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Association Of Renal Calculi With Non-Alcoholic Fatty Liver Disease Detected On Computed Tomography

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ABSTRACT

BACKGROUND: The phrase "non-alcoholic fatty liver disease "is used to describe fatty liver conditions that affect persons who do not consume alcohol. NAFLD is a form of fatty liver diseasethat is characterized by hepatic inflammation and concomitant liver fat buildup. A common kidneyillness known as renal stone disease is characterized by crystal deposition in the renal medulla andurinary system. NAFLD may increase risk of nephrolithiasis. We examined the association of NAFLD with development of renal calculi in Pakistani men and women of all ages. **OBJECTIVE:**To find the association of renal calculi with non-alcoholic fatty liver disease detected in computedtomography. **METHODOLOGY:** It was a cross sectional analytical study conducted in Radiology Department, Lahore General Hospital. A total 298 patients who underwent abdomen- pelvic CT were included. Patients of both genders and with NAFLD were included. Patients with viral liver disease and liver cirrhosis, splenectomy, liver metastasis, chronic renal failure, transplanted kidney. The statistical significance of association between NAFLD and renal stone disease was assessed using chi-square test. **RESULTS:** In comparison to women, men had a stronger association between fatty liver and stones. NAFLD and nephrolithiasis were more prevalent in cases of age more than 40 and less prevalent in cases of age less than 20 (p for intercept
< 0.001). Renal calculi and NAFLD ration were significantly correlated with hypertension (p = 0.06). Diabetes Mellitus had a non-significant relationship (p = 0.024). Mean of renal calculi sizes
4.35 and standard deviation was 4.30. **CONCLUSION:** Study indicates that prevalence of nephrolithiasis was significantly higher in the NAFLD as compare to healthy groups. Renal calculi were significantly associated with hypertension and Diabetes Mellitus in males have higher prevalence of renal calculi than females.

KEYWORDS: Non-alcoholic fatty liver disease, Nephrolithiasis, Computed Tomography.

INTRODUCTION:

The phrase "non-alcoholic fatty liver disease" is used to describe fatty liver conditions that affect persons who do not consume alcohol. There is a modest amount of fat in a healthy liver. When fat makes up 5% to 10% of the weight of the liver, it becomes an issue[1]. NAFLD is a form of fatty liver disease that is characterized by hepatic inflammation and concomitant liver fat buildup. Steatosis refers to a higher level of fat deposition in the liver. NAFLD is now the most prevalent liver condition, with a frequency of roughly 25% to 30% doubling in the last 20 years[2].

According to the most research, the prevalence substantially is higher in people who have metabolic syndrome, which includes obesity, diabetes, hypertension and a large waist circumference[3]. Other cause of steatosis or hepatitis such as hepatotoxic medications, excessive alcohol consumption, congenital

metabolic disorders or viral hepatitis must be checked out to make the diagnosis of NAFLD. The diagnosis of NAFLD is frequently made clinically after rulingout other disorders but a liver biopsy is necessary for a certain diagnosis of NASH/NAFLD.

Insulin resistance is assumed to be a contributing factor in the development of NAFLD, as it is with other diseases of metabolic syndrome. Management techniques aim to reduce liver damage while reversing or improving insulin resistance. Because cardiovascular disease is the primary cause of death among individuals with NAFLD, cardiovascular risk factor control is an essential component of therapy[4]. Due to its ability to rule out other potential causes of liver injury and assess the severity of fatty infiltration into hepatocytes, lobular inflammation, hepatocyte ballooning andfibrosis, liver biopsy is currently the gold standard for diagnosing NAFLD.

Kidney stones also referred to as renal calculi and typically produced in the kidney, are referred toas nephrolithiasis. A frequent renal illness known as renal stone disease is characterized by crystaldeposition in the renal medulla and urinary tract. Our findings demonstrate that metabolic syndrome can alter the concentration and dilution of urine, increasing the risk of uric acid and calcium oxalate stone formation. According to the foundation of these investigations, renal stone disease may be connected to and a part of the metabolic syndrome. Recent epidemiological research has shown a connection between metabolic syndrome, obesity, diabetes, and high blood pressure7. Whether a kidney stone is in the kidney, ureter, or urinary bladder, the symptoms varydepending on where it is. Stone development does not initially result in any symptoms. Subsequently, renal colic (severe cramping pain), flank pain (pain in the back), hematuria (bloodyurine), obstructive uropathy (urinary tract illness), urinary tract infections, obstruction of urine flow, and hydronephrosis are signs and symptoms of the stone disease (dilation of the kidney). These ailments may cause nausea, vomiting as well as pain from the stone event[6].

