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Linking NAFLD and Nephrolithiasis: A CT-Based Investigation

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Abstract
Objectives: To evaluate the association between NAFLD and renal stone detected on computed tomography.
Method: This study encompassed 240 patients who underwent noncontrast CT abdomen-pelvis computed tomography between November 2023 and April 2024. The nonalcoholic fatty liver disease group included those who had a reduced mean Hounsfield unit (HU) of the right lobe, lateral and left medial segment of the liver as compared to that of the spleen. The control group included patients who had liver parenchyma HU larger than spleen HU. All patients were examined for the presence or absence of radiopaque kidney, ureter, or urinary bladder stones, whether symptomatic or not.
Results: From 240 patients, 122 were healthy (50.8%) without NAFLD or renal stone disease. NAFLD was found in 88 individuals with a mean age of 46.8 ± 17.7 years, 42 (47.7%) males and 46 (52.3%) women. Renal stone disease was detected in 70 patients, accounting for 29.1% of the total. The average age of these patients was 43.7 ± 19.3 years, with 32 males and 38 females. Forty individuals with NAFLD had renal stones (45.5%) which was significantly more than the prevalence in those who are NAFLD negative 13 (19.7%), $P < 0.001$. Females with NAFLD had a considerably greater renal stone rate (52.2%) compared to those without NAFLD (16.3%), $P < 0.001$.
Conclusion: Patients with non-alcoholic fatty liver disease (NAFLD) had a significantly higher incidence of renal stone disease compared to persons with a healthy liver, especially among women.
Keywords: Non-alcoholic liver disease, urolithiasis, computed tomography

Introduction

Nonalcoholic fatty liver disease (NAFLD) is the primary cause for chronic liver disease on a global scale, impacting around 17% to 33% of the general population.[1] This prevalence is increasing consistently as a result of the global increase in metabolic syndrome epidemics.[2] NAFLD is defined as the presence of a minimum of 5% fat accumulation in liver, as determined by the identification of steatosis through imaging or histological evidence, with the exclusion of secondary causative factors[3] and other concurrent liver disorders, for example: chronic viral hepatitis, alcohol-related liver disease, and drug induced hepatitis like tamoxifen or herbal remedies that induce hepatic steatosis.

The diverse influence of NAFLD on both hepatic and systemic health is characterized by a complex interaction. It is linked to several liver illnesses, ranging from simple fatty liver to more serious problems including cirrhosis and hepatocellular cancer. In addition, non-alcoholic fatty liver disease (NAFLD) may be linked to many other extra hepatic disorders, such as obesity, dyslipidemia, type 2 diabetes, cardiovascular disease, and kidney dysfunction. Furthermore, NAFLD has the capacity to advance to cirrhosis, hepatic failure, or hepatocellular cancer, ultimately requiring liver transplantation.[4]

Urolithiasis is a common kidney condition defined by the formation of crystals in renal medulla and urinary system. This disease is affected by several factors, both external and internal.[5] Recent research has shown a robust correlation between urolithiasis and prevalent health problems such as diabetes mellitus and obesity, metabolic syndrome and hypertension. These findings highlight the possibility that metabolic syndrome might disrupt the processes that regulate urine formation, therefore enhancing the likelihood of developing calcium oxalate and uric acid kidney stones.[6] CT scan has high sensitivity in detection and characterization of both renal stones and the fatty infiltration of the liver.[7] To diagnose hepatic steatosis, a liver-minus-spleen difference of less than −10 HU or a pure liver HU less than 40 have been utilized.[8] The complicated interplay between NAFLD and metabolic syndrome highlights the complex relationship of both health conditions. In addition to strong association with insulin resistance,[9] NAFLD has been suggested as a potential precursor to metabolic syndrome.[10] This has sparked curiosity in its possible involvement in development and progression of conditions beyond the liver, for example chronic kidney disease (CKD) and urolithiasis.[11,12]

The purported correlation between NAFLD and renal calculi has garnered research attention. A Chinese research study conducted on 3719 men found a significant correlation between non-NAFLD and the occurrence of renal stones. In addition, pooled data from seven observational studies with a total of 226,541 individuals showed that NAFLD patients had a 1.73 times higher chance of developing urolithiasis compared to healthy controls.[13] Overall, NAFLD is becoming more widely acknowledged as a significant risk factor.

