African Journal
of Gastroenterology &

Assessment of Chronic Kidney Disease in Patients with Non-Alcoholic Fatty Liver Disease (NAFLD); A Single Center Experience

Mona Mohammed Abdelrahman[1]*, Shimaa Badawy Hemdan[2], Mohamed Ezeldin [3], Osama Abbas Orabi [4], Shimaa Anwar Rashed[5], Ahmed Nagah Nour Eldin [4]

1. Lecturer of Tropical Medicine and Gastroenterology Department, Faculty of Medicine, Sohag University, Egypt. ORCID: 0000-0002-8784-848X

2. Lecturer of Medical Biochemistry Department, Faculty of Medicine, Sohag University, Egypt.

3. Lecturer of Diagnostic and Interventional Radiology Department, Faculty of Medicine, Sohag University, Egypt. ORCID: 0000-0001-5613-1729.

4. Lecturer of Internal Medicine Department, Faculty of Medicine, Sohag University, Egypt.

5. Clinical and Chemical Pathology Department, Faculty of Medicine, Sohag University, Egypt.

***Corresponding author:** Mona Mohammed Abdelrahman, Tropical medicine and Gastroenterology Department, Faculty of Medicine, Sohag University, Egypt. Postal code: 82524. Telephone: 00201021025895, Email: monamohamed@med.sohag.edu.eg. ORCID: 0000-0002-8784-848X.

- **Running title**: chronic kidney disease in NAFLD.

Original research

Abstract:

Background:

Non-alcoholic fatty liver disease (NAFLD) represents a considerable percentage of chronic liver diseases worldwide. The liver is not the only organ affected by NAFLD but also affects other organs such as the cardiovascular system and the kidney. In recent decades, there has been a growing body of evidence linking NAFLD to kidney function. So, the current study aims to assess the percentage of chronic kidney disease (CKD) in NAFLD patients and its link to different stages of hepatic fibrosis.

Patients and Methods: A case-control study evaluated 62 non-alcoholic fatty liver disease patients and a control group of 38 volunteers with apparently healthy livers (normal echo pattern by ultrasound). All participants underwent serum creatinine measurement, albumin creatinine ratio in urine, calculation of estimated glomerular filtration rate (eGFR), abdominal ultrasound, and fibroScan examination.

Results: The authors showed that the percentage of patients with chronic kidney diseases (patients with GFR less than 60 ml or micro-albuminuria) were significantly higher among NAFLD groups than in healthy controls. There was a significant positive correlation between the albumin creatinine ratio and subcutaneous fat thickness, BMI, and steatosis degrees. The estimated glomerular filtration rate (eGFR) and the age of the patients had a significant negative correlation. In comparison, the eGFR and AST levels had a significant positive correlation.

Conclusions: Our results showed that NAFLD substantially raises the risk of getting CKD.

Keywords: Non-alcoholic fatty liver disease, NAFLD, Estimated glomerular filtration rate, Microalbuminuria. Hepatic fibrosis, Hepatic steatosis, Chronic kidney disease, CKD, fibroscan, Albumin-creatinine ratio.

Introduction:

One of the most frequent triggering factors of chronic liver disorder worldwide is non-alcoholic fatty liver disease (NAFLD) (1). NAFLD is characterized by excessive fat deposition (>5%) in the hepatocytes in the absence of alcohol consumption or other reasons for liver illness, such as autoimmune, drug-induced, or viral hepatitis(2). NAFLD has a wide histologic variety, including simple steatosis, non-alcoholic steatohepatitis (NASH), liver fibrosis, and cirrhosis (2). In Western countries, NAFLD has been found in up to 30% of the general public, particularly in individuals with metabolic syndrome(3,4). In addition, NAFLD is considered an independent risk factor for cardiovascular disease, and there is growing evidence that it plays a causal role in chronic renal disease evolution (CKD)(5).

 Moreover, CKD is a significant health concern in the Western population, affecting more than a quarter of those over 65 (6). CKD is known as reduced estimated glomerular filtration (eGFR) or the occurrence of significant proteinuria (>500 mg)(7). Nearly half a million persons in the United States currently get renal dialysis treatment, which is predicted to rise to 2.2 million by 2030(8).

 In recent decades, there has been a growing body of evidence linking NAFLD to kidney function. Many researchers have confirmed that NAFLD, which can be detected by ultrasonography, liver

Original research

enzymes, or biopsy, is linked to an elevated risk of CKD(9). Moreover, NAFLD, particularly with higher gamma-glutamyl transferase concentrations, appears to contribute to the development of CKD in several prospective investigations; according to the National Kidney Foundation Practice Guidelines, mild kidney function impairment occurs before CKD appears. The unfavorable adverse effects of CKD may be averted or postponed if MKFD can be recognized and treated in time(11). So, this study aims to assess the percentage of chronic kidney disease in NAFLD patients and whether there is a risk between hepatic fibrosis and CKD.