Nephrolithiasis prevalence increased from 5% of American adults in 1980 to over 9% in 2012[7]. Nephrolithiasis is a widespread issue with a considerable negative impact on health and the economy, and both its prevalence and incidence are rising internationally. The most recent studiesrevealed that 9.4% to 11.9% of men and 7% of women in America have nephrolithiasis[8]. Between4.7% to 10% of people in European nations have urinary calculi[9].

Based on a computed tomography (CT) finding in ordinary daily practice, we recently observed aconcurrent diagnosis of fatty liver disease and renal stones disease in the same patient. Reviews ofthe literature utilizing According to papers in Pub Med, there have only been two recent studies that examined the relationship between renal stone disease and fatty liver. As a result, the goal ofour study was to assess the incidence of renal stone disease in NAFLD patients using the CT scan[10].

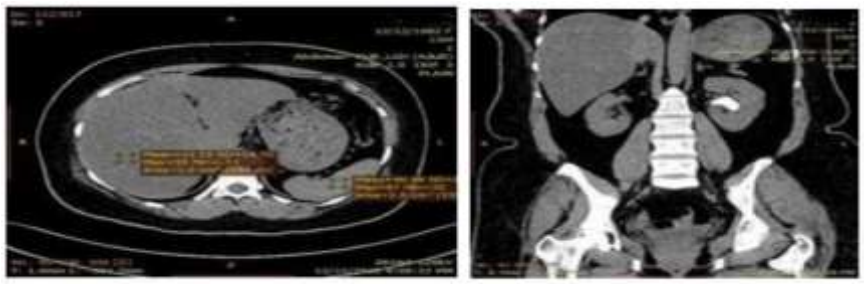
The noninvasive approach of computed tomography (CT) allows for a quick gathering of pictures and a quantitative evaluation of the diagnosis of NAFLD. As a result, it is helpful in clinical practice and provides patient monitoring and follow-up[11].

Although numerous putative processes have been hypothesized including hepatic steatosis, insulin resistance, and oxidative stress, the precise mechanisms relating NAFLD to urolithiasis remain unknown. Recently, sizable Cohort research with 208,578 Korean individuals who received a health assessment was conducted. Indicating that a higher incidence of urolithiasis was substantially correlated with NAFLD. The existing data on the connection between NAFLD and urolithiasis point to a growing body of evidence that NAFLD and an increased risk of urolithiasisare closely related. Yet is quantitatively constrained. Computed tomography (CT), a noninvasive technique that enables quick image

collection and quantitative evaluation of the diagnosis of NAFLD, is helpful in clinical practice and provides patient monitoring and follow-up[12].

MATERIAL AND METHOD:

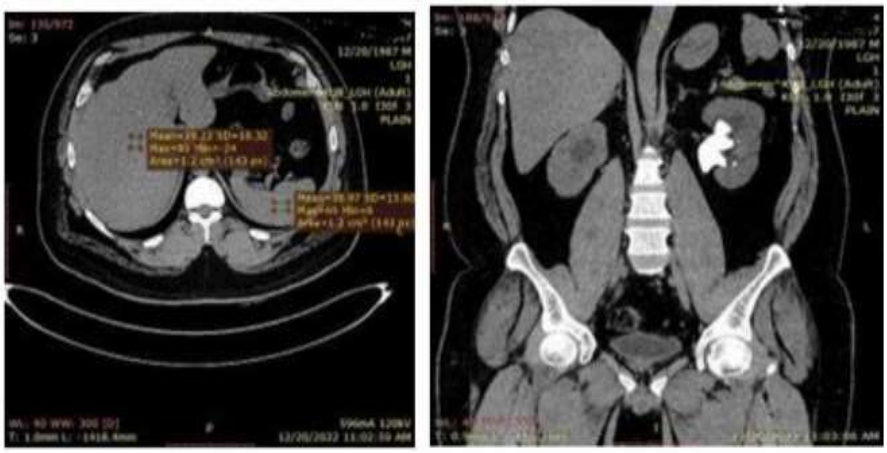
This cross sectional analytical study was conducted from October 2022 to January 2023 in Radiology Department Lahore General Hospital (LGH), Lahore, Pakistan. A total 298 patients who underwent abdomen-pelvic CT were included. Patients of both genders and with NAFLD were included. Patients with viral liver disease and liver cirrhosis, splenectomy, liver metastasis, chronic renal failure, transplanted kidney. Data was collected after taking informed consent fromall the participants. A 128 detectors row CT scanner (SIMENS CT 128 SLICES MODEL SOMATOM DEFINITION EDGE) and 16 slices (TOSHIBA AQUILION 16 SLICES) were used
to perform the abdomen-pelvic CT scan. All patients were in the supine position and were scannedfrom the lung base to the level of pubis symphysis. We performed scan without contrast. The scanning parameter were as follows: Tube voltage 120 KVp, Collimation 128x0.6mm, Rotation speed 0.5sec, Pitch 0.8, Reconstruction thickness 3-5mm and no reconstruction interval. Sagittal and coronal reformatted images were generated with a thickness of 3mm. The statistical



(A) (B)

significance of association between NAFLD and renal stone disease was assessed using chi-square test. The statistical analysis was performed using Medical Software for Windows.

