The Egyptian Journal of Hospital Medicine (July 2020) Vol. 80 (3), Page 1003-1007

Renal Impairment and Nonalcoholic Fatty Liver Disease. Disease – Disease Relationship

Said Abd Elbaky Gad Shams El Deen
Department of Internal Medicine, Faculty of Medicine, Zagazig University, Sharkia, Egypt
Corresponding author: Said Abd Elbaky Gad Shams El Deen, Mobile: 01227517689, Email: saidabdelbaky12345@gmail.com

ABSTRACT

Background: Nonalcoholic fatty liver disease (NAFLD) has emerged as serious growing global health problem worldwide and its association with the progression of renal impairment (RI). Accumulating evidence suggests that NAFLD and RI are sharing the same cardio metabolic risk factors.

Objective: to evaluate and investigate the confounding factors sharing in the relation between NAFLD and renal impairment (RI).

Patients and Methods: 250 Egyptian patients with NAFLD were investigated for creatinine, ALT, AST, lipid profile, fasting blood sugar. Questionnaire and physical examination were done to explore the relationship between NAFLD and RI.

Result: HA1C was 6.0±0.31, cholesterol 210.05±36.67, triglyceride 162.59±35.06, LDL 146.02±16.7 and HDL 43.23±6.15. AST and ALT were 34.12±4.28 and 35.34±4.8 respectively. ALP was 72.49±6.56, Cr 0.99±0.11, urea 29.16±9.41 and e-GFR 89.67±9.95. 39.2% were smokers 39.6% were Hypertensive, 60.8% had dyslipidemia and 27.6% had metabolic syndrome. 22.4% were cardiac patients and asthma represented 17.2% of the studied group. Renal impairment group was significantly associated with higher age and higher HA1C and also with higher Cr and urea but with lower GFR. We found also significant association between RI and males, hypertension, dyslipidemia, metabolic syndrome and asthma, with no other significant relation found.

Conclusion: There is strong and close association between NAFLD and RI as they share the same metabolic risk factors and precipitating factors.

Keywords: Renal impairment, Nonalcoholic fatty liver.

INTRODUCTION

Nonalcoholic fatty liver disease (NAFLD) is growing worldwide global health problem represents about 20-30% of world population. It encompass wide varieties of liver injury range from simple steatosis to progressive inflammation (steatohepatitis), liver fibrosis and cirrhosis with consequent hepatocellular carcinoma [(1)].

Chronic kidney disease (CKD) or renal impairment (RI) is worldwide health problem that results is high morbidity, mortality and socio-economic problems [(1, 2)]. RI is defined as gradually progressive decline in renal function represented by decreased glomerular filtration rate (GFR) with consequent changes in renal mass [(3, 4)] and this abnormalities are diagnosed based on urine analysis, kidney biopsy and imaging studies [(4)].

RI is frequently associated with patients of old age, hypertension, diabetes, obesity and dyslipidemia [(4)]. Nonalcoholic liver disease in Western countries is also associated with obesity[(5)], diabetes, hypertension and dyslipidemia. In some studies there is strong evidence linking between NAFLD and kidney function. Some cross-sectional studies shows that NAFLD diagnosed by ultrasonography[(6)], enzymes or biopsy is highly associated with renal impairment [(7)]. Another study had showed that NAFLD with markedly increased transaminases is associated with kidney troubles. Mild kidney damages occur early before chronic renal failure according to a study by the National Kidney Foundation Practice Guidelines [(8)].

It is important to explore the risk factors affecting kidney function early to prevent progression to chronic renal failure. For these causes we decided to study the effect of confounding factors sharing NAFLD and RI as age, gender, lifestyle factors, diabetes, lipids, hypertension and liver biochemistry on the relationship between NAFLD and RI from volunteers and doing questionnaire as was done in other studies [(9, 10)].

Aim of the work was to evaluate and investigate the confounding factors sharing in the relation between NAFLD and renal impairment (RI).

MATERIALS AND PATIENTS

This study was carried out at Internal Medicine Department, Faculty of Medicine Zagazig University in the period from April 2017 to June 2018.

Ethical approval:

The study was approved by the Institutional Review Board of Ethical Committee. Written informed consent was obtained from all patients.