Methodology:

A case-control study evaluated 62 non-alcoholic fatty liver diseases patients (23 men, 39 women) presented to the Tropical Medicine and Gastroenterology outpatient clinic of Sohag University Hospitals and a control group of 38 volunteers (11 men, 27 women) with apparently healthy liver (normal echo-pattern by ultrasound) from February 2021 to July 2021. On abdominal ultrasound examination, patients showing bright echo patterns of the liver were included in the study. Patients with diabetes Mellitus, hypertension, thyroid disorders, chronic kidney disorders, chronic liver disorders rather than NAFLD, and patients with a history of intake of alcohol, statins, nephrotoxic drugs such as NSAIDs and antibiotics, and steroids were excluded from the study. After approval of the study protocol, informed written consent was taken from patients and volunteers. All included patients were subjected to the following:

1. Comprehensive medical history and physical assessment.
2. Body mass BMI was estimated (BMI (kg/m^2) = weight in kilograms / (height in meters)^2).
3. Waist circumference measurement: assessed horizontally at the level of the umbilicus.
4. **Laboratory investigations: after overnight fasting,10 ml of blood was taken and examined for**
   - Fasting blood sugar
   - Serum lipogram.
   - Liver function tests.
   - Serum creatinine

5. **Spot albumin creatinine ratio test (ACR):** The clean catch method obtained a random urine sample. Albumin in urine was measured by immunoturbidimetry using a Chromatest kit, and creatinine was measured by Jaffe's reaction using a Spin React kit. Both were analyzed by Photometer 5010. The Spot **ACR** was calculated by mg/dl. Normal adult reference range up to 30ug Alb/mg creatinine.
6. **Calculation of estimated Glomerular Filtration Rate (eGFR) according to** Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) (12)**.**
7. **Abdominal ultrasound examination:** to evaluate the echogenicity of the liver and to measure the subcutaneous and preperitoneal fat (13).

   A-Subcutaneous fat (S) – using the linear Probe in a longitudinal plane, measure the line from the skin to the linea alba on the mid-sternal line, 1 cm above the umbilicus.
   B) Preperitoneal fat (P) – extends from the anterior surface of the left lobe of the liver to the posterior surface of the linea alba.

African Journal
of Gastroenterology &

8. **Assessment of the degree of hepatic fibrosis and steatosis using FibroScan:**

After overnight fasting, all patients were examined by FibroScan® Mini+ 530 (M probe and the XL probe, Paris, France) to evaluate hepatic stiffness (fibrosis) and Controlled Attenuation Parameter (CAP) (hepatic steatosis). The patient lay in the left lateral position, and ten valid values of liver stiffness measurements and CAP were taken and evaluated in kilopascals (Kpa) and decibels/meter (dB/m). Then their median value was taken into consideration only if the interquartile range to median ratio was less than 30% (14). According to the median value, the grades of fibrosis were classified into F0 (0-5.4), F1 (5.5-6.9), F2 (7-7.9), F2-3(8-8.9), F3 (9-10.4), F3-4(10.5-11.4) and F4 (11.5-75). In contrast, steatosis grades were classified into S1 (222-242), S1-2 (243-258), S2 (259-300), S2-3 (301-310), and S3 (311-350)(15).

Statistical Analysis:

Data were analyzed using SPSS version 16 (**SPSS Inc., Chicago, USA**). Quantitative data were represented as mean, standard deviation, median, and range. When the data were not normally distributed, *Kruskal Wallis* test for comparison of three or more groups. Qualitative data were presented as numbers and percentages. The *Chi-square* test was used for the comparison of rates in different groups. *Spearman's correlation* test was used to find a correlation between data. *Graphs* were produced by using the Excel program and SPSS program.

Results:

The authors conducted a case-control study on 62 non-alcoholic fatty liver disease patients (23 men,39 women). They had a mean age of 44.7 and ranged from 26 to 65 years. The control group included 38 volunteers (11 men, 27 women) with apparently healthy livers (normal echo pattern by ultrasound). Their mean age was 44.4 years, ranging from 22 to 70 years. There was no significant difference between NAFLD cases and healthy control as regards age and sex (P-value=0.9, 0.4 respectively).

After fibro-scan examination, we detected those 35 patients (56%) had no hepatic fibrosis (F0), while 14 patients (23%) had mild to moderate degree of fibrosis (F1-2), and 13 patients (21%) had advanced liver fibrosis (F3-4) **(Fig 1)**.

Regarding steatosis, 28 patients (45%) had a marked degree of steatosis (S3), 25 patients (40%) had a moderate degree of steatosis (S2), and nine patients (15%) had a mild degree of steatosis (S1) **(Fig 2)**.

By abdominal ultrasound examination, we found that the size of the liver and spleen and the thickness of subcutaneous and preperitoneal fat were significantly larger among NAFLD patients than in the control group. Also, there was a significant increase in serum triglycerides, serum HDL, serum VLDL, fasting blood sugar, and serum creatinine among groups of NAFLD patients than the control group. The glomerular filtration rate was significantly lower in patients with NAFLD than in healthy control **(Tab 1,2).** The occurrence of microalbuminuria was considerably higher in NAFLD patients than in healthy control **(Tab 1).**

When evaluating stages of CKD according to e GFR, stage 1 (patients with GFR more than 90 mL/min/1.73 m2) included 44 patients (65.7%), stage 2(patients with GFR from 60:89

Original research

mL/min/1.73 m2) included 20 patients (29.3%), and stage 3a (patients with GFR 45:59 mL/min/1.73 m2) included three patients (4.5%).

The percentage of patients with chronic kidney diseases (patients with GFR less than 60 ml or micro-albuminuria) were significantly higher among NAFLD groups than in healthy controls **(Tab 3).**

Albumin creatinine ratio had a significant positive correlation with the subcutaneous fat thickness (r= 0.3, P = 0.03) **(Fig 3)**, BMI (r= 0.3, P = 0.03) **(Fig 4),** and steatosis degrees (r= 0.3, P = 0.007) **(Fig 5)**. On the other hand, the estimated glomerular filtration rate and the age of the patients had a significant negative correlation (r= - 0.3, P = 0.04) **(Fig 6).** Conversely, the estimated glomerular filtration rate and the AST level had a significant positive correlation (r= 0.4, P = 0.000) **(Fig 7).**

Table 1. Clinical and laboratory characteristics of all NAFLD patients and healthy control.