The aim of this research was to assess the correlation between NAFLD and the presence of renal stone disease as revealed by computed tomography.

Methods

This is a cross-sectional observational analytical study which was conducted at Al-Kindy Teaching Hospital from 1-11-2023

to 1-4-2024. The Al-Kindy Teaching Hospital's scientific and ethical committee authorized the investigation.

CT evaluation of NAFLD: The Hounsfield unit (HU) was used to evaluate NAFLD. HU is a relative quantitative measure of radio density utilized to assess the adipose content of the liver. Normal livers typically exhibit a CT attenuation of 50–65 HU, with Hounsfield Units 8–10 HU greater than the spleen HU on non-contrast CT scans. Fatty liver infiltration is diagnosed when the liver attenuation is less than 48 HU (The diagnosis of fatty liver is made based on the liver-to-spleen ratio being less than 1.0 or 0.8).

Patients and groups: A total of 240 patients who were scheduled for abdomen-pelvis CT for any indication initially entitled. The inclusion criteria for the NAFLD group were patients who underwent abdominal pelvis non-contrast CT study and had the right lobe of liver, lateral and left medial segment, exhibit a reduced average HU when compared to the spleen. The control group consisted of individuals with greater hepatic parenchymal Hounsfield Units (HU) compared to the HU of the spleen. All patients were then evaluated for the presence or absence of radiopaque stones in the kidneys, ureters, or urinary bladder whether symptomatic or asymptomatic.

Exclusion criteria included a history of diabetes mellitus, a hepatoma, viral hepatitis, hepatic fibrosis, metastasis of other primary cancers, splenectomy, excessive alcohol consumption, or a CT scan with suboptimal image quality (owing to beam hardening artifact).

CT protocol: The abdomen-pelvis CT scan was conducted utilizing a 128-detector row CT scanner (Definition AS+, Siemens) with a slice size of 0.6 mm. The supine posture was used to scan all patients from the base of the lung to the pubic symphysis. A non-contrast scan was implemented. The scanning parameters were as follows: tube voltage of 120 kVp, rotation speed of 0.5 s, pitch of 0.6, reconstruction thickness of 1 or 5 mm, and no reconstruction interval. The radiation dose was reduced by activating the automatic exposure control 120 kVp, 200 mAs. However, the automatic tube potential modulation (Siemens, careKV) was not enabled. Reformatted pictures were generated in the sagittal and coronal planes, with a thickness of 1 mm and 5 mm, respectively.

Statistical analysis: The statistical analysis was performed using IBM Corp.'s Statistical Package for Social Sciences software version 26, located in Armonk, N.Y., USA. Continuous variables were represented as the mean, standard deviation (SD), or range. The relationship between urolithiasis disease and Fatty liver disease was assessed using Chi-Square or Mann Whitney tests, depending on the circumstances. A significant difference was operationally defined as a (P) value below the threshold of 0.05.

Results

From the total of 240 cases, 122 were classified as healthy, with no identified NAFLD or renal stone disease (50.8 % of the total). NAFLD was observed in 88 patients, 42 (47.7%) of them were men and 46 (52.3%) were women. There was no statistically significant association between the gender of the patient and the presence of NAFLD, Table 1.

The mean age of all patients was 43.4 ± 18.2 years ranging between 10–87 years. The mean age of NAFLD patients was 43.7 ± 19.03 ranging between 17–80 years, 46 (52.3%) were younger than 50 years old. There was no significant difference in the age of patients with and without NAFLD, Table 2.

