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Association of non-Alcoholic Fatty Liver Disease with Urolithiasis detected on non-Contrast Computed Tomography

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Abstract

Background & Objectives: We aimed to assess whether there is an association between urolithiasis and non-alcoholic fatty liver disease using non-enhanced computed tomography.

Methods :This is a case control study done from October to December 2019, a total of 284 non-contrasts CT scans of reviewed. The subjects were assigned in to cases of non-alcoholic fatty liver group defined with lower average Hounsfield unit of liver than that of spleen and control involved non-fatty liver defined as patients whose Hounsfield of liver parenchyma higher than that of spleen. We determined the percentage of urolithiasis (patients having radiopaque stones in the urinary tract including kidneys, ureters or urinary bladder) in both groups and calculated their significance of relation.

Results: The non-alcoholic fatty liver group involved 112 cases of which 67 (59.8%) male, 45 (40.2%) female and control of non-fatty liver group involved 172 cases; of which, 89 (51.8%) male, 83 (48.2%) female. The incidence of stone disease was significantly higher in non-alcoholic fatty liver (36.6%) than control group (12.2%) which statistically significant with increasing detection rate of renal stone (OR: 4.1, 95% CI, 2.28-7.54). The correlation was still significant when evaluated among males and females separately. Though the prevalence of stone among males (25.6%) is higher than females (17.2), yet it was not statistically significant. This is also true among males (41.8% stone) and females (28.9% stone) in case subjects.

Conclusion: Non-alcoholic fatty liver has an association with significant increase in prevalence of urolithiasis than those without non-alcoholic fatty liver, that is can be considered an independent risk factor variable for renal stone formation.

Key words: **:** Non-alcoholic fatty liver disease, Urolithiasis, Non-contrast CT.

Introduction

Non-alcoholic fatty liver disease (NAFLD) is a variety of disease that varies from steatosis to non-alcoholic steatohepatitis (NASH) with liver involvement by different stage of liver fibrosis and cirrhosis with progression to hepatocellular carcinoma.[1-3] Although NAFLD is common hepatic disorder occurs in absence of excessive alcohol intake only a minority of patients develop advanced liver disease.[4] Non-alcoholic fatty liver is affecting up to 25% of the population globally so it is a common causes of chronic liver disease.[3,5] When at least 5% of non-diseased liver component is replaced by fat called NAFLD.[6] Non-alcoholic fatty liver is thought to be a metabolic syndrome and is regarded as a part of multisystemic disease because it has association with extra-hepatic chronic organ diseases like cardiovascular and renal systems (like chronic kidney disease (CKD), others like type 2 diabetes mellitus (T2DM). Non-alcoholic fatty liver increases morbidity and mortality among patients suffered from this disorder, cardiovascular disease considered first cause of death.[7-11]Urolithiasis is a common

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disorder of urinary system associated with deposition of crystal in the renal medulla and urinary system pathway.[12] Recent studies demonstrated the association between urolithiasis with some metabolic disorders, including obesity, diabetes mellitus and hypertension. With the support of these studies, urolithiasis may be a component of metabolic syndrome[13-15]. Several studies suggested that there is a close link between urolithiasis and those patients who have NAFLD.[16-17] The exact cause between these relations is still unknown, but some studies claim hepatic steatosis, insulin resistance, and oxidative stress as potential mechanisms.[18-19] A key factor in the pathogenesis of NAFLD; insulin resistance, plays an important role in the development of renal stones through its influence on the urinary PH.[20] In the literature, several articles have been reported on the relation between NAFLD and renal stones, however investigations are still insufficient and quantitatively limited beside that being not reproducible yet and the results are inconsistent across variable researches. Establishing the relationship between NAFLD and urolithiasis is crucial as if the relation is clarified, part of the management strategy of the patients with NAFLD is their screening for the development of renal stone.[3] The aim of our study was to assess whether there is association between urolithiasis and NAFLD using non-enhanced CT scan.