Clinical &d laboratory variables	NAFLD Patients N=62	Control Group N=38	P-value
Age (years), mean±SD	45±10.5	44.4±14.7	0.9
Male, n% Female, n%	23 (37%)/39(63%)	11 (29%)/17(71%)	0.4
BMI (Kg/m2), mean±SD	33.7±6.2	31.5±5.8	0.06
ALT (IU/L), median(IQR))	20 (17-28)	17.5(10.7-21.2)	0.007
AST(IU/L), median(IQR)	22(17.8-30.5)	17 (13-20)	0.000
Albumin(g/dl), mean±SD	4.2±0.4	4.3±0.4	0.4
Total bilirubin (mg/dl), median((IQR)	0.7±0.3	0.6±0.2	0.03
Triglycerides (mg/dl), median(IQR)	145(115-205)	111(71-165)	0.000
Total cholesterol (mg/dl), mean±SD	203±45	193±48.8	0.03
LDL (mg/dl), mean±SD	128±49.9	119.8±39.8	0.6
HDL (mg/dl), mean±SD	39±6	41±3.4	0.06
VLDL (mg/dl), median(IQR)	30(23.8-40.5)	22(12-33)	0.000
Fasting blood sugar (mg/dl), mean±SD	93.6±14.7	78.5±8.8	0.000
Creatinine(mg/dl), mean±SD	0.84±0.18	0.72±0.17	0.000
eGFR (mL/min/1.73 m2), mean±SD	119.7±36.6	117.7±37	0.003
Presence of microalbuminuria (N%)	10 (16%)	0 (0%)	0.003

IQR: interquartile range

Original research

Table 2. Clinical and laboratory characteristics of NAFLD and control groups.

Clinical and laboratory variables	NAFLD Patients N=62			Control Group N=38	P-value
	No fibrosis(F0) N=35	Mild to moderate fibrosis (F1-2) N=14	Advanced fibrosis and cirrhosis (F3-4) N=13		
Age (years), mean±SD	44.7±10	42.4±9.4	47.2±12.7	44.4±14.7	0.8
Male,n% Female, n%	12 (34.3%) 23 (75.7%)	8 (57.2%) 6(42.8%)	3 (23%) 10 (77%)	11 (29%) 17(71%)	0.2
BMI (Kg/m2), mean±SD	32.9±4.7	33.5±6.5	36.6±8.5	31.5±5.8	0.07
Waist circumference (cm), mean±SD	107±11.3	110±13.6	110±25.4	94±12.3	0.000
Abdominal ultrasound measurement, mean±SD					
Liver size (cm)	16±1.5	17±2	16±2	14±1.8	0.000
Spleen size (cm)	11.9±1.6	12.4±2	12±2	9.5±1.5	0.000
Subcutaneous fat thickness (mm)	17±4.8	15±8.3	18±4.3	12±3.6	0.000
Preperitoneal fat thickness (mm)	12±3.4	13±4.3	15±4.2	10.4±3.8	0.002
Steatosis (Fibroscan), mean±SD	221±8.3	224±8.3	257±5.6	-------	0.4
ALT (IU/L), median(IQR)	20 (7-94)	22 (12-43)	18 (11-69)	17.5 (10.7-21.2)	0.04
AST(IU/L), median(IQR)	22 (13-79)	19 (11-30)	22 (15-41)	17 (13-20)	0.000
Albumin(g/dl), mean±SD	4.2±0.4	4.2±0.3	4.3±0.4	4.3±0.4	0.8
Total bilirubin (mg/dl), median(IQR)	0.7 (0.3-1.6)	0.8 (0.2-1.5)	0.8 (0.3-1.1)	0.6 (0.3-1.2)	0.2
Triglycerides (mg/dl), median(IQR)	140 (70-450)	225 (70-395)	150 (77-233)	111 (71-165)	0.000
Total cholesterol (mg/dl), mean±SD	200.1±41.4	197.2±50.9	214.5±48	193±48.8	0.06
LDL (mg/dl), mean±SD	128.9±41.6	117±51.2	139±56	119.8±39.8	0.5
HDL (mg/dl), mean±SD	39.5±5.9	35.6±7.5	41.2±3	41±3.4	0.006
VLDL (mg/dl), median(IQR)	28 (14-90)	41 (14-79)	30 (8-44)	22 (12-33)	0.000
Fasting blood sugar (mg/dl), mean±SD	91.9±15.6	92.5±8.3	99.2±16.5	78.5±8.8	0.000
Creatinine(mg/dl), mean±SD	0.8±0.17	0.95±0.15	78±0.18	0.72±0.17	0.000
eGFR (mL/min/1.73 m2), mean±SD	101±26.9	89.7±20	107.5±39.7	117.7±37	0.03

IQR: interquartile range

Original research

Table 3. Percentage of chronic kidney diseases among NAFLD patients and control group

