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The Role Of Renal Resistive Index (RRI) As Early Non Invasive Predictor Of Renal Dysfunction And Relation To Estimated GFR In NAFLD Patients

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ORIGINAL STUDY

The role of renal resistive index as an early noninvasive predictor of renal dysfunction and relation to estimated glomerular filtration rate in nonalcoholic fatty liver disease patients

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Abstract

Background: **Nonalcoholic fatty liver disease (NAFLD) is the diagnosis of fatty infiltration of the liver (steatosis) in the absence of other reasons, done through histology or imaging, with or without fibrosis or inflammation. We sought to ascertain the function of the renal resistive index (RRI) as early noninvasive predictor of renal dysfunction and the relationship between estimated glomerular filtration rate (eGFR) and RRI in patients with NAFLD.**

Patients and methods: **This cross-sectional research comprised 250 patients and controls gathered from the outpatient clinic of the Hepatogasteroenterology Department, Benha Teaching Hospitals. They were split into three groups: group 1 consisted of 100 nonalcoholic steatohepatitis (NASH) patients, fibrosis-free or with a history of the condition; group 2 comprised 100 patients with simple steatosis; and group 3 consisted of an additional 50 healthy, normal controls. All patients underwent laboratory investigations, including tests for the lipid profile, liver function, kidney function, fasting blood glucose (FBG), and radiological assessment using an abdominal ultrasound.**

Results: **RRI and NAFLD fibrosis scores were significantly greater in group 1 in contrast to groups 2 and 3 ($P < 0.05$) and were significantly higher in group 2 in comparison to group 3 ($P < 0.05$). BMI, hypertension, FBG, eGFR, serum creatinine, total cholesterol, triglycerides, direct bilirubin, NAFLD fibrosis score, and NASH were the significant predictors of RRI indicated in the multiple regression analysis. RRI can significantly predict NASH with an area under the curve of 0.908, *P* value of less than 0.001, at cutoff value more than 0.063, with 100% sensitivity, 60.67% specificity, 62.9% positive predictive value, and 100% negative predictive value.**

Conclusions: **We concluded that NAFLD is associated with higher RRI, NAFLD fibrosis score, FBG, serum creatinine, hazardous lipid profile, liver enzymes, and lower eGFR.**

Keywords: Estimated glomerular filtration rate, Nonalcoholic fatty liver disease, Renal dysfunction, Renal resistive index

1. Introduction

The fatty infiltration of the liver (steatosis) without other causes, with or without inflammation or fibrosis, as established by imaging or histology, is known as nonalcoholic fatty liver disease (NAFLD). NAFLD prevalence varies from 17 to 33% in Western countries' general population, and its incidence is still rising [1]. NAFLD contains a wide range of conditions, comprising simple steatosis, a relatively benign accumulation of lipids, and progressive nonalcoholic steatohepatitis (NASH) caused by inflammation, necrosis, and fibrosis [2]. There is no indication of inflammation in basic hepatic steatosis; however, inflammation of the liver is seen in NASH. Cirrhosis and hepatocellular cancer may develop from NASH [3].

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A variety of events that are connected to impaired kidney function and a persistent reduction in glomerular filtration rate (GFR) are encompassed under chronic kidney disease (CKD). The estimated prevalence of CKD in American adults was 11%. (19.2 million). CKD is becoming more widely acknowledged as a major risk factor for cardiovascular disorders and end-stage renal failure [4].

The cardiometabolic risk factors and pathophysiological processes of NAFLD and CKD are convergent. Oxidative stress, rennin–angiotensin system activation, insulin resistance (IR), and the cytokines released inadequately by the inflammatory and steatotic liver may contribute to the pathophysiology of CKD and NAFLD [5]. The hepatorenal syndrome is observed in liver cell failure patients by the anticipated connection between the kidney and liver [6]. Targher et al. [7,8] completed two cross-sectional investigations, which concluded that the CKD prevalence is greater in patients with NAFLD than in those with no steatosis.

The approximate renal alterations, chronic renal disease prognosis, and clinical consequences can be predicted by utilizing the estimated glomerular filtration rate (eGFR), which is an assessment of the renal's capacity to filter the blood [9]. In addition, renal ultrasonography (USG) and renal Doppler USG are crucial for the assessment of renal diseases or subsequent renal hemodynamic alterations [10]. Greyscale USG is employed to determine the chronic phase of renal disorder by evaluating renal measurement, parenchymal thickness, and parenchymal echogenicity. Renal color Doppler USG is used to assess the systolic/diastolic ratio, end-diastolic velocity, peak systolic velocity, pulsatility index, and renal resistive index (RRI), which aids in the determination of renal hemodynamic alterations. The RRI is the most often employed of these metrics in clinical settings [11,12]. Doppler examination of the renal vascular bed can determine RRI, which is a semiquantitative index. RRI = [(peak systolic velocity−end-diastolic velocity)÷peak systolic velocity]. The RRI score often falls within the range of 0.47–0.70, indicating a variation between the two kidneys of less than 5–8% [13].

