evaluates residual stone fragments after PCNL and SWL [19].

Occasionally, ureteric calculi may not be visible in CT-KUB due to various reasons, such as small size, low density, volume averaging, paucity of retroperitoneal fat, confusion with phleboliths, respiratory movements during image acquisition, or recent passage of the stone [20]. Nevertheless, CT-KUB demonstrates helpful secondary signs to locate a stone, including hydroureter, perinephric fat stranding, tissue rim sign, and renal parenchymal density differences compared to the normal contralateral kidney [20, 21]. Hydroureter is more reliable than hydronephrosis because the latter may be misinterpreted with most of the normal renal pelvis or in an extrarenal baggy pelvis [20,21]. Perinephric fat stranding is thread-like soft tissue densities in surrounding perinephric fatty tissues. This results from inflammation or increased lymphatic pressure secondary to back pressure effects of the ureteric stones [21]. The tissue rim sign represents ureteral wall inflammation and oedema at the level of calculus obstruction. This sign distinguishes calculus from a phlebolith in the pelvis [21]. The renal parenchymal density difference is a critical parameter for ureteric obstruction as it is a measurement-based indicator. Parenchymal density is measured in the upper, middle, and lower segments of each obstructed kidney. A 5 HU or more density difference is an important secondary sign to predict the obstructed urinary system [22].

CT-KUB has been identified as a gold-stranded test to differentiate renal calculi from various differential diagnoses. Up to one-third of patients with acute flank pain, initially suspected of having ureteric calculi, may have alternative diagnoses that significantly impact patient management [22, 23]. These alternative diagnoses include gynaecological conditions (ectopic pregnancy, haemorrhagic ovarian cysts), gastrointestinal and hepatobiliary conditions (acute appendicitis, diverticulitis, cholecystitis, pancreatitis), and vascular conditions (ruptured aneurysms) [23]. Furthermore, CT-KUB can diagnose unrelated incidental findings in the urinary system, such as neoplastic conditions and congenital abnormalities/anatomical variants.

Disadvantages of CT

Despite its immense merits, CT-KUB has a few drawbacks. Radiation exposure is a significant limitation. One significant limitation is the high radiation exposure, ranging from 5 to 10 mSv, which is over three times the radiation dose of IVP [14]. Young patients with urinary stones who undergo repeat CT scans are at risk of accumulating high cumulative radiation doses, which may lead to radiation-induced neoplasms [24]. When the lifetime cumulative radiation dose is more than 100 mSv, it is associated with a 1 in 200 risk of radiation-induced neoplasms [25].

Therefore, to overcome these drawbacks, researchers have proposed various low-dose CT (LDCT) protocols to address these issues, reducing radiation dose by 75% to 90% without compromising diagnostic accuracy [26]. These protocols use techniques like reduced tube voltage (kV) and tube current(mA), while advancements in CT hardware and software enable high diagnostic performance with lower effective radiation doses (1-4 mSv) [27]. (Figure 5A and Figure 5B) LDCT and even ultra-LDCT demonstrate a sensitivity and specificity of 94.1% and 100.0%, respectively, in detecting urinary calculi [27]. It can also detect alternative diagnoses with sensitivity and specificity of around 92% and 96%, respectively [27]. Furthermore, CT-KUB does not provide much information about the functional state of the kidneys. The cost and availability of the test have limited its free usage in certain hospitals.

To minimise unnecessary radiation doses to patients, paramedical teams, physicists, and radiologists should discuss introducing low-dose and ultra-low-dose CT protocols during CT imaging. Additionally, medical teams should consider alternative diagnostic methods and justification before requesting a CT to minimise unnecessary radiation exposure.