Percentage of chronic kidney diseases	NAFLD Patients N=62			Control Group N=38	P-value
	No fibrosis (F0) N=35	Mild to moderate fibrosis (F1-2) N=14	Advanced fibrosis and cirrhosis (F3-4) N=13		
GFR less than 60 mL/min/1.73 m2	1 (2.85%)	0 (0%)	2 (15.4%)	0 (0%)	0.04
Microalbuminuria (30-300mg/g)	5(14%)	2 (14%)	3(23%)	0 (0%)	0.04
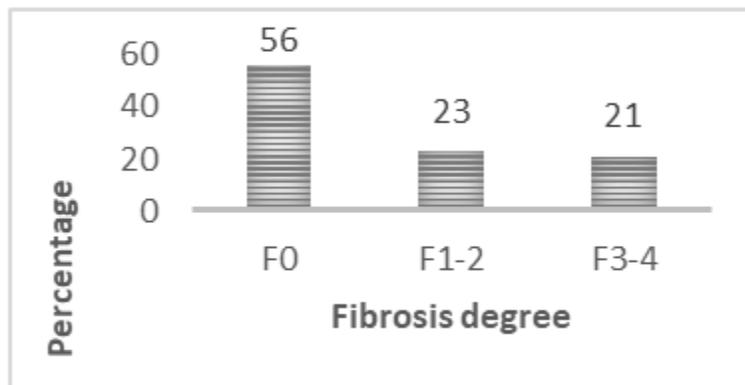
Fig 1. Distribution of stages of fibrosis measured by fibroscan.
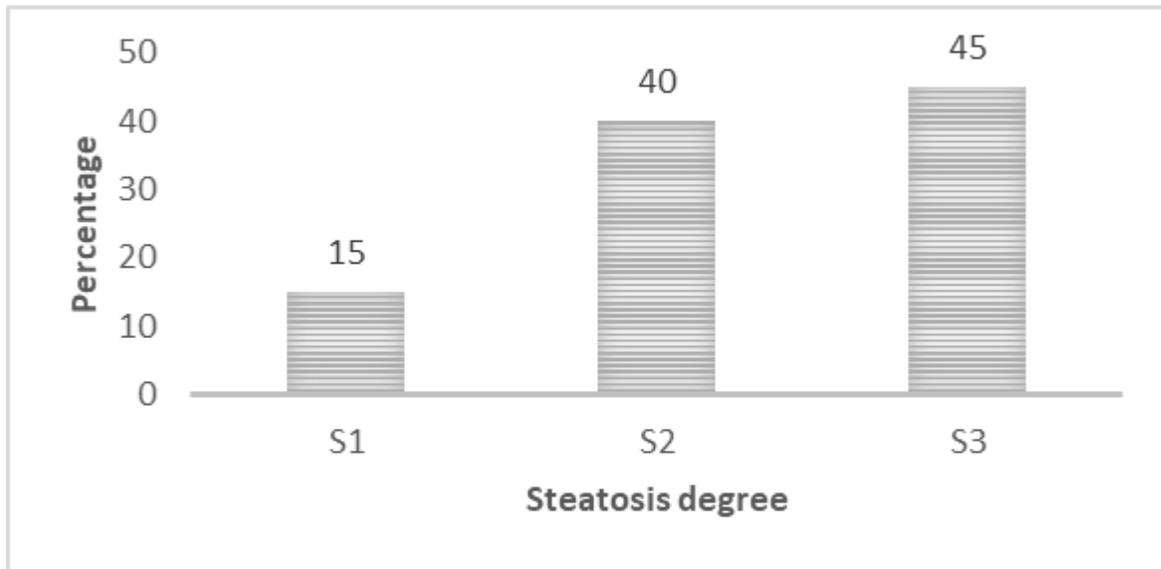
Original research

Fig 2. Distribution of stages of steatosis measured by fibroscan.

Original research
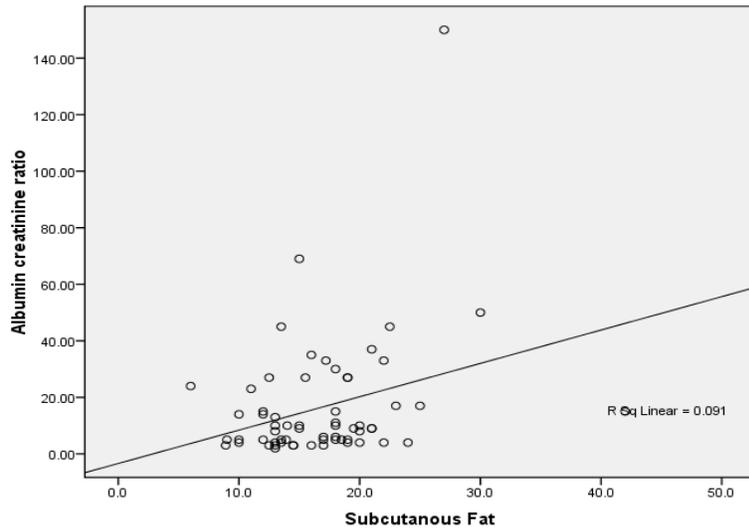
Fig 3. There was a significant positive correlation between the albumin creatinine ratio and subcutaneous fat thickness (r= 0.3, P = 0.03).
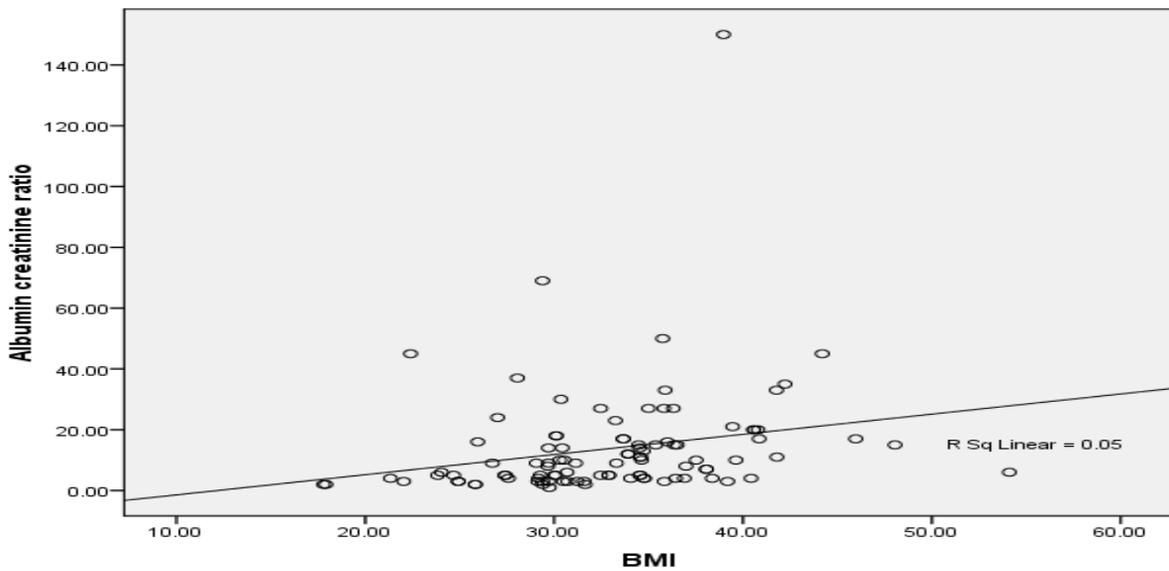