The current research intended to ascertain the function of RRI as an early noninvasive predictor of renal dysfunction and the relationship between eGFR and RRI in patients with NAFLD.

2. Patients and methods

This cross-sectional research recruited 250 patients and controls (age>18 years) from the outpatient clinic of the Hepatogastroenterology Department, Benha Teaching Hospitals, Qalyubia, Egypt. It received the approval of ethics committee of Benha Teaching Hospital from December 2022 to November 2023. All patients gave written informed permission.

The control group consisted of individuals with normal liver size, echogenicity, and shape; normal liver and kidney function tests, normal urine analysis, normal eGFR, and no pertinent medical history.

Exclusion criteria included patients on nephrotoxic medications, having hypertension, diabetes mellitus, liver diseases other than NAFLD, or any kind of structural or functional renal disorder, including acute or chronic renal diseases or renal artery stenosis.

2.1. Grouping

Three groups were formed from the enrolled individuals: group 1 consisted of 100 patients with NASH, either having fibrosis or not; group 2 comprised 100 patients with simple steatosis; and group 3 comprised 50 controls who were normal and healthy.

The diagnosis of NAFLD was made in conjunction with the exclusion of fatty liver, a history of hepatic viral infection, the use of steatogenic or hepatotoxic drugs, and consumption of alcohol in excess (>140 g/week for males and >70 g/week for women). One skilled operator used the usual procedure for hepatic steatosis identification on a USG scan to determine whether or not the liver was fatty. As opposed to the renal cortex of NAFLD patients, the control group's liver was shown to be more echogenic.

Every patient had a thorough medical history taken. All participants and controls underwent physical examinations, and laboratory investigations were conducted. Tests for the liver, including alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyl transferase (GGT), alkaline phosphatase (ALP), serum albumin, total and direct bilirubin, and total proteins; and tests for the kidneys, Complete urine analysis, eGFR, fasting blood glucose (FBG), blood urea nitrogen (BUN), serum creatinine, serum potassium (K), sodium (Na), and complete urine analysis. Viral indicators were determined employing hepatitis C antibodies and hepatitis B surface antigen.

After an 8-h fast, an abdominal ultrasound was used to do a radiological examination on all of the study's patients and controls. Ultrasound device with color Doppler advantage and a 2.8–5 MHz convex linear transducer (LOGIQ P6; G E Medical

Systems, Grandview Boulevard Waukesha, USA) were used to analyze them in order to assess parenchymal echogenicity, size of the liver, and contour of the liver capsule (coarse, smooth, lobulated). Assessment criteria included renal size, echogenicity, cortico-medullary differentiation, and cortical thickness (at least 10 mm).

The ultrasound apparatus automatically determine the RRI. The superior, middle, and inferior zones of each kidney were the three locations where the resistance was measured intrarenal at the interlobar arteries. The mean value was then computed. Next, a mean RRI was calculated using each patient's six readings. RRI formula: RRI=(peak systolic velocity−end-diastolic velocity)÷peak systolic velocity [14].

The distinction between simple steatosis and NASH was made using the sonographic image of elevated liver echogenicity in conjunction with normal or higher liver enzymes; the noninvasive evaluation of the NAFLD fibrosis existence was carried out via computing the fibrosis score of NAFLD [15]. The following information was needed to calculate this score: age, fasting blood sugar, platelet count, AST, ALT, BMI, and albumin.

NAFLD fibrosis score formula [16]: $-1.675 + 0.037 \times$ age (years)$+0.094 \times$ BMI (kg/m^2)$+ 1.13 \times$ IFG÷diabetes (yes = 1, no = 0)$+0.99 \times$ AST/ALT ratio$-0.013 \times$ platelet ($\times 10^9$)$-0.66 \times$ albumin (g/dl).

The findings were explained as follows: less than −1.455: predictor lack of significant fibrosis (F0−F2 fibrosis), more than or equal to −1.455 to less than or equal to 0.675: indeterminate score, and more than 0.675: predictor of existence of significant fibrosis (F3−F4 fibrosis).

