ORIGINAL ARTICLE

DECIPHERING THE ASSOCIATION BETWEEN TYPE OF RENAL STONES AND HEPATIC FATTY INFILTRATION; A RETROSPECTIVE SINGLE INSTITUTE STUDY

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ABSTRACT

AIMS/OBJECTIVE: In this study we aimed to establish a relationship/association between types of renal stone (uric acid and non-uric acid) with hepatic status (fatty and non-fatty). **MATERIALS AND METHODS:** 565 patients with renal stones on NCCT KUB between January 2021 to July 2023 were retrospectively identified. The attenuation ratio value and location on the graph plot of the biggest calculus per scan were utilized to distinguish between uric acid and non-uric acid calculi. Fatty liver status was seen by calculating the difference between spleen and hepatic parenchymal HU. Statistics analysis was done using Chi-square test in SPSS 26 version. **RESULTS:** Amongst total of 565 patients, males were 414 and females were 151. In males, 357(63.2%) had non uric stones and 57 (10.1&) had uric acid stones. In females, 129 (22.8%) had non uric stones and 22 (3.9%) had uric acid stones. In males, 361 (63.9%) had non fatty liver and 53 (9.4%) had fatty liver. In females, 119 (21.1%) had non fatty liver and 32 (5.7%) had fatty liver. Pearsen chi-square came out to be 0.764 representing no association between types of renal stone (uric acid/non uric acid) with fatty infiltration (being less than 0.05 is significant). **CONCLUSIONS:** A pilot study performed resulting in no significance in Pakistani population between fatty infiltration and type of renal stones.

Keywords: Renal Stones, Uric acid stone, Non uric acid stone, Fatty Liver, CT, Radiology.

Introduction

The global occurrence of kidney stones has increased during the last several decades.[1] Urolithiasis is a progressive form of a common kidney disease that can be caused by both internal and external factors. Nonalcoholic fatty liver disease (NAFLD) is associated with metabolic issues and has a well-documented influence on renal function.[2] Uric acid, the last oxidation product of purine metabolism and a cause of kidney stones, has been associated to a number of cardio-metabolic illnesses, including hypertension, renal disease, and metabolic syndrome.[3] Recent research has focused on the processes by which uric acid increases the development of NAFLD. According to one study, uric acid causes hepatic steatosis by producing mitochondrial oxidative species, which promotes de novo lipogenesis in cultured HepG2 cells. Other research has identified an alternate mechanism for uric acid-induced fat accumulation, specifically SREBP-1 activation driven by endoplasmic reticulum stress.[4] So far, little attention has been devoted to the link between fatty liver and renal calculi as an underlying risk factor. However, no studies have been

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conducted to demonstrate a link between the kinds of renal calculi (uric acid/non-uric acid) and hepatic condition (non-fatty/fatty infiltration).

Materials and Methods

This retrospective study was duly approved by institute s ethical review committee. Total 565 individuals with renal stones on NCCT KUB were found retrospectively between January 2021 and July 2023. The attenuation ratio value and position on the graph plot of the largest calculus per scan were used to differentiate between uric acid and non-uric acid calculi. Fatty liver status was determined by determining the difference between splenic and hepatic parenchymal HU.

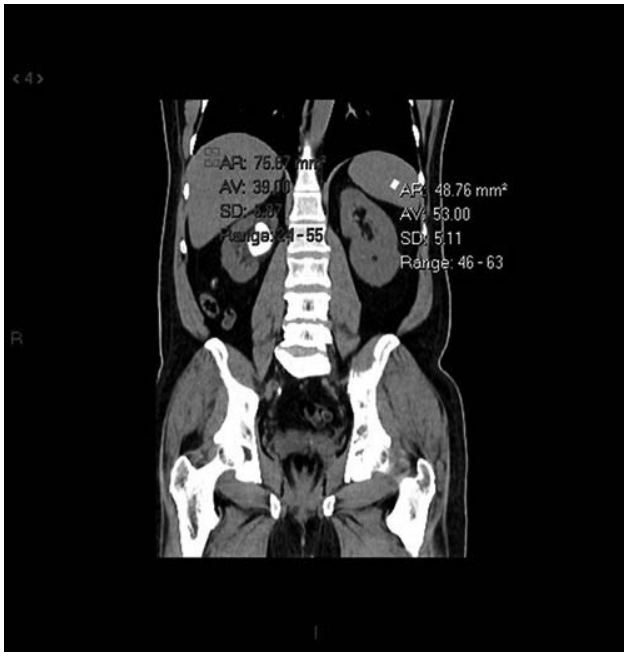


Figure 1: HU value of liver and spleen on NCCT to calculate hepatic fatty status.