Materials and methods

This is a case-control study. It was approved by the ethical committee of Kurdistan Higher council of Medical specialties. The study was carried out on patients visiting the CT scan department of Rizgary teaching hospital in Erbil city and underwent abdomen-pelvis CT eligible from October to December 2019. In this study; we reviewed 284 non-contrast CT scans of patients.The inclusion criteria for NAFLD group were those with lower average Hounsfield unit (HU) of hepatic right lobe, left medial and lateral segment than that of spleen. Control group were defined as patients whose HU of liver parenchyma showed higher than that of spleen.Verbal consent was obtained from each subject beforehand for the purpose of getting patien information. Data concerning demographic characteristics, alcohol consumption, medication use, and comorbidities like hypertension, diabetes, liver disease, were collected by self-administered questionnaires.Exclusion criteria were those who performed abdomen-pelvis CT without non-contrast image, those with suboptimal quality of CT images due to artifacts and those having liver diseases including viral hepatitis, liver cirrhosis, hepatocellular carcinoma, liver metastasis, or chronic liver disease other than NAFLD and participants had a pharmacologic history of drugs that could influence fatty liver; patients with splenectomy or excessive alcohol intake. Participants with polycystic kidney disease, deformity, hypoplasia, dysgenesis, renal tumor, renal cancer and kidney transplantation were also excluded.The CT scanner was a 16-detector row, used in performing the abdomen-pelvis CT scans. The patients were put in supine position and scanning field was from the lung base to the pubic symphysis. We recruited the non-contrast scan phase. The reconstruction thickness, 3 or 5 mm; and no reconstruction interval. Sagittal and coronal reformatted images were generated with a thickness of 3 or 5mm.Liver attenuation measurements were done in at least two liver segments; it was made using a round Region-Of-Interest (ROI) with the maximal possible diameter per segment without including macroscopic vascular or bile structures. The diagnosis of fatty liver was made if the attenuation of the liver was at least 10 HU less than that of the spleen or the

attenuation of the liver was less than 40 HU[21]. Spleen density was measured using the same way.We have determined the percentage of urolithiasis (patients having radiopaque stones in the urinary tract including kidneys, ureters or urinary bladder) in NAFLD and control groups and calculated the significance of relation.
Data entered and analyzed using Statistical Package for Social Sciences version 25 (SPSS Inc., IBM Company, Chicago, Illinois, USA). Descriptive analyses were expressed as frequencies and percentages and the inferential results were compared between the subjects with different variables using a statistical significance level of ≤ 0.05 and analyzed using t-test and Pearson Chi square or Fisher's exact tests if necessary.

Results

Among the 284 total subjects, 156 (54.9%) men and 128 (45.1%) women. The age range of the subjects was 22-76 years (mean 48.88±11.83 years). The subjects were assigned in to cases (NAFLD group) (n.112) {67 (59.8%) male, 45 (40.2%) female} and control group (non-fatty liver) (n.172) {89 (51.8%) male, 83 (48.2%) female}. Sixty-two (21.8%) had stone, of these, 41 (36.6%) were case subjects and 21(12.2%) were control subjects. The difference was significant with p-value of 0.001 as shown in Table (1).

Table:(1): Association between NAFLD and urolithiasis.

			Urolithiasis		Total
			Yes	No	
Groups	Case		41(36.6%)	71(63.4%)	112(100%)
	Control		21(12.2%)	151(87.8%)	172(100%)
Total			62(21.8%)	222(78.2%)	284(100%)
p-value				0.001	

The NAFLD was associated with increasing detection rate of renal stone (OR: 4.1, 95% CI, 2.28-7.54). The correlation was still significant when evaluated among males and females separately with p-values of 0.001 and 0.01 respectively as in Table (2) (for males) and Table (3) (for females).

Table (2): Association between NAFLD and urolithiasis in male subjects.

		Urolithiasis		Total
		Yes	No	
Males	Case	28(41.8%)	39(58.2%)	67(100%)
	Control	12(13.5%)	77(86.5%)	89(100%)
Total		40(25.6%)	116(74.4%)	156(100%)
p-value			0.001	

Table (3): Association between NAFLD and urolithiasis in female subjects.