2.2. Statistical analysis

Using SPSS, v28, statistical analysis was executed (IBM Inc., Armonk, New York, USA). Using the analysis of variance (F) test, quantitative variables were contrasted between the two groups and given as SD and mean. The frequency and percentage (%) of the qualitative variables were analyzed by χ^2 test. A statistically significant outcome was described as a two-tailed P value less than 0.05. To ascertain the level of correlation between two quantitative variables, Pearson correlation analysis was performed. The link between one dependent variable and multiple independent factors was examined using multiple regression. Receiver operating characteristic curve analysis was determined to evaluate each test's overall diagnostic performance. The overall performance of the test is assessed by employing area under the curve.

3. Results

The weight and BMI were markedly bigger in groups 1 and 2 in contrast to group 3 ($P < 0.05$), with no marked variation between groups 1 and 2. Other baseline characteristics (age, sex, and height) and comorbidities (hypertension, diabetes mellitus, and dyslipidemia) were insignificantly different among the groups under study (Table 1).

White blood cells were notably bigger in group 2 in contrast to group 3 ($P = 0.013$), with no significant variation between other groups and each others. Platelets count and H notable DL were significantly reduced in groups 1 and 2 in contrast to group 3 ($P < 0.05$), with no significant variation between

Table 1. Baseline characteristics of the studied groups.

	Group 1 ($N = 100$)	Group 2 ($N = 100$)	Group 3 ($N = 50$)	P value
Age (years)	53.44 ± 6.9	52.17 ± 7.68	52.48 ± 7.54	0.456
Sex				
Male	62 (62)	70 (70)	31 (62)	0.429
Female	38 (38)	30 (30)	19 (38)	
Weight (kg)	88.15 ± 12.25 $P1 = 0.396$, $P2<0.001$[a], $P3<0.001$[a]	89.58 ± 11.53	69.3 ± 5.88	<0.001[a]
Height (m)	1.65 ± 0.04	1.65 ± 0.04	1.66 ± 0.04	0.534
BMI (kg/m^2)	32.31 ± 4.52 $P1 = 0.445$, $P2<0.001$[a], $P3<0.001$[a]	32.81 ± 4.67	25.18± 2.54	<0.001[a]
Comorbidities				
HTN	53 (53)	51 (51)	20 (40)	0.304
DM	36 (36)	38 (38)	17 (34)	0.886
Dyslipidemia	49 (49)	47 (47)	22 (44)	0.845

Data displayed as mean ± SD or frequency (%).
DM, diabetes mellitus; HTN, hypertension.
$P1$: P value between groups 1 and 2.
$P2$: P value between groups 1 and 3.
$P3$: P value between groups 2 and 3.
[a] Statistically significant as P value less than 0.05.

groups 1 and 2. FBG was significantly greater in groups 1 and 2 in contrast to group 3 ($P < 0.001$, 0.001), with no significant variation between groups 1 and 2. eGFR was significantly lower in groups 1 and 2 in contrast to group 3 ($P < 0.05$) and were notably reduced in groups one in contrast to group 2 ($P < 0.05$). Serum creatinine, total cholesterol, triglycerides, and low-density lipoprotein (LDL) were significantly greater in groups 1 and 2 in contrast to group 3 ($P < 0.001$, 0.001) and were significantly larger in group 1 in contrast to group 2 ($P = 0.039$). Liver enzymes (ALT, AST, and ALP) were markedly larger in group 1 in contrast to groups 2 and 3 ($P < 0.05$), with no significant variation between groups 2 and 3. Albumin was significantly reduced in group 1 in contrast to groups 2 and 3 ($P < 0.001$, 0.001), with no significant variation between groups 2 and 3. There was an insignificant difference among groups under study concerning the other laboratory investigations, including hemoglobin, C-reactive protein, BUN, Na^+, K^+, direct bilirubin, and total protein (Table 2).

Table 3 shows that RRI and NAFLD fibrosis scores were significantly greater in group 1 in contrast to groups 2 and 3 ($P < 0.05$) and were significantly higher in group 2 in comparison to group 3 ($P < 0.05$). Renal parenchymal thickness was insignificantly different among the groups under study.

In both groups 1 and 2, there was a substantial positive connection between RRI and the NAFLD fibrosis score, age, BMI, serum creatinine, triglycerides, total cholesterol, LDL, ALT, AST, and

Table 2. Laboratory investigations of the studied groups.