Inclusion Criteria:
Patients having renal stones with or without fatty liver.

Exclusion Criteria:
Known renal or hepatic disease like CLD, Renal mass etc.

Statistics:
Chi-square test was applied using SPSS 26 version.

Results

Males accounted for 414 of the 565 cases, while females made for 151.
In men, 357 (63.2%) had non-uric stones, whereas 57 (10.1%) had uric acid stones. In females, 129 (22.8%) had non-uric stones, whereas 22 (3.9%) had uric acid stones.
In men, 361 (63.9%) had non-fatty livers, whereas 53 (9.4%) had fatty livers. In females, 119 (21.1%) had non-fatty livers, whereas 32 (5.7%) had fatty livers.

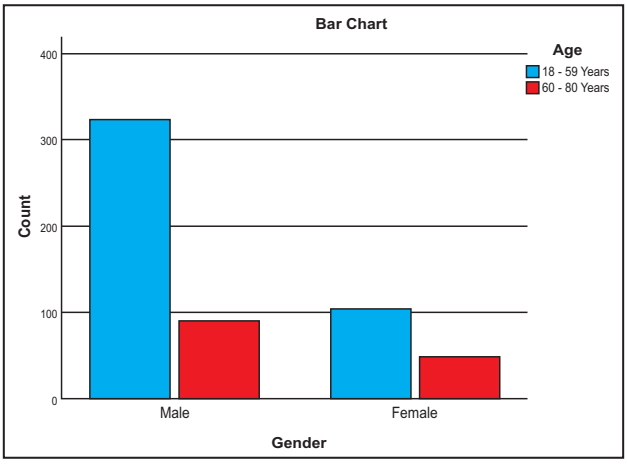
1. Gender vs Age

Irrespective of stones and hepatic status, 324 patients (57.3%) in males were in 18-59 years of age and 90 patients (15.9%) were in 60-80 years of age. Cumulatively, these were total of 414 patients (73.3%). Irrespective of stones and hepatic status, 103 patients (18.2%) in females were in 18-59 years of age and 48 patients (8.5%) were in 60-80 years of age. Altogether, these were total of 151 patients (26.7%).

Geneder* Age Crosstabulation

			Age		Total
			18-59 years	60-80 years	
Gender	Male	Count	324	90	414
		% of Total	57.3%	15.9%	73.3%
	Female	Count	103	48	151
		% of Total	18.2%	8.5%	26.7%
Total		Count	427	138	565
		% of Total	75.6%	24.4%	100.0%

Table 1: Gender X Age cross tabulation.



Graph 1: Gender X Age bar chart.

2. Age vs type of renal calculi

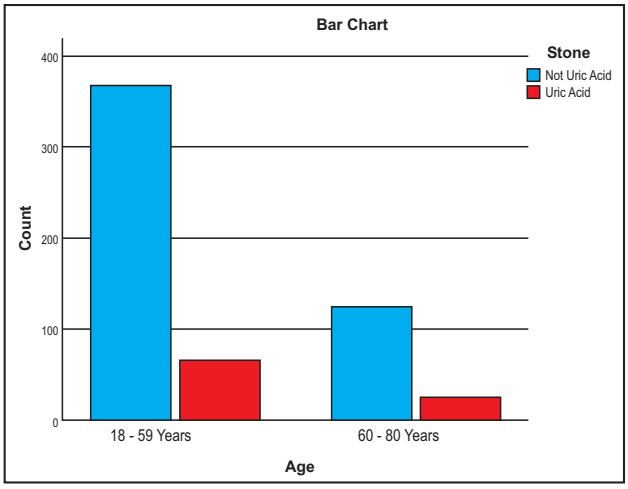
Irrespective of gender, 367 patients (65%) in 18-59 years of age had non uric acid stones and 60 patients (10.6%) had uric acid stones. Collectively, these are total of 427 patients (75.6%).

Irrespective of gender, 119 patients (21.1%) in 60-80 years of age had non uric acid stones and 19 patients (3.4%) had uric acid stones. As a total, these were total of 138 patients (24.4%).

