Renal Dysfunction in Patients With Nonalcoholic Fatty Liver Disease is Related to the Presence of Diabetes Mellitus and Severity of Liver Disease

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Background and aims: There is sparse data on the prevalence of renal dysfunction in patients with nonalcoholic fatty liver disease (NAFLD). The aim of the present study was to evaluate the presence of renal dysfunction in patients with NAFLD and correlate it with the severity of liver disease. **Methods:** One hundred nonalcoholic patients with ultrasound showing hepatic steatosis were enrolled into the study after exclusion of other causes. Presence of renal dysfunction was estimated by glomerular filtration rate and by evaluating 24 h urinary protein and microalbumin. Various risk factors including components of metabolic syndrome, severity of hepatic steatosis (as assessed on ultrasound), hepatic necro-inflammation (as assessed by hepatic transaminases) and hepatic fibrosis (as assessed by transient elastography) were correlated with the presence of renal dysfunction. **Results:** Twenty eight (28%) patients with NAFLD had evidence of impaired renal function with 5 (5%) having abnormal glomerular filtration rate, 18 (18%) having significant proteinuria and 5 (5%) having both. Presence of type 2 diabetes mellitus, raised hepatic transaminases and advanced fibrosis on transient elastography were found as independent predictors of impaired renal function with raised hepatic transaminases having the best sensitivity (89%) and presence of advanced fibrosis the best specificity (90%). A model comprising of these three parameters had good accuracy (AUROC = 0.763) in predicting impaired renal function in patients with NAFLD. **Conclusions:** Around one-third of patients with NAFLD have impaired renal functions. Prevalence of impaired renal function in patients with NAFLD is dependent on the severity of liver disease and presence of diabetes mellitus. (J CLIN EXP HEPATOL 2019;9:22–28)

Nonalcoholic fatty liver disease (NAFLD) is a spectrum of disorders ranging from hepatic steatosis to nonalcoholic steatohepatitis (NASH), NASH related cirrhosis and hepatocellular carcinoma (HCC).^{1,2} More than a quarter of the general population, both in India and abroad have NAFLD of varying severity with a much higher prevalence in patients with diabetes mellitus and metabolic syndrome.³ In spite of established common features between NAFLD and chronic kidney disease (CKD) including associations with obesity, metabolic syndrome, risk of cardiovascular disease,^{4,5} increasing evidence is now suggesting about the independent relationship between NAFLD and impairment of renal

function.⁶ It has also been proposed that mild kidney function damage (MKFD), which occurs before development of CKD, has an independent relationship with NAFLD.⁷ This is more important in public health care as the adverse effects of CKD can be prevented or delayed if it is detected at the early stage of MKFD and appropriate timely treatment given.⁸ There is also upcoming evidence on the correlation between the severity of NAFLD and degree of impairment of renal functions.⁷ Indian patients of NAFLD are significantly different from their Western counterparts in being less obese, and having lower frequency of diabetes mellitus and metabolic syndrome.^{9,10} Except for a recent negative study in a specialized group of

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Abbreviations: CKD: chronic kidney disease; HCC: hepatocellular carcinoma; NAFLD: nonalcoholic fatty liver disease; NASH: nonalcoholic steatohepatitis

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liver donors,¹¹ data on interrelationship between NAFLD and deranged renal function is missing in Indian patients, in whom, the values of renal function parameters like glomerular filtration rate (GFR) may differ¹² from the Western patients.¹²⁻¹⁵ However the predictors of development of impaired renal function in NAFLD patients is largely unknown. Thus we undertook this study was to find the prevalence of renal dysfunction, to correlate it with the severity of liver disease and to find predictive factors for the presence of impaired renal function among Indian patients with NAFLD.

PATIENTS AND METHODS

Consecutive patients with ultrasonography showing features of hepatic steatosis with normal or raised hepatic transaminases were screened over a period of 18 months (July 2014 to December 2015). Ultrasonography was done either for evaluating raised hepatic transaminases or for dyspeptic symptoms. The approval of the Institution Ethics Committee of the Post Graduate Institute of Medical Education and Research, Chandigarh, India, was obtained prior to the commencement of the study. Patients with frank cirrhosis on ultrasound or with high liver stiffness measurement (LSM) ≥ 13 kPa, patients with history of decompensation of liver disease in the past, pregnant females and those with alternate etiology for liver disease were excluded from the study ($n = 23$). A signed informed consent was obtained from all patients included in the study. All included patients were nonalcoholic, had negative viral markers (HBsAg, anti HCV), negative autoimmune hepatitis markers, negative serology for celiac disease and had normal serum ceruloplasmin and normal iron work up. All subjects were subjected to a detailed anthropometric examination and overweight, obesity, central obesity were defined as per the Asia Pacific Guidelines.¹⁶