Figure 1 :



(A) (B)

Non-contrast abdomen CT scan of a 64 years old male shows diffuse fatty liver on axial image (A) and left kidney showing multiple stones (macrolithiasis) on coronal image (B). Patient came to the hospital with the complain of left flank pain and burning urination.

Figure 2 :

RESULTS:

There were 115 women (49.8%) and 174 men (60.2%) among the 289 cases. Using the Chi squared Test, only stones (kidney, ureter, and bladder) were discovered in 235 out of 289 cases (or 81.3%).There was no stone in 54 cases (18.7%) of them. P = 0.05 is the significance level. Gender, Diabetes Mellitus (DM), Hypertension (HTN), Fatty Liver Grading, and Renal Calculi Size were evaluated in our study to determine the relationship between NAFLD and Nephrolithiasis. In comparison to women, men had a stronger association between fatty liver and Stones. NAFLD andnephrolithiasis were more prevalent in cases of age more than 40 and less prevalent in cases of age less than 20 (p for interrelationship.

Renal calculi and the NAFLD ratio are significantly correlated with hypertension (p = 0.06). Diabetes Mellitus has a non-significant relationship (p = 0.23) between renal calculi and the NAFLD ratio. However, when HTN and DM are combined, there is a significant connection between renal calculi and the NAFLD ratio (p = 0.024). Mean of renal calculi sizes 4.35 and standard deviation is 4.30.

Table 1: Comparison between renal calculi and grading of fatty liver.

Renal Calculi	Grade				
	0	1	2	3	
NO	40	10	1	3	54 (18.7%)
YES	159	34	17	25	235 (81.3%)
	199 (68.9%)	44 (15.2%)	18 (6.2%)	28 (9.7%)	289

