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Research Article

Association of chronic kidney disease with non-alcoholic fatty liver disease in cases of type-II diabetes mellitus

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ABSTRACT

Objective: To determine association of chronic kidney disease with non-alcoholic fatty liver disease in cases of type-II diabetes mellitus.

Material and methods: This cross sectional study was conducted at Department of Nephrology, Sahiwal Medical College Sahiwal from March 2018 to September 2018 over the period of six months. Total 200 diagnosed cases of type-II diabetes mellitus having age >30 years either male or female were included in the study. CKD and NAFLD was assessed in selected patients.

Results: Total 200 diabetics were enrolled in present study. Mean age of the patients was 59.77±8.63 years. Total 110 (55%) patients were male and 90 (45%) patients were female. Coronary heart disease was found in 85 (42.5%) patients and 115 (57.5%) patients were found without coronary heart disease. Total 130 (65%) patients were hypertensive and 70 (35%) patients were non-hypertensive. Smokers were 95 (47.5%) and non-smokers were 105 (52.5%). Obese were 80 (40%) and non-obese were 120 (60%). Out of 200 diabetics, CKD was found in 67 (33%) patients and 138 (69%) patients were found with NAFLD.

Conclusion: Results of present study showed significant association between CKD and NAFLD. Most of the patients were hypertensive. Higher number of patients were found with history of coronary artery disease and smoking. Obesity was also prominent.

Keywords: Chronic kidney disease, CKD, NAFLD, MKFD

INTRODUCTION

Metabolic syndrome is not only highly prevalent in patients with NAFLD, also increase the risk of developing NAFLD.[1-4] NAFLD is regarded as the hepaticmanifestation of metabolic syndrome. The spectrum of NAFLD includes nonalcoholic fatty liver (NAFL), nonalcoholic steatohepatitis (NASH), liver cirrhosis and hepatocellular carcinoma.[5] NAFLD is the most common liver disease in world, affects more than a quarter of thegeneral population, with an even higher prevalence in patients with diabetes mellitus and metabolic syndrome.[6] An independent relationship of NAFLD with impairment of renal function and mild kidney function damage (MKFD), which occurs before development of chronic kidney disease (CKD) has been suggested.[7,8] This suggests a possibility of a potential therapeutic window in which occurrence of nephropathy may be prevented or delayed.[9] Indian subjects with NAFLD are significantly different from their

Western counterparts in being less obese and having lower frequency of diabetes mellitus and metabolic syndrome.[10] India is projected to be the next capital of diabetes in world. The prevalence of diabetes has increased tenfold from 1.2% to 12.1%, between 1971 and 2000. It is estimated that the prevalence it's projected to increase from 61.3 million in 2011 to 101.2 million by 2030.[11]There is extremely limited Indian data on association NAFLD and CKD in type 2 diabetes mellitus subjects.

MATERIAL AND METHODS

This cross sectional study was conducted at Department of Nephrology, Sahiwal Medical College Sahiwal from March 2018 to September 2018 over the period of six months. This study was approved by the ethical committee and written informed consent was taken from every patient.Total 200 diagnosed cases of type-II diabetes mellitus having age >30 years either male or female were included in the study.

Patients with ultrasound suggestive of cirrhosis, high liver stiffness measurement (LSM) ≥13 kPa, history of decompensation of liver disease, pregnant females and those with alternate etiology for liver disease were excluded from the study. History of all the patients was taken and noted on pre-designed proforma. All the patients were assessed for CKD and NAFLD as per operational definition.

Operational definitions:

Hypertension:

Hypertension was considered if patient was currently receiving antihypertensive medication or else if the blood pressure was consistently ≥130/85 mmHg.

Chronic Kidney Disease:

For diagnosis of CKD, kidney function was estimated using the simplified modification of diet in renal disease (MDRD) study equation. eGFR = (175 x 9 (Scr)-1.234 x (Age)-0.179x (if female, 0.79)). Urinary albumin excretion rate (ACR, mg/g) was measured as the albumin to creatinine ratio. CKD was defined as eGFR<60 ml/min per 1.73 m2 and/or ACR ≥30 mg/g (>3 mg/mmol).[12]

Nonalcoholic Fatty Liver Disease (NAFLD)

on ultrasonography, hyperechogenicity of the liver relative to the kidneys, ultrasound beam attenuation, and poor visualization of intrahepatic vessel borders and left ventricular diastolic dysfunction was diagnosed by using pulse wave Doppler on the basis of : E/A ratio of less than 1, mitral deceleration time (DT) >240 mitral and Isovolumic relaxation time (IVRT) > 90 msec.