Subjects were considered hypertensive if currently receiving antihypertensive medication or else if the blood pressure was consistently $\geq 130/85$ mm Hg and diabetic if they were already on any treatment for diabetes mellitus or fasting blood sugar was ≥ 110 mg/dl or HbA1c $\geq 6.5\%$.

Blood samples were taken from each subject after an overnight fast and hemogram, liver function tests, coagulogram, fasting blood sugar, fasting plasma insulin, and lipid profile were done. Fasting serum insulin was measured and insulin resistance was calculated using the validated homeostasis model assessment (HOMA-IR) method.¹⁷ An absolute value of HOMA-IR >1.64 was taken as abnormal.¹⁸ Metabolic syndrome was defined as per the National Cholesterol Education Program – Adult treatment panel III criteria¹⁹ with waist circumference modified as per the Asia Pacific criteria.¹⁶ A waist circumference ≥ 90 cm in men and ≥ 85 cm in women were hence considered abnormal. All patients were

subjected to an ultrasound examination of abdomen and hepatic steatosis was graded into mild, moderate and severe steatosis.²⁰ All patients also underwent LSM using transient elastography by Fibroscan machine (Echosens, Paris, France) and LSM of >7 kPa was graded as significant fibrosis ($\geq$ F2 METAVIR stage) and >8.7 kPa as advanced fibrosis ($\geq$ F3).²¹ Patients with LSM ≥ 13 kPa were considered to have overt cirrhosis liver and were excluded from the study. Renal function was assessed in all patients and GFR was calculated using Cockcroft-Gault formula.²² All patients were quantified for their 24 hour urine protein excretion using ALBU-I kit on COBAS INTEGRATM 400 plus systems from Roche Diagnostics[®]. Overt proteinuria was defined as excretion of greater than 500 mg protein/day. Those without overt proteinuria were screened for the presence of microalbuminuria by ELISA technique (reagents from Randox laboratories, Hitachi[®] 917/ModP analyzer). Micro-albuminuria was defined as 24 h urine albumin excretion between 30 and 300 mg/day. Significant proteinuria was defined as presence of overt proteinuria or microalbuminuria. Impaired renal function was defined as GFR less than 80 ml/min/1.73 m² (US National Kidney foundation guidelines with adjustments for Indian average values)^{12,14,15} and/or presence of significant proteinuria. MKFD was defined as eGFR between 60–79 ml/min/1.83 m² and/or significant proteinuria.⁸

Age, gender, weight, BMI, waist circumference, waist hip ratio, components of metabolic syndrome, presence of metabolic syndrome, fasting insulin, HOMA-IR, insulin resistance, fasting blood sugar and serum creatinine were studied as the predictors of impaired renal function in patients with NAFLD. Severity of liver disease as assessed by degree of hepatic steatosis on ultrasonography, hepatic necro-inflammation as assessed by elevated serum transaminases and presence and degree of hepatic fibrosis as measured by transient elastography were also correlated with the presence of renal dysfunction.

SPSS v.20 software was used for the analysis and generation of results. Continuous variables were expressed as mean $\pm$ SD. Categorical variables were expressed as proportions (percentages) and groups were compared using Chi-square or Fischers exact test. For comparison of continuous variables *t*-test and Mann-Whitney test was applied for parametric and non-parametric variables respectively. Significance was set at $P < 0.05$ for all tests. Predictors of impaired renal function were determined using binary logistic regression analysis to adjust for potential confounders and the odds ratio (OR) with 95% confidence interval (CI) of effect of each predictor was calculated.