Renal stone disease was seen in 70 (29.1%) of all patients, 32 of them were men and 38 were women with a mean age of 43.7 ± 19.3 years and an age range of 19–80 years. Renal stones were present in 40 (45.5%) patients with NAFLD (Figure 1), which was considerably higher than the rate of renal stones in the 30 (19.7%) patients who were negative for NAFLD, $P < 0.001$ (Table 3). Among women, renal stone prevalence was much greater in those with NAFLD at 24 cases (52.2%) compared to those who tested negative at 14 cases (16.3%), with a statistically significant difference ($P < 0.001$). The age of NAFLD patients who had renal stones was not significantly different from that of those who did not.

Discussion

The association between NAFLD and renal stones has been the subject of considerable attention for some time.[14,15] It has been reported that the incidence of stone formation can be elevated as a consequence of alterations in urinary constituents caused by the fatty liver. The presence of nephrolithiasis may be influenced by fatty acids as they can affect excretion of calcium and oxalate by phosphorylating arachidonic acid. Arachidonic acid phosphorylation initiates a metabolic cascade in calcium regulation, leading to hypercalciuria. This occurs as a result of the activity of other secondary mediators or the PGE2/vitamin D receptor.[16] The alternative viewpoint holds that mitochondrial lipid peroxidation and systemic generation of oxygen free radicals by the kidneys raise calcium oxalate concentrations. The Carrasco-Valiente research confirmed these results.[17]

We have shown using CT imaging that NAFLD is strongly correlated with a 45.5% higher likelihood of developing renal stones. Several studies have reported the association between renal stone disease and NAFLD in recent years, which is consistent with the findings of the current study. A study reviewed 11245 ultrasonography reports found that the rate of renal

Table 1. **Non-alcoholic fatty liver disease association with gender**

NAFLD		Gender no (%)			*P* value
		Total	F	M	
	Negative	152	86 (56.6)	66 (43.4)	0.590
	Positive	88	46 (52.3)	42 (47.7)	
Total		240	132 (55)	108 (45)	

Table 2. **Non-alcoholic fatty liver disease association with age group**

NAFLD		Age group no (%)			*P* value
		Total	≥50 Y	<50 Y	
	Negative	152	54 (35.5)	98 (64.5)	0.076
	Positive	88	42 (47.7)	46 (52.3)	
Total		240	96 (40)	144 (60)	