	Group 1 ($N = 100$)	Group 2 ($N = 100$)	Group 3 ($N = 50$)	P value
Hb (g/dl)	12.34 ± 0.96	12.55 ± 0.87	12.31 ± 0.88	0.169
WBCs ($\times 10^9$/l)	6.61 ± 1.44 $P1 = 0.398$, $P2 = 0.067$, $P3 = 0.013$[a]	6.78 ± 1.48	6.17 ± 1.21	0.045[a]
PLT ($\times 10^9$/l)	270.19 ± 79.06 $P1 = 0.853$, $P2 = 0.029$[a], $P3 = 0.016$[a]	268.15 ± 76.41	298.3 ± 60.29	0.048[a]
CRP (mg/dl)	2.38 ± 0.67	2.54 ± 0.6	2.52 ± 0.67	0.196
FBG (mg/dl)	102.65 ± 14.62 $P1 = 0.149$, $P2<0.001$[a], $P3<0.001$[a]	105.65 ± 14.67	88.78 ± 6.17	<0.001[a]
eGFR (ml/min/1.73 m^2)	114.3 ± 2.66 $P1 = 0.039$[a], $P2<0.001$[a], $P3<0.001$[a]	115.17 ± 3.25	118.5 ± 6.27	0.389
Serum creatinine (mg/dl)	1.04 ± 0.08 $P1<0.001$[a], $P2<0.001$[a], $P3<0.001$[a]	0.9 ± 0.06	0.59 ± 0.13	<0.001[a]
BUN (g/dl)	15.54 ± 1.39	15.7 ± 1.3	15.6 ± 1.25	0.679
Na^+ (mmol/l)	140.56 ± 3.13	140.02 ± 3.19	140.76 ± 2.97	0.302
K^+ (mmol/l)	4.39 ± 0.54	4.36 ± 0.53	4.33 ± 0.54	0.764
Total cholesterol (mg/dl)	229.76 ± 18.23 $P1<0.001$[a], $P2<0.001$[a], $P3<0.001$[a]	193.78 ± 19.38	119.34 ± 17.18	<0.001[a]
Triglycerides (mg/dl)	195.23 ± 22.81 $P1<0.001$[a], $P2<0.001$[a], $P3<0.001$[a]	175.07 ± 19.78	92.14 ± 17.08	<0.001[a]
HDL (mg/dl)	46.93 ± 7.33 $P1 = 0.590$, $P2 = 0.006$[a], $P3 = 0.016$[a]	47.47 ± 6.83	50.26 ± 6.04	0.017[a]
LDL (mg/dl)	195.01 ± 25.75 $P1<0.001$[a], $P2<0.001$[a], $P3<0.001$[a]	182.12 ± 20.06	93.72 ± 27.76	<0.001[a]
ALT (IU/l)	61.07 ± 12.22 $P1<0.001$[a], $P2<0.001$[a], $P3 = 0.896$	30.18 ± 6.37	30.04 ± 5.81	<0.001[a]
AST (IU/l)	54.59 ± 8.92 $P1<0.001$[a], $P2<0.001$[a], $P3 = 0.310$	29.68 ± 5.29	28.76 ± 5.07	<0.001[a]
ALP (IU/l)	120.84 ± 16.73 $P1<0.001$[a], $P2<0.001$[a], $P3 = 0.278$	60.23 ± 6.08	59.08 ± 6.13	<0.001[a]
Direct bilirubin (mg/dl)	0.51 ± 0.06	0.5 ± 0.06	0.5 ± 0.06	0.384
Total bilirubin (mg/dl)	0.15 ± 0.01	0.16 ± 0.01	0.16 ± 0.01	0.417
Albumin (g/dl)	3.73 ± 0.17 $P1<0.001$[a], $P2<0.001$[a], $P3 = 0.888$	4.14 ± 0.17	4.14 ± 0.16	<0.001[a]
Total protein (g/dl)	6.96 ± 0.2	6.98 ± 0.22	7.03 ± 0.18	0.145

Data presented as mean ± SD.

ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BUN, blood urea nitrogen; CRP, C-reactive protein; eGFR, estimated glomerular filtration rate; FBG, fasting blood glucose; Hb, hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; PLT, platelets; WBCs, white blood cells.

*P*1: *P* value between groups 1 and 2.

*P*2: *P* value between groups 1 and 3.

*P*3: *P* value between groups 2 and 3.

[a] Statistically significant as *P* value less than 0.05.

Table 3. Clinical data of the studied groups.

	Group 1 ($N = 100$)	Group 2 ($N = 100$)	Group 3 ($N = 50$)	P value
Renal parenchymal thickness (mm)	12.02 ± 0.66	11.91 ± 0.58	11.89 ± 0.68	0.341
RRI	0.66 ± 0.01	0.64 ± 0.01	0.60 ± 0.02	<0.001[a]
	$P1$<0.001[a], $P2$<0.001[a], $P3$<0.001[a]			
NAFLD fibrosis score	−1.22 ± 1.18	−2.09 ± 0.9	−3.73 ± 0.92	<0.001[a]
	$P1$<0.001[a], $P2$<0.001[a], $P3$<0.001[a]			

Data displayed as mean ± SD.
NAFLD, nonalcoholic fatty liver disease; RRI, renal resistive index.
$P1$: P value between groups 1 and 2.
$P2$: P value between groups 1 and 3.
$P3$: P value between groups 2 and 3.
[a] Statistically significant as P value less than 0.05.