Fig 4. There was also a significant positive correlation between the albumin creatinine ratio and BMI (r= 0.3, P = 0.03).
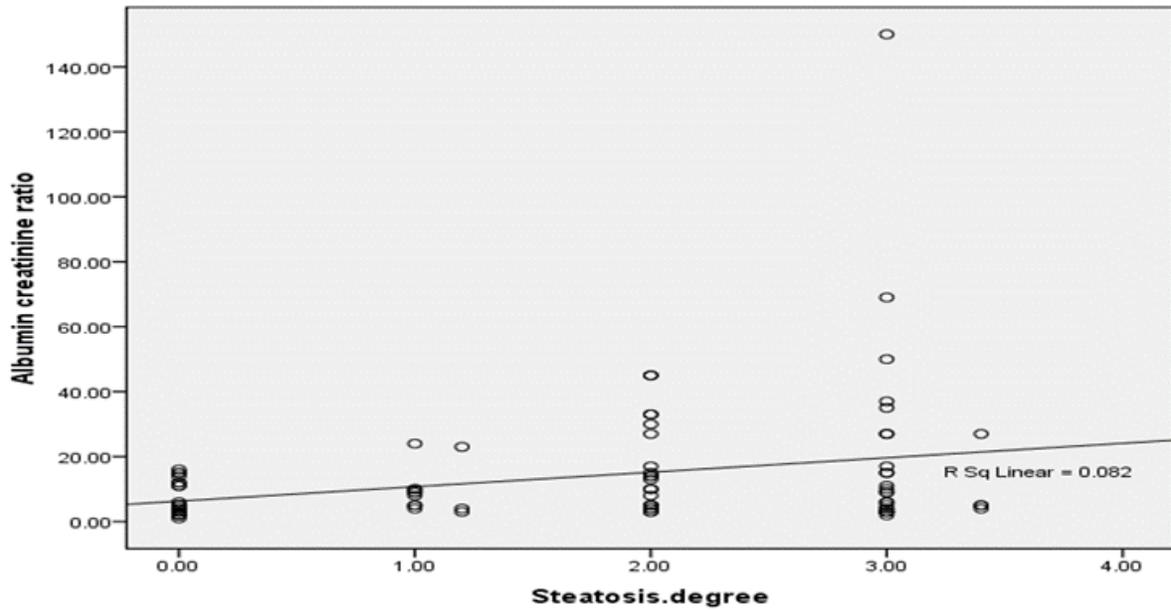
Fig 5. There was a significant positive correlation between albumin creatinine ratio and steatosis degrees (r= 0.3, P = 0.007)

Original research
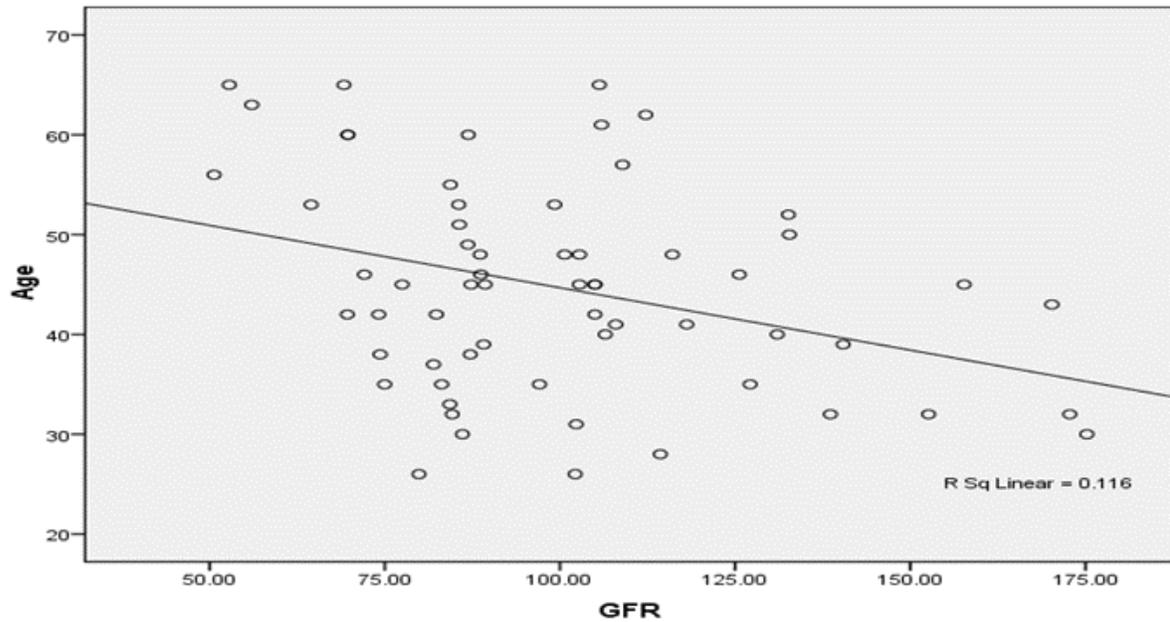
Fig 6. There was a significant negative correlation between the estimated glomerular filtration rate and the age of the patients (r= - 0.3, P = 0.04).