Age* Stone Crosstabulation

			Stone		Total
			Not Uric Acid	Uric Acid	
Age	15-59 Years	Count	367	60	427
		% of Total	65.0%	10.6%	75.6%
	60-80 Years	Count	119	19	138
		% of Total	21.1%	3.4%	24.4%
Total		Count	486	79	565
		% of Total	86.0%	14.0%	100.0%

Table 2: Age X Stone type cross tabulation.



Graph 2: Gender X Stone type bar chart.

3. Age vs hepatic status

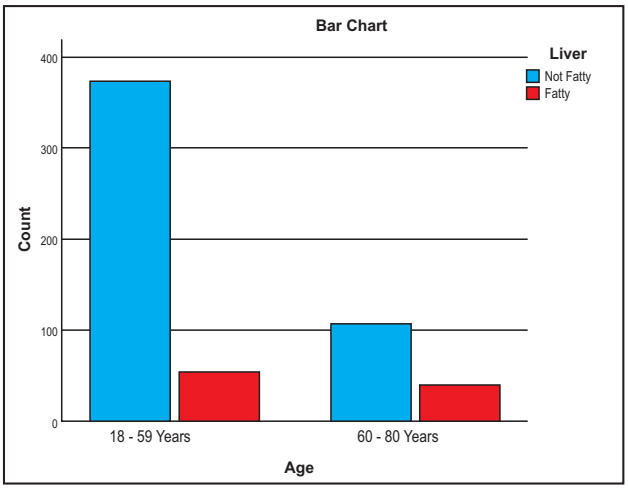
Irrespective of gender, 377 patients (66.7%) in 18-59 years of age had non fatty liver and 50 patients (8.8%) had fatty liver. Combining these, these are total of 427 patients (75.6%).

Irrespective of gender, 103 patients (18.2%) in 60-80 years of age had non fatty liver and 35 patients (6.2%) had uric acid stones. After summing, these are total of 138 patients (24.4%).

Age* Liver Crosstabulation

			Liver		Total
			Not Fatty	Fatty	
Age	18 - 59 Years	Count	377	50	427
		% of Total	66.7%	8.8%	75.6%
	60 - 80 Years	Count	103	35	138
		% of Total	18.2%	6.2%	24.4%
Total		Count	480	85	565
		% of Total	85.0%	15.0%	100.0%

Table 3: Age X Hepatic status cross tabulation.



Graph 3: Age X Hepatic status bar chart.

4. Gender vs type of renal calculi

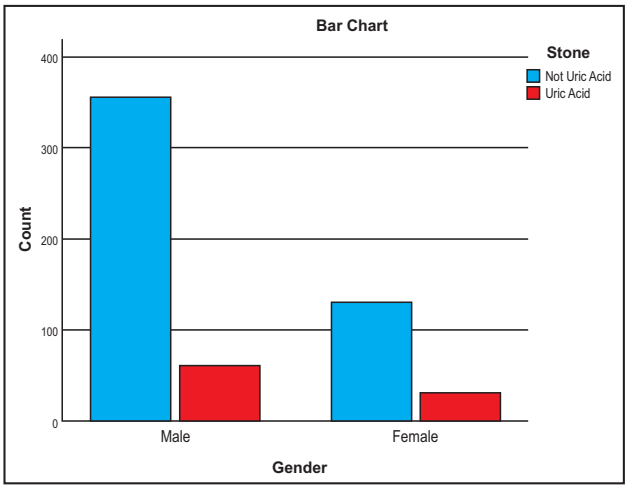
Irrespective of age, 357 patients (63.2%) in males had non uric acid stones and 57 patients (10.1%) had uric acid stones. Entirely, these were total of 414 patients (73.3%).

Irrespective of age, 129 patients (22.8%) in females had non uric acid stones and 22 patients (3.9%) had uric acid stones. As a total, these were total of 151 patients (26.7%).

Geneder* Stone Crosstabulation

			Stone		Total
			Not Uric Acid	Uric Acid	
Gender	Male	Count	357	57	414
		% of Total	63.2%	10.1%	43.3%
	Female	Count	129	22	151
		% of Total	22.8%	3.9%	26.7%
Total		Count	486	79	565
		% of Total	86.0%	14.0%	100.0%

Table 4: Gender X Type of stone cross tabulation.



Graph 4: Gender X Type of stone bar chart.