RESULTS

One hundred and twenty-three consecutive adults with hepatic steatosis (M:F = 70:53, mean age 42 ± 11 years)

were screened for inclusion. Of these 14 patients with frank cirrhosis on transient elastography, 8 patients' positive for either HBsAg or anti HCV and 1 patient who was pregnant, were excluded. Finally, one hundred patients with NAFLD (56 males, mean age of 42 ± 11 years and body mass index (BMI) of 27.7 ± 4.2 kg/m²) meeting the inclusion criteria were included. Thirteen patients (13%) had normal BMI and eighty seven (87%) patients were either overweight (BMI 23–25 kg/m²) ($n = 17$) or obese (BMI >25–30 kg/m²) ($n = 41$) or severely obese (BMI >30 kg/m²) ($n = 29$). Forty eight patients (48%) had metabolic syndrome (≥ 3 out of the 5 components) as per the modified ATP III criteria²³ with abdominal obesity, hypertension, diabetes mellitus, low serum HDL and high serum triglycerides present in 86%, 26%, 20%, 59% and 56% of patients respectively. At least one component of metabolic syndrome was present in 96 (96%) patients with only four (4%) patients having no components of metabolic syndrome. Insulin resistance (HOMA-IR ≥ 1.64) was present in 60 (60%) patients.

Raised transaminases [either AST or ALT] were present in 68 (68%) of the NAFLD patients (median AST 40 (27–59) IU/L and median ALT 66 (38–99) IU/L). Thirty five patients had mild steatosis (35%), 52 (52%) had moderate steatosis and 13 (13%) patients had severe steatosis as assessed on ultrasound. Severity of hepatic fibrosis by transient elastography (Fibroscan), was assessed in all patients ($n = 94$; 6 patients had invalid readings). There was no fibrosis (LSM ≤ 5.7 kPa) in 39 (41%) patients, significant fibrosis (LSM > 7 kPa) in 33 (35%) patients and advanced fibrosis in 22 (23%) patients. Demographic, anthropometric, biochemical, metabolic and imaging details of all patients are shown in Table 1.

Prevalence of Impaired Renal Function in Patients With NAFLD

Twenty-eight (28%) patients with NAFLD were found to have impaired renal function in our study. Isolated abnormal GFR of <80 ml/min/1.73 m² was present in only 5 (5%) patients and all of them had eGFR between 60 and 79 ml/min/1.73 m². Isolated significant proteinuria (overt proteinuria/microalbuminuria) was present in 18 (18%) patients. 5 (5%) patients had both significant proteinuria and abnormal GFR of which 3 had GFR less than 60 ml/min/1.73 m². Hence, 10 (10%) patients had abnormal GFR, of which 7 (7%) had GFR between 60 and 79 ml/min/1.73 m² and 3 (3%) had GFR less than 60 ml/min/1.73 m². Significant proteinuria (overt proteinuria/microalbuminuria) was present in 23 (23%) patients. Overt proteinuria was present in 4 (4%) patients and microalbuminuria was present in rest 19 (19%) patients (Table 2). MKFD was present in 25 (25%) patients.

Table 1 Demographic Characteristics, Anthropometry, Metabolic and Imaging Parameters in 100 Patients With NAFLD.

<i>n</i> = 100	
Mean age (yrs)	42 $\pm$ 11
Male <i>n</i> (%)	56 (56)
Mean weight (kg)	73 $\pm$ 11
Mean BMI (kg/m ²)	27.7 $\pm$ 4.2
Abnormal BMI <i>n</i> (%)	87 (87%)
Overweight <i>n</i> (%)	17 (17%)
Obese <i>n</i> (%)	41 (41%)
Severely obese <i>n</i> (%)	29 (29%)
Mean waist circumference (cm)	96.5 $\pm$ 8.4
Abnormal waist circumference <i>n</i> (%)	86 (86)
Hypertension <i>n</i> (%)	26 (26)
Mean fasting blood sugar (mg/dl)	105 $\pm$ 20
Type 2 diabetes mellitus <i>n</i> (%)	20 (20)
Median fasting insulin (mU/L) ^a	9.0 (4.4–13.4)
Median HOMA-IR ^a	2.27 (1.13–3.54)
Abnormal HOMA-IR <i>n</i> (%)	60 (60)
Mean triglyceride (mg/dl)	160 $\pm$ 57
Hypertriglyceridemia <i>n</i> (%)	56 (56)
Mean HDL (mg/dl)	43 $\pm$ 11
Low HDL <i>n</i> (%)	59 (59)
Metabolic syndrome <i>n</i> (%)	48 (48%)
Median AST (IU/L) ^a	40 (27–59)
Median ALT (IU/L) ^a	66 (38–99)
Raised transaminases <i>n</i> (%)	68 (68%)
Steatosis on ultrasound	
Mild <i>n</i> (%)	35 (35%)
Moderate <i>n</i> (%)	52 (52%)
Severe <i>n</i> (%)	13 (13%)
Median liver stiffness measurement (kPa) ^a	6.1 (5.0–8.6)
Fibrosis on transient elastography^b	
No fibrosis (LSM ≤ 5.7 kPa) <i>n</i> (%)	39 (41%)
Significant ($\geq F2$; LSM > 7 kPa) <i>n</i> (%)	33 (35%)
Advanced ($\geq F3$; LSM > 8.7 kPa) <i>n</i> (%)	22 (23%)