Original research
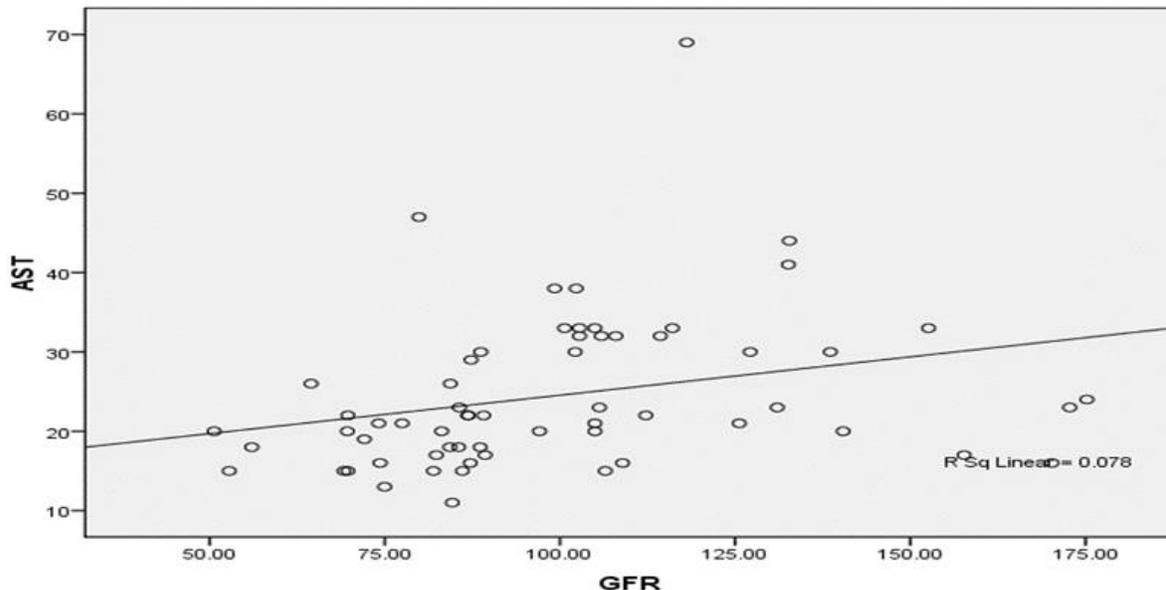
Fig 7. There was a significant positive correlation between the estimated glomerular filtration rate and AST level (r= 0.4, P = 0.000).

Discussion:

Non-alcoholic fatty liver disease (NAFLD) represents a considerable percentage of chronic liver diseases worldwide. The liver is not the only organ affected by NAFLD but also affects other organs such as the cardiovascular system and the kidney. In recent decades, there has been a growing body of evidence linking NAFLD to kidney function.

The increased risk for CKD is related to certain risk variables such as diabetes, hypertension, and chronic renal diseases(16). all these risk factors for CKD were excluded at the start of the current study. However, in this analysis, NAFLD and CKD association remained continuously strong. We found that the percentage of patients with chronic kidney diseases (patients with GFR less than 60 ml or micro-albuminuria) were significantly higher among NAFLD groups than in healthy controls. Also, the incidence of micro-albuminuria was substantially higher among NAFLD groups than in healthy controls (P-value=0.04).

Furthermore, there was a significant positive correlation between the albumin creatinine ratio and subcutaneous fat thickness, BMI, and steatosis degrees. Obesity is one of the main risk factors for NAFLD and CKD(17,18). Even in the absence of hypertension, obesity is linked to the development of proteinuria and pathologic signs of podocyte hypertrophy and focal segmental glomerular sclerosis(19). The estimated glomerular filtration rate and the age of the patients had a significant negative correlation. On the other hand, the estimated glomerular filtration rate and

Original research

AST level had a significant positive correlation. The current findings support those of a recent Asian cohort study which found that NAFLD was linked to a nearly 40% increased risk of CKD(20). In addition, the authors discovered that the risk of CKD rose as the degree of NAFLD severity grew, as shown by a significant positive correlation between albumin creatinine ratio and steatosis degree, BMI, and subcutaneous fat thickness. Also, the risk increases with age and increases AST enzyme.

Though various possible explanations have been proposed, the pathophysiologic mechanisms associated with NAFLD and CKD are yet unknown(21,22). Researchers supposed that NAFLD might increase insulin resistance, leading to dyslipidemia and the release of specific pro-inflammatory, pro-oxidant, and pro-fibrogenic mediators contributing to the occurrence and progression of CKD(23,24). Therefore, therapy to prevent or decrease damage has yet to be advised unless the mechanisms linking NAFLD and CKD are entirely known. However, the improvement in kidney function tests was noticed after the histopathological regression in NAFLD related to changes in lifestyle for one year(25).