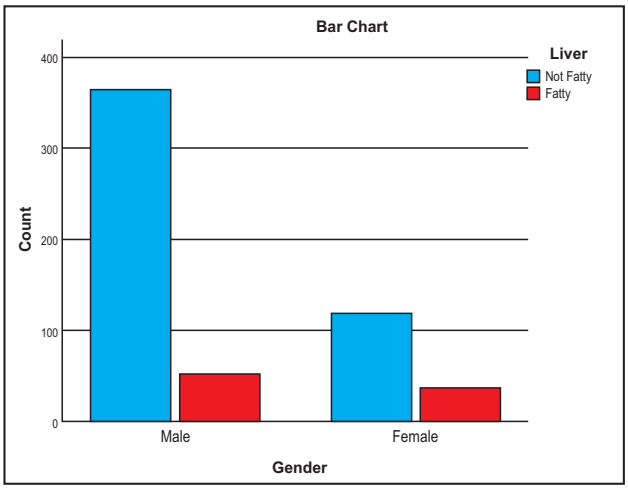
5. Gender vs hepatic status

Irrespective of age, 361 patients (63.29%) in males had non fatty liver and 53 patients (9.4%) had fatty liver. In tandem, these were total of 414 patients (73.3%).

Geneder* Liver Crosstabulation

			Liver		Total
			Not Fatty	Fatty	
Gender	Male	Count	361	53	414
		% of Total	63.9%	9.4%	73.3%
	Female	Count	119	32	151
		% of Total	21.1%	5.7%	26.7%
Total		Count	480	85	565
		% of Total	85.0%	15.0%	100.0%

Table 5: Gender X Hepatic Status cross tabulation.



Graph 5: Gender X Hepatic Status bar chart.

Irrespective of age, 119 patients (21.1%) in females had non fatty liver and 32 patients (5.7%) had fatty liver. Collectively, these were total of 151 patients (26.7%).

6. CRUX

Uric-acid stone in non-fatty liver

= 68/480

= 14.16%

Uric-acid stone in fatty liver

= 11/85

= 12.94%

Non-uric-acid stone in non-fatty liver

= 412/480

= 85.83%

Non-uric-acid stone in fatty liver

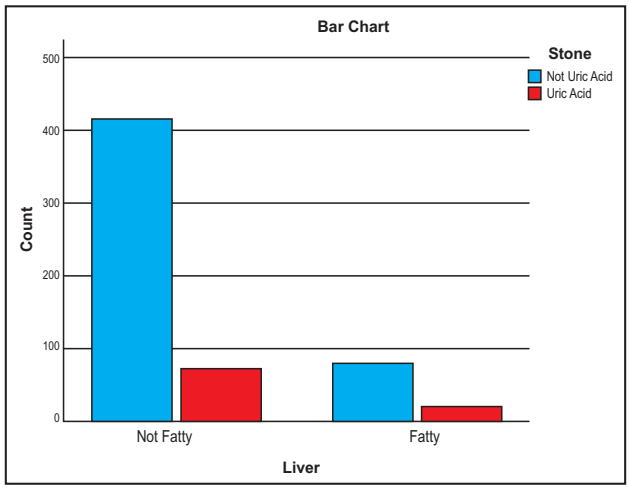
= 74/85

= 87.05%

Liver* Stone Crosstabulation

			Stone		Total
			Not Uric Acid	Uric Acid	
Liver	Not Fatty	Count	412	68	480
		% of Total	72.9%	12.0%	85.0%
	Fatty	Count	74	11	85
		% of Total	13.1%	1.9%	15.0%
Total		Count	486	79	565
		% of Total	86.0%	14.0%	100.0%

Table 6: Hepatic Status X Stone type cross tabulation.



Graph 6: Hepatic Status X Stone bar chart.

Pearsen chi-square came out to be 0.764 representing no association between types of renal stone (uric acid/non uric acid) with fatty infiltration (being less than 0.05 is significant).