^aData presented as median (interquartile range). All other data presented as mean $\pm$ SD or *n* (%).

^bValid readings in 94 patients.

ALT: alanine aminotransferase; AST: aspartate aminotransferase; BMI: body mass index; HDL: high density lipoprotein; HOMA-IR: homeostasis model assessment for insulin resistance; LDL: low density lipoprotein.

Comparison of Patients of NAFLD With and Without Impaired Renal Function

Comparison of demographic characteristics, anthropometry, metabolic and imaging parameters were done between patients of NAFLD with ($n = 28$) and without

Table 2 Prevalence of Impaired Renal Function, eGFR and Microalbuminuria in 100 Patients With NAFLD.

	<i>n</i> (%)
Impaired renal function present	28 (28%)
GFR <i>n</i> (%)	
GFR ≥ 80 ml/min/1.73 m ² (normal)	90 (90%)
GFR 60–79.9 ml/min/1.73 m ²	7 (7%)
GFR < 60 ml/min/1.73 m ²	3 (3%)
Proteinuria	23 (23%)
Overt proteinuria <i>n</i> (%)	4 (4%)
Microalbuminuria <i>n</i> (%)	19 (19%)

Data presented as *n* (%). GFR: glomerular filtration rate.

(*n* = 72) impaired renal function. Patients of NAFLD with impaired renal function had statistically significant higher mean age, higher mean BMI, fasting blood sugar, and serum creatinine than NAFLD patients without impaired renal function. Proportion of patients with diabetes mellitus, metabolic syndrome and insulin resistance were also significantly higher in NAFLD patients with impaired renal function. Comparison of demographic characteristics, anthropometry and metabolic parameters between patients of NAFLD with and without Impaired renal function is given in Table 1 in Supplementary material. Proportion of patients with raised transaminases was significantly higher in the impaired renal function group as were the median AST and ALT levels (Table 3). Even though there was no significant difference in the prevalence of mild and moderate hepatic steatosis in patients with NAFLD with and without impaired renal function, there were more patients with severe steatosis in the

impaired renal function group. Higher proportion of patients in the impaired renal function group had significant fibrosis (Median LSM >7 kPa) and advanced fibrosis (Median LSM >8.7 kPa) in comparison to patients with normal renal function. Absolute value of liver stiffness measurement was also significantly higher in patients with impaired renal function.

Predictors of Impaired Renal Function in Patients With NAFLD

On univariate analysis, age, BMI, presence of severe obesity, metabolic syndrome, presence of insulin resistance, serum creatinine, presence of raised transaminases, higher AST & ALT values, higher LSM on transient elastography, presence of significant and advanced fibrosis on transient elastography and severe steatosis on ultrasound were found to be predictors of impaired renal function in patients with NAFLD. Results of univariate analysis are given in Table 2 in Supplementary material. On multivariate analysis, presence of type 2 diabetes mellitus, raised hepatic transaminases and advanced fibrosis on transient elastography were found to be the independent predictors of impaired renal function in patients with NAFLD (Table 4). The sensitivity, specificity positive predictive value, negative predictive value and diagnostic accuracy of these factors were also calculated. Advanced fibrosis on transient elastography had the best diagnostic accuracy and specificity (diagnostic accuracy – 81%, sensitivity – 58%, specificity – 90%) in predicting impaired renal function in patients with NAFLD followed by presence of Type 2 diabetes mellitus (diagnostic accuracy – 76%, sensitivity – 43%, specificity – 89%), while presence of raised hepatic transaminases had the best sensitivity (diagnostic

Table 3 Comparison of Severity of Liver Disease (Hepatic Steatosis, Hepatic Transaminases and Hepatic Fibrosis) Amongst Patients With and Without Impaired Renal Function.