On the other hand, a study of Caucasian men from Finland found no association between NAFLD (discovered by elevated serum gamma-glutamyltransferase) and CKD(26). This can be explained by the small sample size and low incident rate despite the long duration of follow-up (over 20 years)(26). Furthermore, they depend only on elevated serum gamma-glutamyltransferase, which is not specific to the hepatic pathology, and most NAFLD patients have normal liver enzymes(27). A European study did not recognize the connection between NAFLD and CKD as statistically significant due to the small sample size, different populations, and absence of thorough adjustment for variables (28). Furthermore, according to Qin et al., liver stiffness measurement(LSM) by transient elastography (TE) is a possible indication of CKD in patients with NAFLD; patients with a more excellent value of LSM have a higher chance of developing CKD(29). Therefore, the risk of CKD might rise with the advancement in the hepatic fibrosis stage.

This study had some limitations. First, a cross-sectional design of the study did not determine if NAFLD affects CKD progression on its own. Second, we had a small sample size and a single-center study. Third, we used only the eGFR and albumin creatinine ratio to identify CKD without renal biopsy. However, eGFR is the most prevalent variable assessed for CKD in clinical practice and epidemiological investigations, and eGFR is utilized for CKD classification.

Fourth, the authors did not do a liver biopsy which is the principal method in determining the severity of hepatic fibrosis and inflammation. Unfortunately, we could not do a liver biopsy since most participants were not eligible. Finally, autoimmune liver disorders such as autoimmune hepatitis and primary biliary cholangitis were not ruled out. However, because of its rarity, this may have little impact on the study's findings.

Conclusion:

Our findings showed that NAFLD diagnosis is associated with a considerably higher risk of CKD. Our results indicated that screening for CKD in NAFLD patients is needed. More studies are recommended to establish the underlying mechanism of this link and the therapies required to treat people with NAFLD who are at increased risk of getting CKD.

Footnotes.

Original research

Declaration of competing interest

There are no conflicts of interest related to this study.

Authors' contributions: All authors contributed equally to this work.

ClinicalTrials.gov Identifier: NCT04779905.

The institutional review board of Sohag University, Faculty of Medicine, approved this research.

Data Availability Statement: Available upon reasonable request from the corresponding author.

All authors had direct exposure to the study data and read and agreed with the final text.

E- Editor: Salem Youssef Mohamed, Osama Ahmed Khalil.

Disclaimer: All claims expressed in this article are solely those of the authors and do not necessarily represent their affiliated organizations or those of the publisher, the editors, and the reviewers. Any product evaluated in this article or its manufacturer's claim is not guaranteed or endorsed by the publisher.

Data availability

Original research

The corresponding author will supply the data supporting our study's findings upon reasonable request.

References:
1.   Vernon G, Baranova A, Younossi ZM. Systematic review: The epidemiology and natural history of non-alcoholic fatty liver disease and non-alcoholic steatohepatitis in adults. Alimentary Pharmacology and Therapeutics. 2011;34(3):274–85.
2.   Chalasani N, Younossi Z, Lavine JE, Diehl AM, Brunt EM, Cusi K, et al. The diagnosis and management of non-alcoholic fatty liver disease: Practice Guideline by the American Association for the Study of Liver Diseases, American College of Gastroenterology, and the American Gastroenterological Association. Hepatology. 2012;55(6):2005–23.
3.   Wedemeyer H, Thursz M. The role of different EASL-papers: Clinical practice guidelines vs. position papers vs. conference summaries [Internet]. Vol. 53, Journal of Hepatology. J Hepatol; 2010 [cited 2022 7 May]. p. 372–84. Available from: https://pubmed.ncbi.nlm.nih.gov/20494470/
4.   Loomba R, Sanyal AJ. The global NAFLD epidemic. Nature Reviews Gastroenterology and Hepatology. 2013;10(11):686–90.
5.   Marcuccilli M, Chonchol M. NAFLD, and chronic kidney disease. International Journal of Molecular Sciences. 2016;17(4):1–15.
6.   McCullough K, Sharma P, Ali T, Khan I, Smith WCS, MacLeod A, et al. Measuring the population burden of chronic kidney disease: a systematic literature review of the estimated prevalence of impaired kidney function. Vol. 27, Nephrology, dialysis, transplantation : official publication of the European Dialysis and Transplant Association - European Renal Association. 2012. p. 1812–21.
7.   Targher G, Chonchol MB, Byrne CD. CKD and Nonalcoholic Fatty Liver Disease. American Journal of Kidney Diseases [Internet]. 2014 Oct 1 [cited 2022 May 7];64(4):638–52. Available from: http://www.ajkd.org/article/S0272638614009718/fulltext
8.   Black C, Sharma P, Scotland G, McCullough K, McGurn D, Robertson L, et al. Early referral strategies for management of people with markers of renal disease: A systematic review of the evidence of clinical effectiveness, cost-effectiveness and economic analysis. Health Technology Assessment. 2010;14(21):1–184.
9.   Yasui K, Sumida Y, Mori Y, Mitsuyoshi H, Minami M, Itoh Y, et al. Nonalcoholic steatohepatitis and increased risk of chronic kidney disease. Metabolism - Clinical and Experimental [Internet]. 2011 May 1 [cited 2022 May 7];60(5):735–9. Available from: http://www.metabolismjournal.com/article/S0026049510002507/fulltext
10.   Chang Y, Ryu S, Sung E, Woo HY, Oh E, Cha K, et al. Nonalcoholic fatty liver disease predicts chronic kidney disease in nonhypertensive and nondiabetic Korean men. Metabolism - Clinical and Experimental [Internet]. 2008 Apr 1 [cited 2022 May 7];57(4):569–76. Available from: http://www.metabolismjournal.com/article/S0026049507004167/fulltext
11.   Levey AS, Coresh J, Balk E, Kausz AT, Levin A, Steffes MW, et al. National Kidney Foundation Practice Guidelines for Chronic Kidney Disease: Evaluation, Classification, and Stratification. Annals of Internal Medicine. 2003 Jul 15;139(2).
12.   Silveiro SP, Araújo GN, Ferreira MN, Souza FDS, Yamaguchi HM, Camargo EG. Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation pronouncedly underestimates glomerular filtration rate in type 2 diabetes. Diabetes Care. 2011;34(11):2353–5.
13.   Cuatrecasas G, de Cabo F, Coves MJ, Patrascioiu I, Aguilar G, March S, et al. Ultrasound measures of abdominal fat layers correlate with metabolic syndrome features in patients with obesity. Obesity Science and Practice. 2020;6(6):660–7.
14.   Pathik P, Ravindra S, Ajay C, Prasad B, Jatin P, Prabha S. Fibroscan versus simple noninvasive screening tools in predicting fibrosis in high-risk nonalcoholic fatty liver disease patients from western India. Annals of Gastroenterology. 2015;28(2):281–6.
15.   Zhang X, Wong GLH, Wong VWS. Application of transient elastography in nonalcoholic fatty liver disease.