ALP. There was a notable inverse connection between eGFR, RRI, high-density lipoprotein (HDL), total protein, and albumin. There was an insignificant correlation between RRI and FBG as well as between BUN and direct and total bilirubin (Table 4).

The multiple regression analysis revealed that BMI, hypertension, FBG, eGFR, serum creatinine, total cholesterol, triglycerides, direct bilirubin, NAFLD fibrosis score, and NASH were significant predictors of RRI (Table 5).

RRI can significantly predict NASH with area under the curve of 0.908, P value of less than 0.001, at cutoff value more than 0.063, with 100% sensitivity, 60.67% specificity, 62.9% positive predictive value, and 100% negative predictive value (Table 6, Figs. 1 and 2).

4. Discussion

Both NAFLD and CKD have similar pathogeneses, including a large number of mechanistic molecular pathways and cardiometabolic risk factors. According to the latest research, even after common risk variables were taken into account, NAFLD was linked to a noticeably higher risk for the onset and progression of CKD [17,18]. NAFLD may worsen hypertension and hepatic IR, resulting in inflammatory mediators and atherogenic dyslipidemia in CKD [19–21]. The biology and clinical characteristics of the bidirectional links between NAFLD and CKD remain unclear despite a number of studies demonstrating their connection. In particular, there are few investigations on the attributes of CKD NAFLD patients [22,23].

Table 4. Correlation between renal resistive index and other parameters in the studied groups.

	Group 1 ($N = 100$)		Group 2 ($N = 100$)	
	r	P	r	P
Age (years)	0.259	0.009[a]	0.224	0.025[a]
BMI (kg/m^2)	0.282	0.004[a]	0.264	0.007[a]
FBG (mg/dl)	−0.048	0.639	0.029	0.769
eGFR (mL/min/1.73 m^2)	−0.373	<0.001[a]	−0.210	0.036[a]
Serum creatinine (mg/dl)	0.304	0.002[a]	0.327	0.001[a]
BUN (g/dl)	−0.014	0.889	−0.120	0.236
Total cholesterol (mg/dl)	0.447	<0.001[a]	0.238	0.016[a]
Triglycerides (mg/dl)	0.325	0.001[a]	0.285	0.004[a]
HDL (mg/dl)	−0.320	0.001[a]	−0.214	0.032[a]
LDL (mg/dl)	0.295	0.003[a]	0.271	0.006[a]
ALT (IU/l)	0.239	0.017[a]	0.212	0.034[a]
AST (IU/l)	0.288	0.004[a]	0.217	0.029[a]
ALP (IU/l)	0.301	0.002[a]	0.201	0.045[a]
Direct bilirubin (mg/dl)	0.026	0.798	−0.010	0.919
Total bilirubin (mg/dl)	0.104	0.301	0.065	0.517
Albumin (g/dl)	−0.239	0.016[a]	−0.253	0.011[a]
Total protein (g/dl)	−0.219	0.028[a]	−0.214	0.032[a]
NAFLD fibrosis score	0.236	0.018[a]	0.249	0.013[a]

ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; BUN, blood urea nitrogen; eGFR, estimated glomerular filtration rate; FBG, fasting blood glucose; HDL, high-density lipoprotein; LDL, low-density lipoprotein; NAFLD, nonalcoholic fatty liver disease; r, correlation coefficient.
[a] Statistically significant as P value less than 0.05.

Table 5. Multiple regression analysis for prediction of renal resistive index.