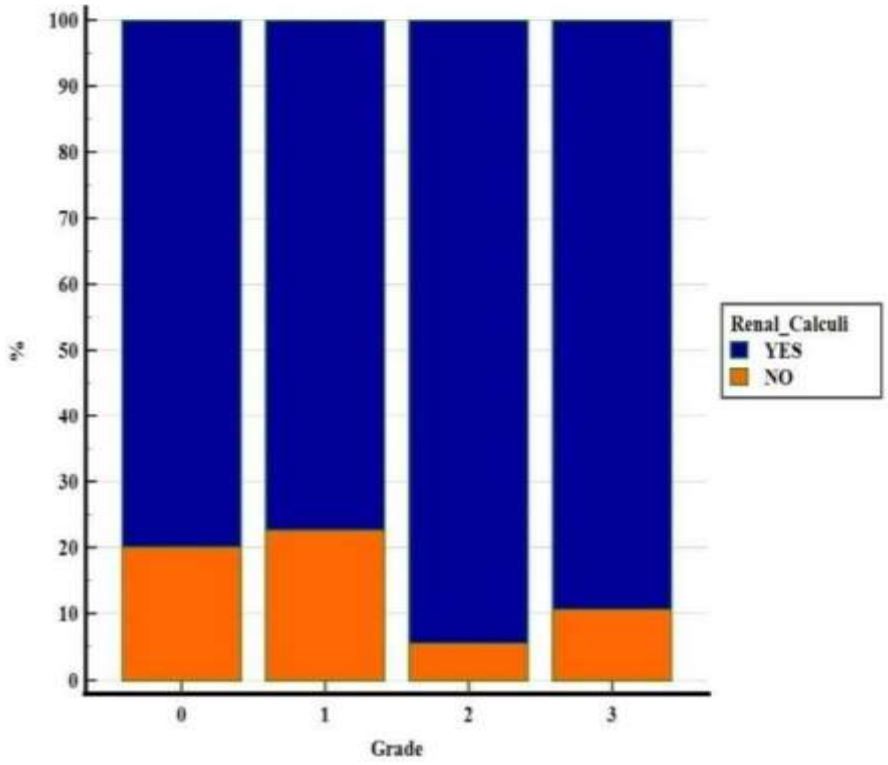
Chi-squared test

Chi-squared	3.949
DF	3
Significance level	P = 0.2671

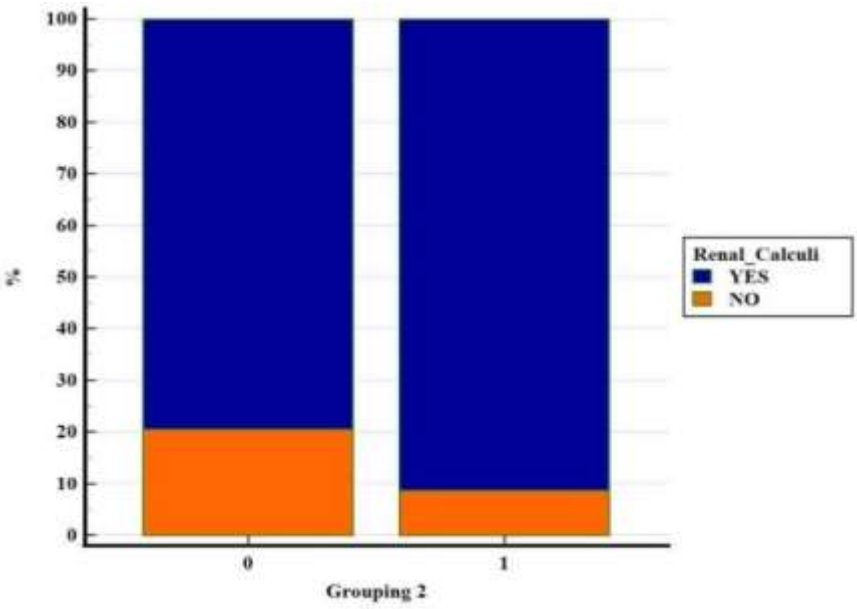
Chi-squared test for trend

Chi-squared (trend)	2.226
DF	1
Significance level	P = 0.1357

On chi-square analysis it was observed that there was increased risk of renal calculi as the severity of fatty liver progressed to Grade II and III, but there was no significant difference on the presenceof stones in patients with no and mild fatty changes in the liver.



Graph 2:



Then we regrouped the patients either without or with mild fatty changes in group 1 and with moderate or severe changes in group 2. On performing chi-square analysis, significant differencein risk of renal stones was seen in group 2.

Table 3: Analysis of covariance

Levene's test for equality of error variances

F	DF 1	DF 2	P
13.9423	3	285	<0.001

Homogeneity of regression slopes

Source	Sum of Squares	DF	Mean Square	F	P
Heterogeneity of slopes	2.840	3	0.947	7.030	<0.001
Individual residual	37.834	281	0.135		

Tests of Between-Subjects Effects

Source	Sum of Squares	DF	Mean Square	F	P
Corrected Model	3.237	4	0.809	5.650	<0.001
Intercept	59.580	1	59.580	416.020	<0.001
Group	0.822	1	0.822	5.740	0.017
HTN	1.084	1	1.084	7.566	0.006
DM	0.206	1	0.206	1.435	0.232
HTN*DM	0.733	1	0.733	5.115	0.024
Residual	40.673	284	0.143		
Total	235.000	289			
Corrected Total	43.910	288			
Coefficient of determination R^2	0.07372				
R^2-adjusted	0.06067				

DISCUSSION:

The present study investigated the association between NAFLD and risk of urolithiasis using other factors such as DM, HTN and BMI representing comprehensive assessment of this association todate. The data provides evidence of increased risk of urolithiasis among patients with NAFLD. Several studies have assessed the relationship between NAFLD and risk of developing urolithiasis. Several studies have assessed the relationship between NAFLD and risk of developing urolithiasis. According to a 2016 study NAFLD was associated with renal stone disease, with a substantially elevated detection rate of renal stone disease in individuals with NAFLD[13]. According to a cohort research published in 2017.About 16,442 participants developed nephrolithiasis throughout the course of 1,054,887.6 person-years of follow-up. Male participants with NAFLD had a significantly higher risk of nephrolithiasis than those without NAFLD[14,15]. In 2015 total of 100 CT studies were enrolled in study. Among the patients with renal stone disease 37.5% had fatty liver. Statistically the frequency of the fatty liver disease in the patient group with urinary stones was significantly higher when compared with the non-urinary stone group. In the subgroups analysis, only the male subgroup was statistically significant. so there was a significant relationship between NAFLD and urolithiasis[16]. According to a study done in 2022 there were 112 cases of non-alcoholic fatty liver, with 67 (59.8%) men and

45 (40.2%) women, and 172 cases of non-fatty liver, with 89 (51.8% men and 83 (48.2% women) men. Both men (41.8% stone) and women (28.9% stone) had a significant relationship between NAFLD and urolithiasis[17].