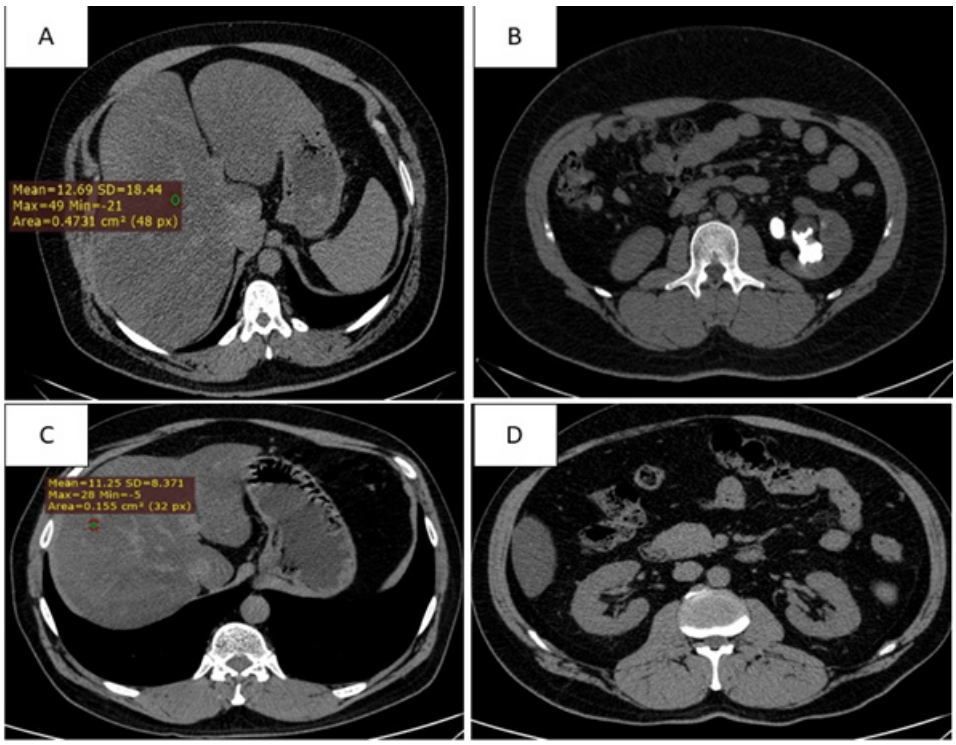

Fig. 1 **Axial section of a non-contrast abdominal CT scan showing the correlation between renal stones and nonalcoholic fatty liver changes. A 35-year-old female presented with left loin pain; A) Diffuse fatty infiltration of the hepatic parenchyma, as well as B) multiple large calyceal stones and a proximal ureteric stone in the left lower pole. A 50-year-old male presented with abdominal pain; C) Diffuse fatty infiltration of the hepatic parenchyma, and D) The kidneys did not demonstrate renal stones.**

Table 3. **Fatty liver association with renal stone**

NAFLD			Renal Stone			
			Total	Negative	Positive	*P* value
All patients No (%)	NAFLD	Negative	152	122 (80.3)	30 (19.7)	<0.001
		Positive	88	48 (54.5)	40 (45.5)	
	Total		240	170	70	
Age Y Mean (SD)	NAFLD	Negative	–	42 (18)	40 (20)	0.394
		Positive	–	47 (17)	46 (19)	0.699
Males No (%)	NAFLD	Negative	66	50 (75.8)	16 (24.2)	0.136
		Positive	42	26 (61.9)	16 (38.1)	
	Total		108	76 (70.4)	32 (29.6)	
Females No (%)	NAFLD	Negative	86	72 (83.7)	14 (16.3)	<0.001
		Positive	46	22 (47.8)	24 (52.2)	
	Total		132	94 (71.2)	38 (28.8)	

stones in NAFLD patients was 17% compared to 8% in those with no evident NAFLD.[18] CT scan is superior to ultrasound in detecting fatty liver changes with higher sensitivity and specificity in addition to its ability to quantify liver fat accumulation.[19,20] Nam and colleagues (2016) discovered that the occurrence of renal stone disease, in a non-contrast CT scan image, was around 19% greater in individuals with non-alcoholic fatty liver disease (NAFLD) compared to those without NAFLD. This incidence is almost half of what was seen in our research.

In addition, they established a correlation between the occurrence of NAFLD and renal stone disease. They showed that likelihood of having renal stone disease was considerably higher in NAFLD cases (odds ratio: 5, 95% CI, 3–8.2) ($P < 0.05$) according their multivariate analysis.[21]

We did not observe a significant age predilection regarding association between NAFLD and nephrolithiasis although it was more frequent in those over 50 years. Kim S et al. reported that such association was significantly more prevalent among individuals under the age of 50 ($P < .001$).[18]

In the current study, the prevalence of the stones was slightly higher in females but not significant, however, the association between renal stones and NAFLD was significant in females compared to males. Other studies found a significant association between renal stones and NAFLD in both sexes.[21,22] In contrast, a separate research found that the association between NAFLD and renal stone disease was statistically significant just among men and those aged 50 and above.[23]

The study's shortcomings include a paucity of clinical, nutritional, and anthropometric data, as well as the related diseases, therapies, and lifestyle factors.

Conclusion

The rate of renal stone disease was considerably greater in patients with NAFLD compared to patients with normal liver. There is a female gender predilection in the association between NAFLD and urolithiasis. Furthermore, the presence of NAFLD may be a risk factor for renal stone disease.

Conflicts of Interest

No conflict of interests was declared by authors.

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