Zaigham A et al. reported fatty liver to be in 15% of population. Our values are likewise comparable, currently 15% of our sample size (85/465 x 100).[5]

Our study showed 15% uric stones in population, results being similar to study conducted by Afshan B et al.[6]

Incidence of stone formation in our study in males(75%) and females(25%), close to data mentioned in above cited studies i.e 79% in males and 21% in females.[6]

Discussion

Kidneys are the excretory organs for eliminating metabolic waste from the body. Azotemia means accumulation of nitrogenous waste in body in case of renal dysfunction.[7]

Normal kidneys and adrenals are retroperitoneal structures enclosed in renal fascia and lie between T12 and L3 vertebrae. Right kidney is slightly lower in position than left because of displacement by right lobe liver.[8] Renal function is to filter the blood, regulate body fluid volume and regulate blood pressure and can be assessed by serum creatinine, electrolyte level, blood urea nitrogen however is best assessed by glomerular filtration rate (GFR).[9]

Renal stones are very common entity and are found to be associated with various causes such as low fluid intake, urinary tract infections, systemic diseases like diabetes mellitus, hypertension and dyslipidemia. Certain urinary tract malformations such as duplex collecting system and horse shoe kidney also predisposes to renal calculi formation. Peak incidence is in persons aged 20-49 years. Males are more prone to have renal stones than females. Symptomatology includes sudden onset severe sharp flank pain with fluctuation and severity episodes lasting over 15-45 minutes duration. It can become unbearable and thence with nausea and vomiting as well. When renal stone migrates into ureter or urinary bladder, pain radiates to groin region.[10] Whenever clinical suspicion of nephrolithiasis arises, the whole urinary tract should be imaged for localizing the stone from renal parenchyma up to urethra. The size of stone and its localization has significance in management whether to choose medications, surgery, or lithotripsy.[10]

Renal stones are composed primarily (75%) of calcium oxalate, of which 50% are calcium phosphate (also known as calcium hydroxyapatite). Magnesium ammonium phosphate (struvite or triple phosphate) stones comprise 10-20 % of renal stones whereas 5% are uric acid stones and 1-2 % are cysteine stones.[11] Ultrasound is cost effective modality for diagnosing renal stones with no radiation hazards, however it is observer dependent.[10] Abdominal computed tomography (CT) is commonest initial imaging test for suspected nephrolithiasis and dual energy CT is a technique allowing calculus composition to be determined by using two different KVP and assessing stone attenuation, Non contrast CT has high sensitivity for the diagnosis of renal stone disease.[11] Calcium stones are radio-opaque and can even be seen on plain radiograph. Generally, calcium, struvite and cysteine stones are radio dense, however cysteine stones are less radio dense than calcium containing stones. Uric acid stones are radiolucent. Sturviute stone are usually large and seen filling the entire pelvi-calyceal system and uric acid stones are generally small.[10]

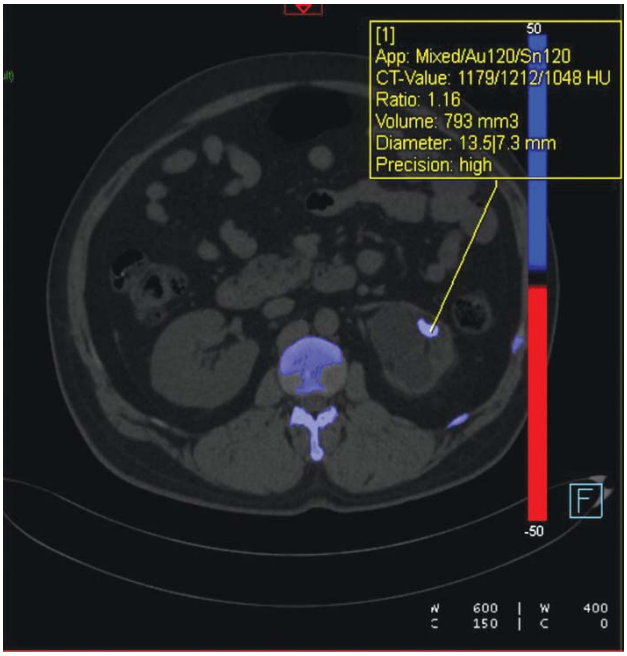


Figure 2: Stone density on NCCT using dual energy CT.

Dual-energy CT is effective for characterizing chemical composition of the urinary stones and specifies uric acid and non uric acid renal stones very precisely. Differentiating between uric and non- uric acid stone is vital as patient with uric acid stones can undergo urinary alkalization instead of undergoing any intervention.[12]