	Coefficient	SE	*t*	*P*	$r_{partial}$	$r_{semipartial}$
Age (years)	0.0001	0.0002	0.291	0.771	0.019	0.019
Sex	0.0012	0.0031	0.398	0.691	0.025	0.025
BMI (kg/m^2)	0.0018	0.0003	6.984	<0.001[a]	0.405	0.405
HTN	0.0180	0.0074	−2.427	0.016[a]	−0.153	0.153
DM	−0.0030	0.0041	−0.728	0.467	−0.046	0.046
Dyslipidemia	−0.0012	0.0029	−0.422	0.673	−0.027	0.027
Hb (g/dl)	−0.0015	0.0015	−0.984	0.326	−0.063	0.059
WBCs ($\times 10^9$/l)	0.0018	0.0010	1.866	0.063	0.119	0.113
PLT ($\times 10^9$/l)	0.0000	0.0000	−1.497	0.136	−0.095	0.090
CRP (mg/dl)	−0.0011	0.0021	−0.499	0.618	−0.032	0.030
FBG (mg/dl)	0.0004	0.0001	4.769	<0.001[a]	0.292	0.288
eGFR (mL/min/1.73 m^2)	−0.0016	0.0003	−4.684	<0.001[a]	−0.285	0.285
Serum creatinine (mg/dl)	0.0945	0.0054	17.366	<0.001[a]	0.744	0.710
BUN (g/dl)	−0.0007	0.0007	−1.000	0.318	−0.064	0.041
Na^+ (mmol/l)	0.0002	0.0003	0.517	0.606	0.033	0.021
K^+ (mmol/l)	0.0000	0.0018	−0.024	0.981	−0.002	0.001
Total cholesterol (mg/dl)	0.0002	0.0000	5.761	<0.001[a]	0.350	0.197
Triglycerides (mg/dl)	0.0001	0.0000	4.580	<0.001[a]	0.285	0.157
HDL (mg/dl)	−0.0001	0.0001	−1.154	0.250	−0.075	0.040
LDL (mg/dl)	0.0001	0.0000	1.917	0.056	0.123	0.066
ALT (IU/l)	0.0000	0.0001	0.385	0.700	0.025	0.013
AST (IU/l)	0.0002	0.0001	1.930	0.055	0.124	0.066
ALP (IU/l)	0.0000	0.0001	0.166	0.868	0.011	0.006
Direct bilirubin (mg/dl)	−0.0413	0.0134	−3.080	0.002[a]	−0.196	0.106
Total bilirubin (mg/dl)	−0.0528	0.0734	−0.720	0.473	−0.047	0.025
Albumin (g/dl)	0.0029	0.0045	0.635	0.526	0.041	0.022
Total protein (g/dl)	−0.0021	0.0040	−0.518	0.605	−0.034	0.018
Renal parenchymal thickness (mm)	0.0012	0.0017	0.682	0.496	0.043	0.032
NAFLD fibrosis score	0.0057	0.0009	6.385	<0.001[a]	0.377	0.296
NASH	0.0206	0.0025	8.168	<0.001[a]	0.462	0.379

ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BUN, blood urea nitrogen; CRP, C-reactive protein; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; FBG, fasting blood glucose; Hb, hemoglobin; HDL, high-density lipoprotein; HTN, hypertension; LDL, low-density lipoprotein; NAFLD, nonalcoholic fatty liver disease; NASH, nonalcoholic steatohepatitis; PLT, platelets; WBCs, white blood cells.

[a] Statistically significant as *P* value less than 0.05.

Table 6. Diagnostic accuracy of renal resistive index for prediction of nonalcoholic steatohepatitis.

	Cutoff	Sensitivity	Specificity	PPV	NPV	AUC	*P* value
RRI	>0.63	100.00	60.67	62.9	100.0	0.908	<0.001[a]

AUC, area under the curve; NPV, negative predictive value; PPV, positive predictive value; RRI, renal resistive index.

[a] Statistically significant as *P* value less than 0.05.

According to a number of cross-sectional studies, NAFLD is linked to a larger prevalence of CKD, which ranges from about 20 to 25% [24,25]. Patients with NAFLD, therefore, need to be screened for CKD. NAFLD is the most quickly growing sign of concurrent liver and renal transplantation and an independent risk factor for CKD [26]. Furthermore, because of altered glucocorticoid metabolism, altered barrier function and gut microbiota, and the buildup of toxic uremic metabolites, CKD may make NAFLD worse. Examining the existence and severity of NAFLD in CKD patients makes sense overall. It is still unknown, though, how precisely the pathophysiology and clinical characteristics of CKD and NAFLD are related to each other [27].

Our study revealed that HDL was significantly reduced in groups 1 and 2 in contrast to group 3 ($P < 0.05$), total cholesterol, triglycerides, and LDL were significantly greater in groups 1 and 2 in comparison to group 3 ($P < 0.001$, 0.001) and were significantly larger in groups 1 in contrast to group 2 ($P = 0.039$). FBG was significantly greater in groups 1 and 2 in contrast to group 3 ($P < 0.001$, 0.001).