	NAFLD with impaired renal function (<i>n</i> = 28)	NAFLD without impaired renal function (<i>n</i> = 72)	<i>P</i> value
Median AST (IU/L) ^a	51 (35–73)	35 (25–56)	.008
Median ALT (IU/L) ^a	75 (62–116)	53 (35–96)	.014
Raised transaminases <i>n</i> (%)	25 (89)	43 (60)	.04
Steatosis on ultrasound			
Mild <i>n</i> (%)	5 (18)	30 (42)	.45
Moderate <i>n</i> (%)	12 (43)	40 (56)	.74
Severe <i>n</i> (%)	11 (39)	2 (3)	.00
Median liver stiffness measurement (kPa) ^a	8.7 (5.7–9.3)	5.7 (4.8–7.1)	.00
Fibrosis on transient elastography ^b			
Significant ($\geq F2$) <i>n</i> (%)	17 (65)	16 (24)	.00
Advanced ($\geq F3$) <i>n</i> (%)	9 (35)	52 (77)	.00

^aData presented as median (interquartile range). All other data presented as mean $\pm$ SD or *n* (%).

^bValid readings in 94 patients of NAFLD.

ALT: alanine aminotransferase; AST: aspartate aminotransferase.

Table 4 Significant Predictors of Impaired Renal Function in Patients With NAFLD on Multivariate Analysis.

Characteristic	Adjusted OR (95%CI)	P value
Diabetes mellitus	5.72 (1.4–23.8)	.016
Advanced fibrosis	5.19 (1.42–19.0)	.013
Presence of raised hepatic enzymes	5.55 (1.006–31.25)	.05

accuracy – 54%, sensitivity – 89%, specificity – 40%) (Supplementary material Table 3). Area under the receiver operating curves (AUROC) was drawn to know the diagnostic accuracy of a model comprising of these three significant parameters (type 2 diabetes mellitus, raised hepatic transaminases and advanced fibrosis), in predicting impaired renal function in patients with NAFLD (Figure 1). Overall this model had significant accuracy in predicting impaired renal function in patients with NAFLD with an area under receiver operating curve (AUROC) of 0.763 (Table 5).

DISCUSSION

This is the first study from India to report the prevalence and predictors of impaired renal function in patients with NAFLD. We found that 28% of patients with NAFLD had impaired renal function, with severity of liver disease (raised hepatic transaminases and advanced fibrosis)

and presence of type 2 diabetes mellitus being predictors for the presence of impaired renal function.

Even though our patients lacked histological diagnosis, taking hepatic fibrosis (as assessed on Fibroscan) as a surrogate marker for severe liver disease, our results suggest that at least 35% (significant + advanced fibrosis on Fibroscan) of our patients could have NASH. This is similar to the histological prevalence of NASH in liver biopsy proven patients of NAFLD from India.^{24,25} Even though hepatic transaminases do not have good correlation with liver histology in patients with NAFLD, elevated hepatic transaminases in our patients could be taken as indirect marker of hepatic necro-inflammation. Since both hepatic transaminases and advanced fibrosis were found as independent predictors of renal dysfunction, our results indirectly may suggest that the severity of liver disease or histological NASH could determine the renal dysfunction patients with NAFLD. Raised ALT and hepatic fibrosis on Fibroscan have the advantage of being the non-invasive modalities and could be used as the screening tool for predicting renal dysfunction in patients with NAFLD.

In addition to raised transaminases and advanced fibrosis, we also found presence of type 2 diabetes mellitus as a significant predictor of impaired renal function in patients with NAFLD.

Presence of type 2 diabetes mellitus is an important risk factor for development of impaired renal function in the general population.^{26,27} However there are only few studies which have studied the causative role of presence of type 2 diabetes mellitus in causing impaired renal function in patients with NAFLD. Studies from Asian population have found significant association of presence of type 2 diabetes mellitus and impaired renal function in patients with NAFLD.^{28,29} Musso et al.³⁰ in their meta analysis of correlation between impaired renal function and NAFLD found no association between presence of type 2 diabetes mellitus and impaired renal function in patients with NAFLD. This meta-analysis comprised of predominantly data from studies done on the Western population and thus cannot be considered representative of the Asian population. Our data and available Asian data show that in the Asian population, type 2 diabetes mellitus is a significant predictor of renal dysfunction in patients with NAFLD.