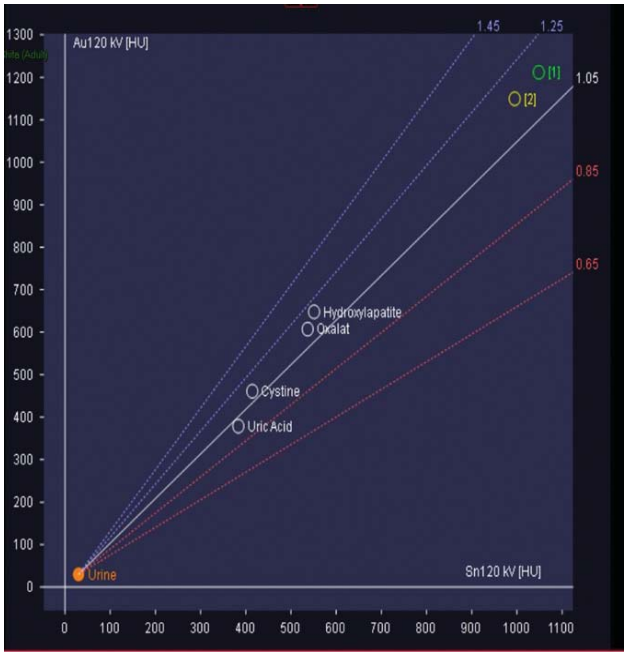


Figure 3: Non uric acid stone attenuation graph.

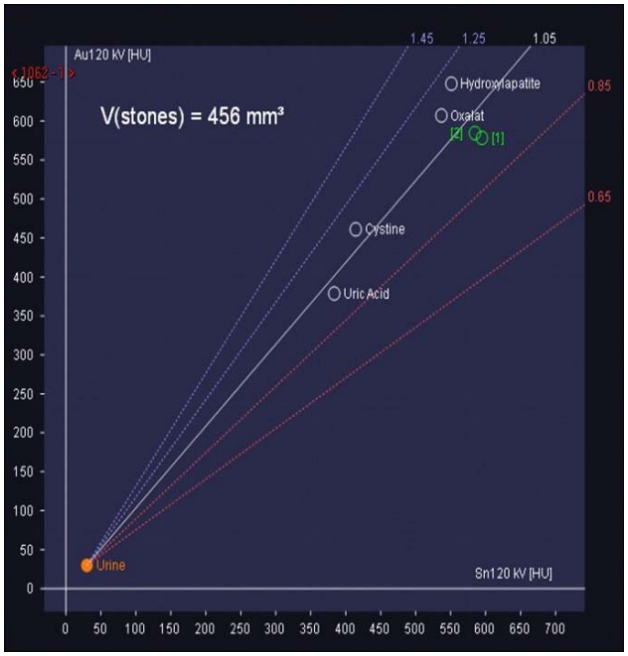


Figure 4: Uric acid stone attenuation graph.

Diffuse hepatic steatosis/ fatty liver disease is a common condition with prevalence of 20 30% in adults and can lead to difficulty in assessing liver parenchyma. Radiologists must report fatty infiltration of liver because it may have serious long-term consequences and can lead to non-alcoholic steato-hepatitis (NASH) and cirrhosis if untreated.[13]

Non-alcoholic fatty liver disease (NAFLD) refers to accumulation of fat in the liver, usually as a result of insulin resistance. Ultrasound is the initial, cost effective imaging modality best used for screening for NAFLD. Fatty liver appears echogenic, featureless/ bland with loss of well demarcated diaphragm. Diagnostic imaging modality for fatty liver is unenhanced CT. Hepatic HU decrease by about 1.6 for each milligram deposition of TGs per gram of liver. On unenhanced CT, severe steatosis is predicted by by relative hypo attenuation of liver more than 10 HU less than spleen and absolute low attenuation, lower than 40 HU. On conventional T1-weighted MR images, severe fatty infiltrate the liver appears as increased hepatic signal intensity (T1: hyper intense T2: mildly hyper intense) and show signal drop out on out of phase imaging.[14]

Prior studies have showed that there is some linkage present between NAFLD and renal stone disease and presence of NAFLD was even attributed as risk factor for renal stone disease as it was thought that fatty liver changes the urinary composition predisposing to formation of stones.[15]

One study found that males have a greater link between fatty liver and urinary stone production than women, which is consistent with our data.[16] Our study sought to demonstrate a link between the kind of renal stone and hepatic function.

Conclusion

Thus, a pilot research conducted in Pakistan found no significant relationship between fatty liver infiltration and the kind of renal stone (uric acid or non-uric stone). Our findings are comparable to those of previous studies described above, with a fatty liver status of 15% in the Pakistani population, a higher prevalence of stones in males, and proportion of uric acid stones in 15% of population.

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