FBG was considerably bigger in the NASH group in contrast to the simple steatosis and control groups, according to a prior study [28]. These findings align with those of Jimba et al. [29]. They discovered that NAFLD showed a substantial positive correlation with rising FBG in nondiabetic

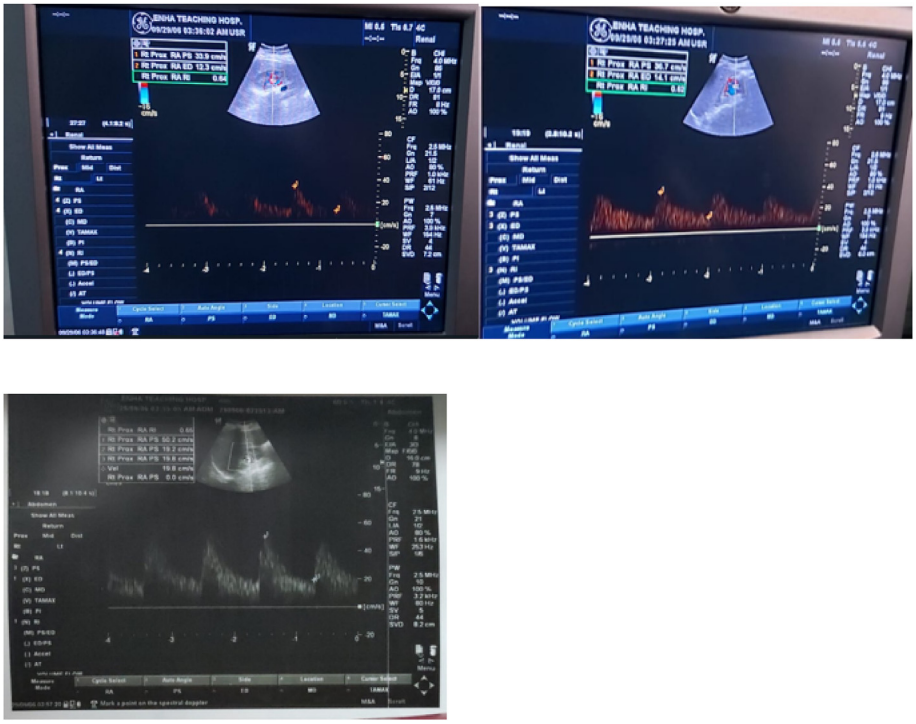

Fig. 1. Ultrasound color Doppler of the right interlobar renal artery of three different cases showed elevated renal resistive index.

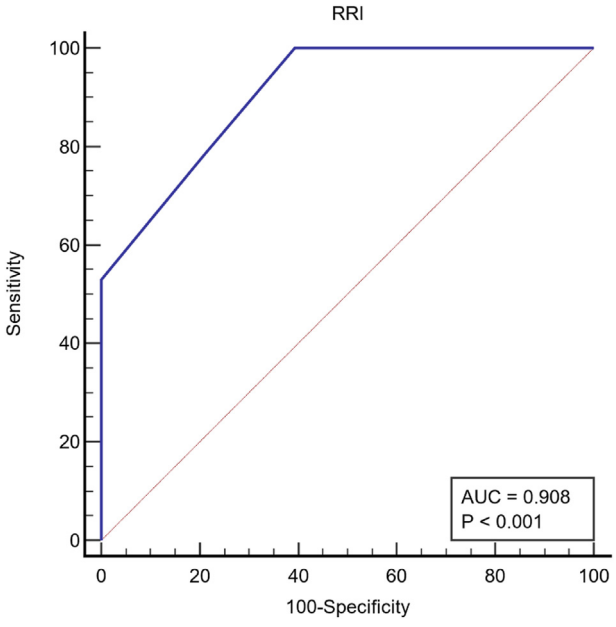

Fig. 2. ROC curve analysis of RRI for prediction of NASH. NASH, nonalcoholic steatohepatitis; ROC, receiver operating characteristic; RRI, renal resistive index.

people. Compared to the simple steatosis and control groups, the NASH group had substantially higher levels of total cholesterol, LDL, and triglyceride, and substantially reduced levels of HDL. These findings are in line with earlier research that found serum HDL cholesterol was lowest in patients with NASH, highest in normal individuals, and followed by simple steatosis patients, while total cholesterol, triglyceride, and LDL cholesterol in NAFLD grow gradually from simple steatosis to NASH [30–32].

In the current research, liver enzymes (ALT, AST, and ALP) were significantly larger in group 1 in contrast to groups 2 and 3 ($P < 0.05$).

Patients with CKD who had NAFLD had noticeably increased serum levels of ALT. IR is the process that leads to the development of NAFLD by activating lipolysis [33]. The hepatocytes are immediately harmed by this increased hepatic fat buildup. Therefore, rather than being the reason for NAFLD, elevated serum ALT levels appear to be a result of NAFLD. Even while serum ALT is commonly used as a substitute measure for NAFLD in clinical practice or epidemiological studies, the application of a high level of ALT alone could potentially overstate the extent of impairment of the liver. This is due to the possibility that notable histological anomalies are connected to either a normal or slightly raised ALT [34].