In a study published in 2018, it was reported that a total of eight studies with 238.400 people.In patients with NAFLD, the incidence of urolithiasis was substantially higher than in those without NAFLD[18]. According to a study done. In 2020, participants with NAFLD were and showed higher prevalence of all metabolic syndrome symptoms, including obesity, impaired glucose tolerance, diabetes mellitus, hypertension NAFLD was linked to an increased incidence of nephrolithiasis[19]. Researchers conducted a study in 2020 in which they claimed that they had "investigated the connection between NAFLD and the risk of urolithiasis." It was discovered that patients with NAFLD had a noticeably higher chance of developing urolithiasis. There is, however, a paucity of information on the relationship between obesity, NAFLD, and urolithiasis. Only one study looked into this connection[20]. So the large number of total subjects with urolithiasis provide adequate statistical power in the detection of the association between NAFLD and urolithiasis. In present study There were 115 women (49.8%) and 174 men (60.2%) among the 289 cases. Using the Chi- squared Test, only stones (kidney, ureter, and bladder) were discovered in 235 out of 289 cases (or 81.3%). There was no stone in 54 cases (18.7%) of them. P = 0.05 is the significance level. In comparison to women, men had a stronger association between fatty liver and stones (p for intercept <0.001).

In a study published in 2014, severity of NAFLD was correlated with an increase in the incidence rate of hypertension The hazard ratios for hypertension were greater in the mild group and moderate to severe group compared with the normal group[21]. In a cross-sectional population-based study carried out in 2022 showed the likelihood of developing kidney stones was found to be 1.17 times higher in people with diabetes, 1.43 times higher in people with hypertension, 2.21 times higher in people with fatty liver, and 1.35 times higher in people who were overweight[22]. A population-based study carried out in 1990, and 509 of the 688 subjects were found to be normotensive. Hypertensive subjects had a relative risk of kidney stones that was twice that of the normotensive group[23]. A past history of nephrolithiasis is linked to an elevated risk of hypertension of compared to patients with a negative history, after correcting for age, according to a study in 2001[24]. In a study published in 2017 nephrolithiasis significantly raised the risk of hypertension in comparison to those who did not have it[27]. In present study Renal calculi and the NAFLD ratio are significantly correlated with hypertension (p = 0.06). In a study published in 2004, 44 (33%) of the 132 individuals with NAFLD had a confirmed diagnosis of diabetes mellitus[26]. In 2006, a population-based case-control study A higher percentage of DM was found in patients with uric acid in 2006, A higher percentage of DM was found in patients with uric acid stones compared to all other stone types[27]. According to a study in 2015 patients with NAFLD had a 50% increased risk of developing metabolic syndrome and a threefold increased risk of developing diabetes compared to the general ppopulation[28]. In a 2005 study found that: 1.38 for older women, 1. For younger women, and 1.31 for men were the multivariate relative risks of prevalent stone disease in adults with DM compared to individuals without. Prospectively, older women had a multivariate relative risk of kidney stone occurrence of 1.29, younger women had a multivariate relative risk of 1. And men had a multivariate relative risk of 0.81 in participants with DM compared to participants without DM. In older women, there was a multivariate relative risk of incident DM of 1. Compared to that of those without a history of kidney stones[29].

According to a 2009 study, family history of diabetes mellitus did not predict the existence or severity of NAFLD or fibrosis. Metabolic syndrome was seen in all patients with severe fibrosis[30]. A study in 2022 found that the presence of non-alcoholic fatty liver disease, atherosclerosis, high- density lipoprotein, low-

density lipoprotein, and cholesterol levels, as well as the thickness of subcutaneous adipose tissue, had no bearing on the development of kidney stones. On the other hand, the production of kidney stones was statistically significantly influenced by triglyceride levels and waist circumference[31].But in present study Diabetes Mellitus has a non-significant relationship (p = 0.23) between renal calculi and the NAFLD ratio. However, when HTN and DM are combined, there is a significant connection between renal calculi and the NAFLD ratio (p = 0.024). Mean of renal calculi sizes 4.35 and standard deviation is 4.30.

CONCLUSION:

Study concluded that the prevalence of urolithiasis is significantly higher in the NAFLD as compared to healthy groups. Renal calculi are significantly associated with hypertension and Diabetes mellitus. Males had a higher prevalence of renal calculi than females.

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