All the collected data was entered in SPSS version 18 and analyzed. Mean and SD was calculated for numerical data. Frequencies and percentages were calculated for categorical data.

RESULTS

Total 200 diabetics were enrolled in present study. Mean age of the patients was 59.77±8.63 years.

Out of 200 diabetics, CKD was found in 67 (33%) patients. (Fig. 1) Total 138 (69%) patients were found with NAFLD. (Fig. 2)Total 110 (55%) patients were male and 90 (45%) patients were female. Coronary heart disease was found in 85 (42.5%) patients and 115 (57.5%) patients were found without coronary heart disease. Total 130 (65%) patients were hypertensive and 70 (35%) patients were non-hypertensive. Smokers were 95 (47.5%) and non-smokers were 105 (52.5%). Obese were 80 (40%) and non-obese were 120 (60%). (Table 1) Out of 138 (69%) patients of NAFLD, CKD was found in 54 (39.13%) patients. Total 62 (31%) patients were found without NAFLD and CKD was found in 13 (20.97%) patients. Statistically significant association between CKD and NAFLD was noted with p value 0.014. (Table 2)

Fig. 1 Frequency of CKD

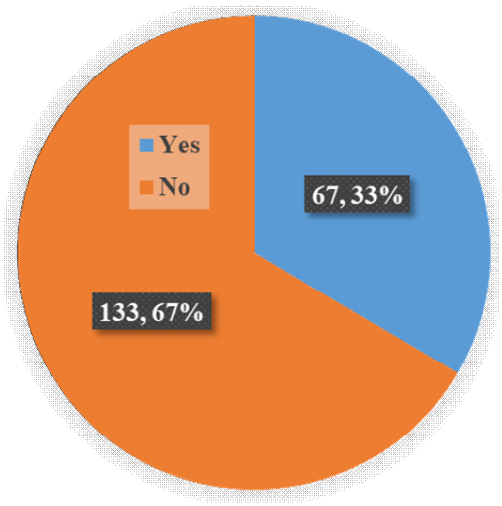

Fig. 2: Frequency of NAFLD

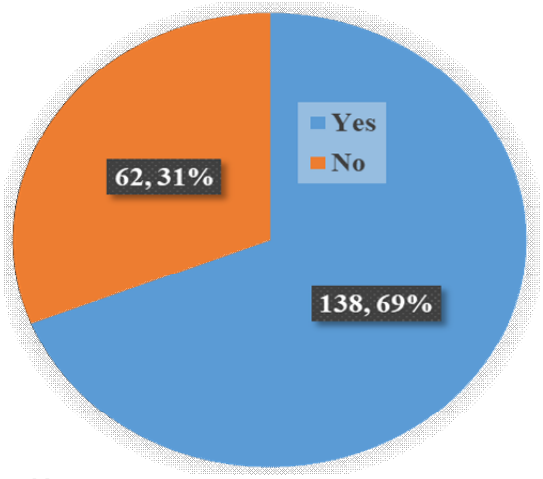

Table 1: Frequencies for different variables

Variable	**N**	**%**
Gender		
Male	**110**	**55**
Female	**90**	**45**
Coronary heart disease		
Yes	**85**	**42.5**
No	**115**	**57.5**
Hypertension		
Yes	**130**	**65**
No	**70**	**35**
Smoking		
Yes	**95**	**47.5**
No	**105**	**52.5**
Obesity		
Obese	**80**	**40**
Non-obese	**120**	**60**

Table 2: Association of CKD with NAFLD

NAFLD	CKD		Total	P value
	Yes	No		
Yes	54 (39.13)	84 (60.87)	138 (69)	0.014
No	13 (20.97)	49 (79.03)	62 (31)	
Total	67 (33.5)	133 (66.5)	200	