Magnetic resonance urography

Magnetic resonance imaging (MRI) is a non-ionic imaging modality to acquire comprehensive soft tissue images using a powerful magnetic field, radio waves and a complex computer system. Magnetic resonance urography (MRU) is a modified MRI technique that provides a detailed assessment of the urinary system, including the collecting system, renal parenchyma, and surrounding structures, with or without IV contrast. Two different methods of MRU studies are available. Heavily T2-weighted turbo spin-echo sequences visualise static water in the urinary system for image contrast without intravenous contrast material. (Figure 6A) On the other hand, gadolinium contrast material is injected



Figure 5A: Standard dose axial view of CT-KUB (120 kVp and effective dose of 12mSv)

Figure 5B: Low dose axial CT-KUB (100 kVp and effective dose of 2 mSv). Despite high image noise, small calculus (<3mm) is still visible. (arrow)

intravenously, and renal excretion of Gadolinium-containing urine is imaged using fast T1-weighted gradient-echo sequences, mimicking IVU [28]. (Figure 6B)

MRU is considered a second-line investigation in obstructive uropathy, particularly in pregnancy and children [28]. It has many advantages over other imaging modalities, such as demonstrating the 3D anatomy of renal parenchyma, pelvicalyceal system, ureters, and bladder without ionising radiation. Semins et al. described that the MRU has a sensitivity of 84 % and a specificity of 100 % to detect calculus using a half-Fourier acquisition single-shot turbo spin-echo (HASTE) MRU with a 3-T MR scanner [29]. Additionally, MRU can differentiate physiological urinary tract dilatation in pregnancy from hydronephrosis caused by urolithiasis [30]. The HASTE technique is used in pregnancy during the second and third trimesters without intravenous Gadolinium as a complementary test to sonography. Additionally, MRI can provide functional information on the kidney in obstructive uropathy for non-pregnant subjects, mainly when chemical exchange saturation transfer (CEST) MRI is utilised with an intravenous contrast medium [30].

A few drawbacks of MRU are poor sensitivity in detecting non-obstructing and small obstructing calculi, relatively high cost, not being freely available in most centres, and time-consuming. Furthermore, it is not recommended during the first trimester of pregnancy.

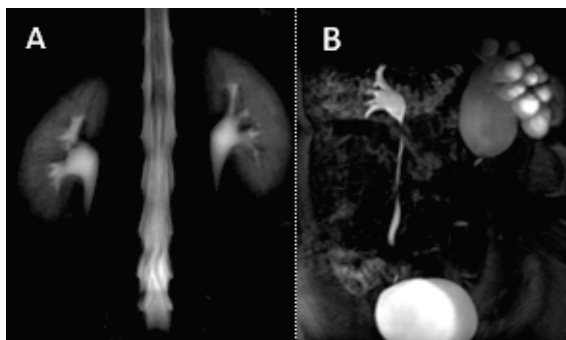


Figure 6A: Magnetic resonance urogram (MRU) to demonstrate the renal pelvi-calyceal system. Static water in the urinary system used as image contrast without intravenous contrast material.

Figure 6B: A male patient with incidental left hydronephrosis. Excretory phase of contrast MRU demonstrates dilated left renal pelvis with markedly narrowed pelviureteric junction. Case courtesy of Roberto Schubert, Radiopaedia.org,

Conclusion

Early diagnosis of urinary calculi and understanding the nature of urinary tract obstruction are crucial in managing urolithiasis. Different radiological modalities play a vital and sometimes complementary role in this regard, with their selection depending on clinical features, availability, and patient factors. X-ray KUB is commonly utilised in follow-up patient care in many centres despite its low sensitivity. However, the value of IVP is currently limited, and many contemporary modalities have replaced it. Ultrasonography is the first-line imaging tool in paediatrics, non-obese patients, and pregnancy. However, non-contrast CT-KUB is considered the gold standard technique for diagnosing urolithiasis despite radiation being a significant drawback. To address this concern, many centres have modified conventional CT protocols, especially for follow-up examinations, using LDCT and ultra-LDCT protocols, which have shown promising results. Being a recent non-ionic investigation, MRU plays a vital role in pregnancy and children. Urology and radiology professionals should collaborate to identify individualised and optimal radiological investigations for each patient, carefully considering the risks and benefits associated with each modality.

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