Even though there is paucity of data from the Indian sub continent, multiple hospital-based, as well as community based cross sectional studies from the West have evaluated the prevalence of renal dysfunction in NAFLD patients and have obtained prevalence percentages ranging from 14% to 47%.^{29,31–34} The only available study from Indian subcontinent suggested no increase in prevalence in chronic kidney disease in patients of nonalcoholic fatty liver.¹¹ However this study is limited to a group of liver donors with histological evidence of fatty liver without

Figure 1 Receiver operating curve of a model comprising of type 2 diabetes mellitus, raised transaminases, and advanced fibrosis in predicting impaired renal function in patients with NAFLD.

Table 5 Sensitivity Specificity and Diagnostic Accuracy of Significant Parameters in Predicting Impaired Renal Function in Patients With NAFLD.

Characteristic	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Diagnostic accuracy (%)
Type 2 diabetes mellitus	43	89	60	80	76
Raised transaminases	89	40	37	91	54
Advanced fibrosis	58	90	68	85	81

PPV: positive predictive value; NPV: negative predictive value.

inflammation or fibrosis. A prospective study amongst Asian population by Chang et al.⁶ found that NAFLD was associated with the development of impaired renal function with relative risk 2.18 (95% confidence interval [CI], 1.75–2.71). The risk of renal dysfunction in NAFLD was irrespective of the risk factors of metabolic syndrome. Thus they concluded that NAFLD was associated with an increased risk of renal dysfunction irrespective of presence or absence of metabolic syndrome or its components. Available longitudinal studies have also connected NAFLD with renal dysfunction and have obtained incidence of renal dysfunction (after average 10 year follow up) ranging from 9 to 31%.^{35–37}

We applied a different cut off of GFR (<80 ml/min/1.73 m²) as applicable to Indian patients based on multiple studies which showed that healthy Indian subjects had a much lesser GFR when compared to the Western population.^{12–14} If we apply the eGFR cutoff of <60 ml/min/1.73 m² and/or significant proteinuria as definition of renal dysfunction in our study, the prevalence would be 23%. The importance of keeping a higher cut off was to detect more cases of MKFD which was defined as eGFR between 60 and 79 ml/min/1.83 m² and/or significant proteinuria. MKFD, according to the National Kidney Foundation practice guidelines, occurs early before CKD appearance, and the adverse outcomes of CKD may be prevented or delayed if MKFD can be detected and treated on time.⁸ The prevalence of MKFD in our study is 25%. We could only find one previous study which defined impaired renal function in patients with NAFLD using a higher cutoff for eGFR (less than 90 ml/min).⁷ Multivariate-adjusted odds ratio in this study illustrated that, compared to subjects with normal liver, NAFLD subjects had a significantly higher risk of MKFD with or without adjusted for blood glucose and other covariates ($P = 0.041$). Further results from multi-interaction analysis demonstrated that the underlying mechanisms that linked NAFLD with impaired kidney were common risk factors and similar pathological processes.

A major limitation of our study was that the diagnosis of NAFLD in our patients was based on the presence of hepatic steatosis on USG with exclusion of other causes of hepatic steatosis and raised transaminases, rather than the histological diagnosis of NAFLD on liver biopsy. In the absence of liver biopsy, presence of significant fibrosis and

the severity of liver disease was evaluated by transient elastography which is now an established modality in patients with NAFLD, although it does not take into account severity of lobular inflammation, ballooning degeneration, and degree of steatosis which are other markers of NASH. Although our patients lacked a histological diagnosis of NASH, which is the severe form of NAFLD, surrogate markers for NASH like advanced fibrosis by transient elastography and presence of raised transaminases were evaluated in all patients.

In conclusion our study observed a significant prevalence of impaired renal function in patients with NAFLD. Presence of impaired renal function in patients with NAFLD was predicted by presence of diabetes mellitus, raised hepatic transaminases and presence of advanced fibrosis with raised enzymes having the best sensitivity and presence of severe fibrosis having the best specificity in predicting renal dysfunction. For the timely therapeutic intervention, it may be prudent to screen patients with NAFLD with raised liver enzymes and advanced fibrosis on Fibroscan for the presence of renal dysfunction.

CONFLICTS OF INTEREST

The authors have none to declare.

APPENDIX A SUPPLEMENTARY DATA

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.jceh.2017.12.005.

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