250 Egyptian patients with NAFLD were investigated for creatinine, ALT, AST, lipid profile, fasting blood

Received:11 /5 /2020
Accepted: 20/1 /2020

sugar. Questionnaire and physical examination were done to explore the relationship between NAFLD and RI.

Patients:

- This study included 250 volunteers; candidates of both sexes from rural as well as urban areas attending Zagazig University Hospitals.
- The subjects with hepatitis, autoimmune disorders, metabolic or hereditary factors, drugs and toxins were excluded.
- Questionnaire strictly focused on age, sex life style habits, smoking, and body built. Questionnaire also focused on cardiac troubles, history, medications, interventional procedures complications, chest troubles as bronchial asthma frequency of attacks, medications, follow up and complications.

Blood sampling:

Blood sample of 5 ml was needed from suitable vein and collected into vacationer tubes according to blood collection standards and stored at 0.4ºC and according to the study desiorm [9, 10]. ALT, AST, serum lipids, glucose, kidney function were measured using chromatographic enzymatic method (Ray automated analyser).

According to American Guidelines of Hepatology Society; diagnosis of NAFLD was done by using ultrasonic examination using MINDRAY 9900 plus digital B/W ultrasound system (MINDRAY Co. Ltd., Shenzhen, China) with the following 5 criteria.

1- diffuse enhancement of near field echo in near hepatic region.
2- Unclear display of intrahepatic lacuna structure.
3- Mild to moderate hepatomegaly.
4- Color Doppler U/S shows reduction of blood flow signal in the liver.
5- Unclear or noncontact display of envelope of right liver lobe [11, 12].

Physical examination:

Body mass index (BMI) by using ultrasonographic body scale SK/CK (Sonka Electronic Technologies Co. Ltd., Shenzhen, China) was 25 kg/m^2 according to WHO (world health organization) [13].

Statistical analysis

Data were collected and outcome measures were coded, entered and analyzed using Microsoft Excel software. Data were then imported into Statistical Package for the Social Sciences (SPSS version 20.0) software for analysis. Qualitative data were represented as number and percentage and were compared by Chi square test (X^2). Quantitative continues data were represented by mean ± SD and were compared by independent t-test. P value was set at <0.05 for significant results and <0.001 for high significant result.

RESULTS

Age and BMI and sex distribution are presented in table 1 and 2.

Table (1): Age and BMI distribution among studied group

	Age (years)	**BMI** (kg/m^2)
Mean	53.2920	32.0776
Median	53.0000	31.5000
Std. Deviation	3.70915	2.30358

Table (2): Sex distribution among studied group.

		Frequency	**Percent**
Sex	**Male**	140	56.0
	Female	110	44.0
	Total	250	100.0

Values of Ha1C, lipid profile, and liver and kidney function test are in tables 3 and 4.

Table (3): HA1C and lipid profile.

	HA1C	**Cholesterol(mg/dl)**	**Triglyc. (mg/dl)**	**LDL(mg/dl)**	**HDL(mg/dl)**
Mean	6.0036	210.0520	162.5920	146.0280	43.2320
Median	6.1000	208.0000	168.0000	145.0000	41.0000
Std. Deviation	1.449	36.67333	35.06989	16.70062	6.15546

Table (4): Liver and kidney function test.

	AST (U/L)	**ALT** (U/L)	**ALP** (U/L)	**Cr** (mg/dL)	**Urea** (mg/dL)	**GFR** (mL/min)
Mean	34.120	35.340	72.496	0.991	29.164	89.672
Median	35.0000	38.0000	72.0000	1.0000	26.0000	95.0000
Std. Deviation	4.286	4.809	6.56341	0.113	9.41337	9.95433

Dyslipidemia was the most common risk factor (Table 5).

Table (5): Risk factors distribution.

		N	**%**
Smoker	**No**	152	60.8
	Yes	98	39.2
Hypertension	**No**	151	60.4
	Yes	99	39.6
Dyslipidemia	**No**	98	39.2
	Yes	152	60.8
Metabolic	**No**	181	72.4
	Yes	69	27.6
Cardiac	**No**	194	77.6
	Yes	56	22.4
Asthma	**No**	207	82.8
	Yes	43	17.2
	Total	250	100.0

22.4% of patients had renal impairment (Table 6).