DISCUSSION

Present observational cross-sectional study specifically aimed at assessing the association between NAFLD with CKD in T2DM subjects. In this study, type 2 diabetics with NAFLD were closely associated with hypertension, obesity and hyperlipidemia, which have consistently been suggested in several studies. Present results were consistent with previous data.[15-19] NAFLD and CKD share many common characteristics including visceral obesity, diabetes mellitus, metabolic syndrome and insulin resistance.[19]Targher G et al, followed 1760 type 2 diabetics for 6.5 years, suggest that nonalcoholic fatty liver disease is associated with an increased incidence of CKD (hazard ratio 1.49, 95% confidence interval 1.1 to 2.2, P <0.01).[15] A Korean study Ahn AL et al, suggested positive association between NAFLD and CKD among population aged 50 years or older.[19] In this study, 35.34% T2DM subjects with NAFLD had CKD. Though Indian literature is lacking several cross-sectional studies from the West have suggested the prevalence of CKD in NAFLD patients to be 14% to 47%.[20-24] Chang Y et al, found that subjects with NAFLD had a relative risk 2.18 (95% confidence interval (CI), 1.75-2.71) for development of impaired renal function.[7] In this study, after multivariate regression analysis adjusting for confounding factors, type 2 diabetics with NAFLD were more than two times prone to develop CKD (OR 2.88 (1.1-6.78), p 0.03)). Whereas Sirota JC et al, found no association between NAFLD and CKD in individuals with diabetes.[21]The possible mechanisms for the association may be through inflammation and oxidative stress. Several cytokines and inflammatory mediator such as IL-6, TGF-b and TNF-are released in NAFLD[22], which promote the progress of the proteinuria.[23] The liver-kidney crosstalk in NAFLD includes altered renin-angiotensin system (RAS) and activated protein kinase (AMPK) activation, impaired antioxidant defense, and excessive dietary fructose intake, which affects renal injury through altered lipogenesis and inflammatory response. In turn, kidney reacts by promoting further RAS activation, increased angiotensin II and uric acid production in a vicious cycle leading to fibrosis.[24] Diagnosis of NAFLD in this study was based on the presence of hepatic steatosis on ultrasound along with exclusion of other causes of hepatic steatosis. It has a sensitivity of 89% and a specificity of 95% in detecting moderate and severe steatosis, but this sensitivity is reduced when hepatic fat infiltration upon liver biopsy is less than 33%.[25,27,28] Author also used transient elastography which is now an established modality for presence of significant fibrosis and the severity of liver disease. But liver biopsy is ideal diagnostic tool for quantification and assessment of prognosis in NAFLD.[29] Exposing clinically asymptomatic subjects to invasive procedure like liver biopsy poses an ethical dilemma.

CONCLUSION

Results of present study showed significant association between CKD and NAFLD. Most of the patients were hypertensive. Higher number of patients were found with history of coronary artery disease and smoking. Obesity was also prominent.

REFERENCES

1. Younossi ZM, Koenig AB, Abdelatif D, Fazel Y, Henry L, Wymer M. Global epidemiology of nonalcoholic fatty liver disease-meta□analytic assessment of prevalence, incidence, and outcomes. Hepatol. 2016;64(1):73-84.