Original research

Clinical and Molecular Hepatology. 2020;26(2):128–41.

16. Kazanciog R, Lu ˇ. Risk factors for chronic kidney disease: An update. Kidney International Supplements [Internet]. 2013 Dec 1 [cited 2022 May 10];3(4):368–71. Available from: http://www.kidney-international.org

17. Sarwar R, Pierce N, Koppe S. Obesity and nonalcoholic fatty liver disease: current perspectives. Diabetes, Metabolic Syndrome and Obesity: Targets and Therapy [Internet]. 2018 [cited 2022 10 May];11:533. Available from: /pmc/articles/PMC6163009/

18. Kovesdy CP, Furth SL, Zoccali C. Obesity and Kidney Disease: Hidden Consequences of the Epidemic. Canadian Journal of Kidney Health and Disease. 2017;4.

19. Chalasani N, Younossi Z, Lavine JE, Charlton M, Cusi K, Rinella M, et al. The diagnosis and management of nonalcoholic fatty liver disease: Practice guidance from the American Association for the Study of Liver Diseases. Hepatology [Internet]. 2018 Jan 1 [cited 2022 May 7];67(1):328–57. Available from: https://onlinelibrary.wiley.com/doi/full/10.1002/hep.29367

20. Sinn DH, Kang D, Jang HR, Gu S, Cho SJ, Paik SW, et al. Development of chronic kidney disease in patients with non-alcoholic fatty liver disease: A cohort study. Journal of Hepatology [Internet]. 2017 Dec 1 [cited 2022 May 7];67(6):1274–80. Available from: http://www.journal-of-hepatology.eu/article/S016882781732264X/fulltext

21. James MT, Hemmelgarn BR, Tonelli M. Early recognition and prevention of chronic kidney disease. The Lancet [Internet]. 2010 Apr 10 [cited 2022 May 7];375(9722):1296–309. Available from: http://www.thelancet.com/article/S0140673609620043/fulltext

22. Yki-Järvinen H. Liver fat in the pathogenesis of insulin resistance and type 2 diabetes [Internet]. Vol. 28, Digestive Diseases. Karger Publishers; 2010 [cited 2022 7 May]. p. 203–9. Available from: https://www.karger.com/Article/FullText/282087

23. Guebre-Egziabher F, Alix PM, Koppe L, Pelletier CC, Kalbacher E, Fouque D, et al. Ectopic lipid accumulation: A potential cause for metabolic disturbances and a contributor to the alteration of kidney function. Vol. 95, Biochimie. Elsevier; 2013. p. 1971–9.

24. Targher G, Byrne CD. Non-alcoholic fatty liver disease: an emerging driving force in chronic kidney disease. Nature Reviews Nephrology 2017 13:5 [Internet]. 2017 Feb 20 [cited 2022 May 7];13(5):297–310. Available from: https://www.nature.com/articles/nrneph.2017.16

25. Vilar-Gomez E, Calzadilla-Bertot L, Friedman SL, Gra-Oramas B, Gonzalez-Fabian L, Villa-Jimenez O, et al. Improvement in liver histology due to lifestyle modification is independently associated with improved kidney function in patients with non-alcoholic steatohepatitis. Alimentary Pharmacology & Therapeutics [Internet]. 2017 Jan 1 [cited 2022 May 7];45(2):332–44. Available from: https://onlinelibrary.wiley.com/doi/full/10.1111/apt.13860

26. Kunutsor SK, Laukkanen JA. glutamyltransferase and risk of chronic kidney disease : A prospective University of Bristol - Explore Bristol Research. Clinica chimica acta. 2017;473:39–44.

27. Younossi ZM, Loomba R, Anstee QM, Rinella ME, Bugianesi E, Marchesini G, et al. Diagnostic modalities for nonalcoholic fatty liver disease, nonalcoholic steatohepatitis, and associated fibrosis. Hepatology [Internet]. 2018 Jul 1 [cited 2022 May 7];68(1):349–60. Available from: https://onlinelibrary.wiley.com/doi/full/10.1002/hep.29721

28. Mantovani A, Zaza G, Byrne CD, Lonardo A, Zoppini G, Bonora E, et al. Nonalcoholic fatty liver disease increases risk of incident chronic kidney disease: A systematic review and meta-analysis. Metabolism - Clinical and Experimental [Internet]. 2018 1 February [cited 2022 7 May];79:64–76. Available from: http://www.metabolismjournal.com/article/S0026049517303062/fulltext

29. Qin S, Wang S, Wang X, Wang J. Liver stiffness assessed by transient elastography as a potential indicator of chronic kidney disease in patients with nonalcoholic fatty liver disease. Journal of Clinical Laboratory Analysis. 2019;33(2):1–8.