Table (6): Renal function impairment prevalence.

		N	**%**
RI	**-VE**	194	77.6
	+VE	56	22.4
	Total	250	100.0

Renal impairment group significantly associated with higher age and higher HA1C also with higher Cr and Urea but with lower GFR, we found also significant association between RI and male, HTN, Dyslipidemia, metabolic syndrome and asthma, with no other significant relation founded (Table 7).

Table (7): Relation with renal impairment.

			No RI N=194	RI N=56	t/X^2	P
Age (Years)			52.94±3.32	54.48±4.65	-2.776	0.006*
BMI (kg/m^2)			32.08±2.41	32.06±1.9	0.057	0.955
HA1C			5.95±0.32	6.18±0.17	-5.167	0.001**
Cholesterol (mg/dL)			212.71±40.77	209.82±11.96	0.5233	0.601
Triglycerides(mg/dL)			162.18±36.37	164.0±30.37	-0.342	0.733
LDL (mg/dL)			145.94±17.8	142.37±9.63	1.458	0.095
HDL (mg/dL)			44.07±6.7	42.5±1.11	1.772	0.075
AST (units/L)			34.27±4.07	33.58±4.94	1.052	0.294
ALT (U/L)			35.54±4.62	34.62±5.39	1.264	0.207
ALP (U/L)			72.67±6.58	71.87±6.52	0.803	0.423
Cr (mg/dL)			0.94±0.06	1.14±0.11	-17.802	0.001**
Urea (mg/dL)			24.75±4.88	44.42±3.43	-28.185	0.001**
GFR (mL/min**)**			94.81±2.74	71.83±2.19	57.452	0.001**
Sex	**Male**	N	127	13		
		%	65.5%	23.2%		
	Female	N	67	43	31.482	0.001**
		%	34.5%	76.8%		
Smoker	**No**	N	109	28		
		%	56.2%	50.0%		
	Smoker	N	85	28	0.671	0.41
		%	43.8%	50.0%		
Hypertension	**No**	N	138	13		
		%	71.1%	23.2%		
	Yes	N	56	43	41.72	0.001**
		%	28.9%	76.8%		
Dyslipidemia	**No**	N	85	13		
		%	43.8%	23.2%		
	Yes	N	109	43	7.738	0.005*
		%	56.2%	76.8%		
Metabolic	**No**	N	168	13		
		%	86.6%	23.2%		
	Yes	N	26	43	87.369	0.001**
		%	13.4%	76.8%		
Cardiac	**No**	N	153	41		
		%	78.9%	73.2%		
	Yes	N	41	15	0.799	0.372
		%	21.1%	26.8%		
Asthma	**No**	N	166	41		
		%	85.6%	73.2%		
	Yes	N	28	15	4.656	0.031*
		%	14.4%	26.8%		
Total		N	194	56		
		%	100.0%	100.0%		

DISCUSSION

Nonalcoholic fatty liver disease (NAFLD) and renal impairment share many comorbid factors as obesity, impaired glucose tolerance, dyslipidemia so there is an interrelationship between NAFLD and RI. From pathophysiological point of view a question must be asked; is NAFLD and RI share the same metabolic risk factors or NAFLD is the main contributor for the development of RI? So we decided to study the variable factors as impaired glucose tolerance, dyslipidemia, BMI, hypertension which are shared between NAFLD and RI.

In our study there was a strong association between renal impaired functions and advanced age, which is in agreement with a study done by **Targher *et al.* [(2)].** Our study also revealed that there was strong significant correlation between Glycated Hb, NAFLD and renal impairment, which is in close association with a study done by **Yasui *et al.* [(14)].** This can be explained by the expanded and inflamed adipose tissue, which impose the liver to release certain inflammatory mediators as interleukin's, toxic free fatty acids and some hormones that may affect kidney function. Impaired glucose tolerance also leads to activation and release of proinflammatory cytokines and chemokines, adipocytokines and tumor necrosis factor, which leads to changes in signaling transcription factor that may lead to renal impairment.