2. Byrne CD. Targher G NAFLD: a multisystem disease. J Hepatol. 2015;62(1):S47-64.
3. Argo CK, Caldwell SH. Epidemiology and natural history of non-alcoholic steatohepatitis. Clin Liver Dis. 2009;13(4):511-31.
4. Younossi ZM, Stepanova M, Afendy M, Fang Y, Younossi Y, Mir H, et al. Changes in the prevalence of the most common causes of chronic liver diseases in the United States from 1988 to 2008. ClinGastroenterolHepatol. 2011;9(6):524-30.
5. Starley BQ, Calcagno CJ, Harrison SA. Non alcoholic fatty liver disease and hepatocellular carcinoma: a weighty connection. Hepatol. 2010;51(5):1820-32.
6. Duseja A, Singh SP, Saraswat VA, Acharya SK, Chawla YK, Chowdhury S, et al. Non-alcoholic fatty liver disease and metabolic syndrome-position paper of the Indian national association for the study of the liver, endocrine society of india, Indian college of cardiology and Indian society of gastroenterology. J ClinExpHepatol. 2015;5(1):51-68.
7. Chang Y, Ryu S, Sung E, Woo HY, Oh E, Cha K, et al. Nonalcoholic fatty liver disease predicts chronic kidney disease in non hypertensive and nondiabetic Korean men. Metab. 2008;57(4):569-76.
8. Li G, Shi W, Hu H, Chan Y, Liu L, Yin D. Non-alcoholic fatty liver associated with impairment of kidney function in non-diabetes population. Biochem Med. 2012;22(1):92-9.
9. 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. Ann Inter Med. 2003;139(2):137-47.
10. Duseja A, Das A, Das R, Dhiman RK, Chawla Y, Bhansali A, et al. The clinicopathological profile of Indian patients with nonalcoholic fatty liver disease (NAFLD) is different from that in the West. Dig Dis Sci. 2007;52(9):2368-74.
11. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. Diab Care. 2004;27(5):1047-53.
12. Levin A, Stevens PE, Bilous RW, Coresh J, De Francisco AL, De Jong PE, et al. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney Int Supp. 2013;3(1):1-50.
13. Wilson SR, Rosen IE, Chin-Sang HB, Arenson AM. Fatty infiltration of the liver--an imaging challenge. J Can AssocRadiol. 1982;33(4):227-32.
14. Musso G, Gambino R, Cassader M, Pagano G. Meta-analysis: natural history of non-alcoholic fatty liver disease (NAFLD) and diagnostic accuracy of non-invasive tests for liver disease severity. Ann Med. 2011;43(8):617-49.
15. Targher G, Chonchol M, Bertolini L, Rodella S, Zenari L, Lippi G, et al. Increased risk of CKD among type 2 diabetics with nonalcoholic fatty liver disease. J Am SocNephrol. 2008;19(8):1564-70.
16. Targher G, Pichiri I, Zoppini G, Trombetta M, Bonora E. Increased prevalence of chronic kidney disease in patients with Type 1 diabetes and non□alcoholic fatty liver. Diab Med. 2012;29(2):220-6.
17. Zhan YT, Zhang C, Li L, Bi CS, Song X, Zhang ST. Non-alcoholic fatty liver disease is not related to the incidence of diabetic nephropathy in type 2 diabetes. Int J Mol Sci. 2012;13(11):14698-706.
18. Yasui K, Sumida Y, Mori Y, Mitsuyoshi H, Minami M, Itoh Y, et al. Nonalcoholic steatohepatitis and increased risk of chronic kidney disease. Metab. 2011;60(5):735-9.
19. Ahn AL, Choi JK, Kim MN, Kim SA, Oh EJ, Kweon HJ, et al. Non-alcoholic fatty liver

disease and chronic kidney disease in Koreans aged 50 years or older. Korean J Family Med. 2013;34(3):199.
20. Hwang ST, Cho YK, Yun JW, Park JH, Kim HJ, Park DI, et al. Impact of non□alcoholic fatty liver disease on microalbuminuria in patients with prediabetes and diabetes. Inter Med J. 2010;40(6):437-42.
21. Sirota JC, McFann K, Targher G, Chonchol M, Jalal DI. Association between nonalcoholic liver disease and chronic kidney disease: an ultrasound analysis from NHANES 1988–1994. Am J Nephrol. 2012;36(5):466-71.
22. Targher G, Chonchol M, Zoppini G, Abaterusso C, Bonora E. Risk of chronic kidney disease in patients with non-alcoholic fatty liver disease: is there a link?. J Hepatol. 2011;54(5):1020-9.
23. Navarro-González JF, Mora C, Muros M, Garcia J, Donate J, Cazana V. Relationship between inflammation and microalbuminuria in prehypertension. J Human Hypertension. 2013;27(2):119.
24. Angulo P, Keach JC, Batts KP, Lindor KD. Independent predictors of liver fibrosis in patients with non-alcoholic steatohepatitis. Hepatol. 1999;30(6):1356-62.
25. Adams LA, Angulo P, Lindor KD. Nonalcoholic fatty liver disease. CMAJ. 2005;172(7):899-905.
26. Day CP. Non-alcoholic fatty liver disease: current concepts and management strategies. Clin Med. 2006;6(1):19-25.
27. Tolman KG, Fonseca V, Dalpiaz A, Tan MH. Spectrum of liver disease in type 2 diabetes and management of patients with diabetes and liver disease. Diab Care. 2007;30(3):734-43.
28. Saadeh S, Younossi ZM, Remer EM, Gramlich T, Ong JP, Hurley M, et al. The utility of radiological imaging in nonalcoholic fatty liver disease. Gastroenterol. 2002;123(3):745-50.
29. Angulo P. Nonalcoholic fatty liver disease. New Eng J Med. 2002;346(16):1221-31.