		Urolithiasis		Total
		Yes	No	
Females	Case	13(28.9%)	32(71.1%)	45(100%)
	Control	9(10.8%)	74(89.2%)	83(100%)
Total		22(17.2%)	106(82.8%)	128(100%)
p-value			0.01	

Though the prevalence of stone among males (25.6%) is higher than females (17.2), yet it was not statistically significant and p-value was 0.086, as shown in Table (4).

Table (4): Difference of urolithiasis in in males and female subjects (both case and control subjects).

		Urolithiasis		Total
		Yes	No	
Gender	Male	40(25.6%)	116(74.4%)	156(100%)
	Female	22(17.2%)	106(82.8%)	128(100%)
Total		62(21.8%)	222(78.2%)	284(100%)
p-value			0.086	

This is also true among males (41.8% stone) and females (28.9% stone) in case subjects, p-value 0.165, Table (5).

Table (5): Difference of urolithiasis in in males and female subjects (both case subjects).

		Urolithiasis		Total
		Yes	No	
Gender	Male	28(41.8%)	39(58.2%)	67(100%)
	Female	13(28.9%)	32(71.1%)	45(100%)
Total		41(36.6%)	71(63.4%)	112(100%)
p-value		0.165		

Among the total 284 cases, the mean age of those with stone (48.68 year ± 13.74) was higher than those without stone (46.84year± 17.73), but statistically not significant, p-value 0.385. While among the 112-case subject the age of those with stone was significantly lower (45.78 year±11.01) than those without stone (50.68year±11.99) with p-value of 0.035

Discussion

In our study we found that incidence of renal stone was 36.6% in those with NAFLD and 12 .2% in those without NAFLD i.e. 24% higher (3 folds). We also showed that the propensity of renal stone is significantly increased among patients

with NAFLD with OR of 4.1, 95% confidence interval, (2.28-7.54), this significant correlation was after adjustment for other confounding variables, as diabetes mellitus and hypertension. This is in agreement with the work Nam[6], a population based retrospective study, who showed that the incidence of urolithiasis was 27% in NAFLD and 8% in non-NAFLD group (19% higher, 3.3 folds) with the prevalence of renal stone was markedly higher in patient with NAFLD than non-NAFLD in multivariate analysis (OR: 5, 95% CI, 3-8.2).Another study by Zeina[22], found a 3.24-fold increased risk of CT diagnosed urolithiasis in NAFLD patients compared to non-NAFLD individuals with higher chance of renal stone in patients with fatty liver changes, OR= 2.52 (95% CI, 1.02-6.26), p-value is 0.046.Equivalent result is found in a met-analysis, studying seven observational studies; they found 1.73-fold higher risk of stone formation in NAFLD than non-NAFLD subjects[3].The incidence of urolithiasis was significantly higher in males with NAFLD than non-NAFLD and again in females in NAFLD than non-NAFLD with P value of 0.001 and 0.01 respectively. In a large Korean cohort study using ultrasound; they found significantly increased risk of urolithiasis in men but not in women[17].Although in our study the prevalence of urolithiasis among men was higher than women in both among cases alone and in comparing cases with control subjects, it was not statistically significant with p-value of 0.165 and 0.086 respectively. This is in accordance with previous work by Nam[6], who found 31% and 21.7% stone in men and women respectively with p-value 0.208.A limitation of our study may be small sample size.

Conclusion

Non-alcoholic fatty liver disease is associated with significant increase in the prevalence of urolithiasis than those without NAFLD, that is can be considered an independent risk factor variable for renal stone formation.We recommend further large-scale study with larger sample size and also to evaluate the association of the severity of NAFLD with renal stone, and also to show the correlation reversely, to find the effect of urolithiasis on NAFLD development.Conflicts of interest statement and funding: There is no conflict of interest to disclose.

Conflicts of interest

The author reports conflicts of interest.

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