Jung and Choi [(15)] showed that NAFLD and RI are closely associated with obesity, dyslipidemia and metabolic syndrome, which is in agreement with the results of our study. These results can be explained by the fact that increased liver uptake of free fatty acids that derived from inflamed adipose tissue (toxic fatty acids), dietary chylomicrons due to impaired glucose tolerance may lead to pathogenic harmful effects on the kidney by direct lipotoxicity on renal parenchyma or indirect by increased release of reactive free oxygen radical plasminogen activator inhibitor 1, transforming growth factor-β and other proinflammatory cytokine.

Our study had revealed that NAFLD is associated with decreased glomerular filtration rate as approved by a study done by **Loomis *et al.* [(16)].** There is no significant correlation between NAFLD and RI as regard BMI, liver enzymes, creatinine and smoking. There was a strong association between bronchial asthma and NAFLD and renal impairment. The most possible explanation is release of inflammatory mediators and side effects of drugs used to treatment of asthma.

CONCLUSION

There is strong and close association between NAFLD and RI as they share the same metabolic risk factors and precipitating factors.

RECOMMENDATIONS

Further experimental studies are needed to define the main sources and types of inflammatory mediator and association between liver and visceral adipose tissue producing renal impairment and to identify other pathogenetic mechanisms by which NAFLD leads to CKD.

REFERENCES

1. **Ghouri N, Preiss D, Sattar N (2010):** Liver enzymes, nonalcoholic fatty liver disease, and incident cardiovascular disease: a narrative review and clinical perspective of prospective data. Hepatology, 52:1156-61.
2. **Targher G, Bertolini L, Padovani R *et al.* (2010):** Prevalence of non-alcoholic fatty liver disease and its association with cardiovascular disease in patients with type 1 diabetes. J Hepatol., 53:713-8.
3. **Targher G, Day CP, Bonora E (2010):** Risk of cardiovascular disease in patients with nonalcoholic fatty liver disease. N Engl J Med., 363:1341-50.
4. **Targher G, Chonchol M, Zoppini G *et al.* (2011):** Risk of chronic kidney disease in patients with nonalcoholic fatty liver. J Hepatol., 2011;54:1020-9.
5. **Levey AS, Stevens LA, Schmid CH *et al.* (2009):** A new equation to estimate glomerular fi ltration rate. Ann Intern Med., 150:604-12.
6. **Chan HL, de Silva HJ, Leung NW *et al.* (2007):** How should we manage patients with non-alcoholic fatty liver disease in 2007?. J Gastroenterol Hepatol., 22:801-8.
7. **Chen K, Xie F, Liu S *et al.* (2011):** Plasma reactive carbonyl species: Potential risk factor for hypertension. Free Radic Res., 45:568-74.
8. **Baskurt OK, Boynard M, Cokelet GC *et al.* (2009):** New guidelines for hemorheological laboratory techniques. Clin Hemorheol Microcirc., 42:75-97.
9. **National-Kidney-Foundation (2002):** K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Am J Kidney Dis., 39:1-266.
10. **Levey AS, Coresh J, Balk E *et al.* (2003):** National Kidney Foundation practice guidelines for chronic kidney disease: evaluation, classifi cation, and stratify cation. Ann Intern Med., 139:137-47.
11. **Ryu S, Chang Y, Kim DI *et al.* (2007):** Gamma glutamyltransferase as a predictor of chronic kidney disease in nonhypertensive and nondiabetic Korean men. Clin Chem., 53:71-7.
12. **Chang Y, Ryu S, Sung E *et al.* (2008):** Nonalcoholic fatty liver disease predicts chronic kidney disease in nonhypertensive and nondiabetic Korean men. Metabolism, 57:569-76.
13. **WHO (2012):** Mean body mass index (BMI). https://www. who.int/ gho/ncd/risk_factors/bmi_text/en/
14. **Yasui K, Sumida Y, Mori Y *et al.* (2011):** Nonalcoholic steatohepatitis and increased risk of chronic kidney disease. Metabolism, 60:735-9.
15. **Jung UJ and Choi MS (2014):** Obesity and its metabolic complications: The role of adipokines and the relationship between obesity, inflammation, insulin resistance, dyslipidemia and nonalcoholic fatty liver disease. Int J Mol Sci., 15(4): 6184–6223.
16. **Loomis AK, Kabadi S, Preiss D *et al.* (2016):** Body mass index and risk of nonalcoholic fatty liver disease: Two electronic health record prospective studies. J Clin Endocrinol Metab., 101(3): 945–952.