Frantzides et al. [19] and Puri et al. [30] claimed that NASH patients had higher AST and ALT readings, which were then lower in patients with simple steatosis and least in controls who are normal. Puri et al. [30] indicated that the ALP mean

was lowest in normal controls and greater in NASH patients, NAFLD patients, and so on.

We discovered that group 1 had considerably bigger RRI and NAFLD fibrosis scores than groups 2 and 3 ($P < 0.05$), and group 2 had markedly bigger scores than group 3 ($P < 0.05$).

Since RRI has been linked to parameters in histology such as glomerulosclerosis and tubulointerstitial lesions, it has been thoroughly investigated in connection with numerous renal disorders as a precursor to endothelial dysfunction and arterial stiffness, which may result in serious end-organ damage [20,21].

Mahmoud et al. [28] exhibited that the RRI was substantially greater in the NASH group in contrast to the control group and those with simple steatosis. RRI was greater in NASH individuals who had fibrosis of the liver (mean = 0.74) than in those without fibrosis (mean = 0.65). Catalano et al. [35] claimed that no significant variation in RRI was found between NAFLD patients and healthy controls. Furthermore, no significant variation was noted between NAFLD individuals with normal liver enzyme levels and those with elevated liver enzyme levels.

In terms of the relationship between RRI and other parameters, the NAFLD fibrosis score, age, BMI, serum creatinine, total cholesterol, triglycerides, LDL, ALT, AST, and ALP were all significantly positively correlated with RRI in both groups 1 and 2. RRI significantly correlated negatively with total protein, albumin, and HDL. The relationship between RRI and FBG, BUN, direct, and total bilirubin was not statistically significant.

Mahmoud et al. [28] demonstrated that RRI was significantly positively connected to BMI, age, cholesterol, triglycerides, AST, gamma-glutamyl transferase, ALT, ALP, and liver fibrosis. Conversely, a significant negative relationship was seen between RRI and HDL.

In regular clinical practice, the eGFR is a frequent, easily administered, and practical indication of kidney function and patients' clinical prognosis [36]. The current evidence suggests that there is a strong correlation between decreased eGFR and the existence and/or severity of NAFLD.

Whatever the cardiovascular risk factors, the existence of NAFLD anticipates the onset and course of CKD [8]. Chen et al. [37] demonstrated that eGFR declined greatly in NAFLD patients than in healthy ones. Hsieh et al. [38] found that in NAFLD patients, there was a substantial connection between a larger fibrosis score and a reduced eGFR. Jang et al. [39] determined that patients with a high NAFLD fibrosis score had a greater decline in NAFLD-related eGFR. They added that there was an independent link between NAFLD and the evolution of chronic renal disease. In spite of the risk variables in NAFLD patients, these investigations also showed a favorable correlation between increasing renal disease and histological severity.

We discovered a substantial negative relationship between eGFR and RRI. Aksu et al. [40] observed lower eGFR levels and higher RRI values in NAFLD patients in contrast to the controls. In NAFLD patients, there was a reverse connection between eGFR and RRI.

An earlier study found that increased RRI at ICU admission was an early, marked, independent predictor for the advancement of AKI stages 2–3 over the first week but not for AKI stage 1. Despite the fact that RRI by itself could not discriminate sensitively for the AKI development, high RRI is an early warning indicator when the condition is severe and the fluid balance is positive [41].

Limitations: first, the cross-sectional study design makes it challenging to determine if NASH and CKD are causally related. Second, renal disease was identified and categorized using an eGFR rather than more accurate metrics. For epidemiological research and clinical practice, however, equations that predict GFR are advised when assessing renal function.

4.1. Conclusions

We concluded that NAFLD is associated with higher RRI, NAFLD fibrosis score, FBG, serum creatinine, hazardous lipid profile and liver enzymes, and lower eGFR. A significant connection was found between age, BMI, RRI, serum creatinine, lipid and liver profile, NAFLD fibrosis score, and eGFR.

Institutional review board (IRB) approval number

HB000120.

Ethical information

The Benha Teaching Hospitals Ethical Committee gave approval before the research started the purpose and nature of the study as well as the risks were be explained to the patients or their relatives. The participants first guardians agreed that he/she would have the investigational nature of the study, its inherent risks and benefits.

Confidentiality of data was assured in which Participants' information was replaced with research

identification codes (ID Codes), data collection forms were be anonymous. patients could withdraw from the study at any time and still get the full medical service with in the facility. Patients could refuse to participate and still get the standard and their right to know the research results were ensured.

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Author contributions

Atteyat A. Semeya: wrote paper and collect cases. Hala A.-E. Tabl: radiological examination and measures. Naglaa F. Al-Mihy: Conceived and designed the analysis and help in writing paper.

Conflict of interest

There are no conflicts of interest.

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