

SONOGRAPHIC ASSOCIATION OF NON – ALCOHOLIC FATTY LIVER DISEASE AND CHRONIC KIDNEY DISEASE WITH METABOLIC SYNDROME

Hafiza Aimon Baqar^a, Muhammad Uzair^b, Muhammad Abdul Hannan^c, Sara Sarfraz Iqbal^a, Muhammad Ahmed Ehsan^a, Zain ul Abideen^a, Huzaifa Afzal^a, Rafia Suleman Naseer^a

^aThe University of Lahore ^b Gilani Ultrasound Center, Ferozpur Road, Lahore. ^c The University of Sialkot.

Correspondence: aimanbaqar1121@gmail.com

ABSTRACT

Background and Objectives: Metabolic syndrome, a complex cluster of metabolic disturbances, has become a global health concern due to its association with increased cardiovascular risks and organ-related disorders. Non-alcoholic fatty liver disease (NAFLD) and chronic kidney disease (CKD) are two significant conditions closely linked to metabolic syndrome, reflecting potential shared pathophysiological mechanisms. Ultrasonography has emerged as a vital tool for non-invasive assessment of NAFLD and CKD within the context of metabolic syndrome. To find the sonographic association of non – alcoholic fatty liver disease with chronic kidney disease in patients with metabolic syndrome methodology.

METHODOLOGY: This descriptive study was performed at Sharif city hospital, Lahore. Total 210 participants, age 18-80 years comprising 107 (51%) males and 103 (49%) females were scanned. The study included CKD and NAFLD patients having metabolic syndrome and patients having any other liver or kidney disease related to metabolic syndrome were excluded.

RESULTS: The study revealed significant associations between diabetes and CKD, as well as between hypertension and stages of CKD. However, no significant associations were observed between diabetes and fatty liver grading, hypertension and fatty liver grading, or obesity and stages of CKD. Similarly, no significant associations were found between obese/non-obese status and fatty liver disease or chronic kidney disease.

CONCLUSION: In conclusion, this study contributes valuable insights into the complex interplay of metabolic syndrome, NAFLD, and CKD. The significant associations observed highlight the need for comprehensive assessment and management of these conditions to reduce their individual and collective burden on global health-care systems.

KEYWORDS: Non-Alcoholic Fatty Liver Disease, Chronic Kidney Disease, Metabolic Syndrome.

INTRODUCTION

Metabolic syndrome, a multifaceted cluster of metabolic disturbances, has risen to epidemic proportions globally, warranting significant attention from the medical community. The syndrome's intricate interplay of central obesity, insulin resistance, dyslipidemia, and hypertension not only heighten the risk of cardiovascular diseases but also influences the development of specific organ-related disorders. Two such prominent conditions are non-alcoholic fatty liver disease (NAFLD) and chronic kidney disease (CKD), both closely associated with metabolic syndrome, offering a window into potential shared pathophysiological mechanisms and clinical implications.

NAFLD, characterized by lipid accumulation within hepatocytes, stands as the most prevalent chronic liver ailment across the world [1]. Concurrently, CKD, characterized by a gradual loss of kidney function, poses a formidable global health challenge with its escalating incidence [2]. The intricate ties between NAFLD, CKD, and metabolic syndrome weave a complex narrative of interconnected factors that propel disease progression.

In the realm of non-invasive diagnostic tools, medical imaging techniques, particularly ultrasonography, have emerged as indispensable assets for assessing NAFLD and CKD. Ultrasonography enables the visu-

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alization of hepatic steatosis and renal anomalies, offering pivotal insights into disease severity and advancement [3]. Moreover, it empowers clinicians to monitor alterations in liver and kidney structure, thus facilitating the evaluation of treatment effectiveness and patient well-being [4].

This article embarks on an exploration of the sonographic relationships between NAFLD and CKD in conjunction with metabolic syndrome. By meticulously surveying contemporary research and pertinent literature, we endeavor to unravel the intricate connections among these entities and their shared underlying mechanisms [5][6]. Furthermore, we will underscore the significance of early-stage identification through ultrasonographic evaluations, accentuating its pivotal role in steering therapeutic modalities and augmenting patient care [7].

The role of medical imaging, particularly sonography, in the assessment of NAFLD and CKD within the context of metabolic syndrome has witnessed remarkable advancements.[6] Ultrasonography, with its non-invasive nature and ability to provide real-time imaging of liver and kidney structures, has become an indispensable tool for early detection, risk stratification, and monitoring of these conditions [8]. The Sonographic Association of Non-Alcoholic Fatty Liver Disease and Chronic Kidney Disease with Metabolic Syndrome forms a critical nexus that demands comprehensive exploration.

Earlier studies were inconclusive of the association of CKD and NAFLD and required more research to be done in order to achieve definite results. Advances in technology help us to determine the risks of having CKD and NAFLD in patients with metabolic syndrome. It can help us to treat these conditions timely without them having to get complicated. The aim of our study is to determine the factors that closely link these three conditions together so that they can either be avoided or managed.

METHODOLOGY

Study Design: This cross-sectional study aimed to investigate the sonographic association of non-alcoholic fatty liver disease (NAFLD) and chronic kidney disease (CKD) with metabolic syndrome. Total 210 participants, age range from 22 to 80 years, out of which 103 (49.0%) were female, and 107 (51.0%) were male.

Inclusion Criteria:

Group 1: patients having metabolic syndrome and CKD

Group 2: patients having metabolic syndrome and NAFLD

Group 3: patients having only metabolic syndrome

Exclusion Criteria

Patients having any other liver or kidney disease related to metabolic syndrome

Data Collection

Clinical data were collected Department of Radiology, Sharif City Hospital, Lahore, including age, gender, presence of diabetes, hypertension, and obesity, as well as ultrasonography findings for NAFLD and CKD staging using a Toshiba Xario 100 with convex probe having frequency of 2-5 MHz by experienced sonographers

Statistical Analysis

Statistical analysis was conducted using SPSS software. Descriptive statistics were used to summarize participant characteristics. Cross-tabulations and Chi-square tests were performed to assess associations between NAFLD, CKD, metabolic syndrome components, and their respective stages. A p-value < 0.05 was considered statistically significant.

RESULTS

In table.1 out of 210 participants, 106 (50.5%) were non diabetes, while 104 (49.5%) were diabetes. 116 (55.2%) were non hypertensive, while 94 (44.8%) were hypertension. 101 (48.1%) were non obese, while 109 (51.9%) were Obese. 2 of them (1.0%) did not have Fatty Liver Disease, while 208 (99.0%), had Fatty Liver Disease. 124 (59.0%) did not had chronic kidney disease, while 86 (41.0%) had chronic kidney disease.

Table 1: Descriptive statistics.

	Frequency				
	Diabetes	Hypertension	Obesity	NAFLD	CKD
No	106 (50.5 %)	116 (55.2 %)	101 (48.1 %)	2 (1 %)	124 (59 %)
Yes	104 (49.5 %)	94 (44.8 %)	109 (51.9 %)	208 (99 %)	86 (41 %)
Total			210 (100 %)		

In Table 2 out of 124 participants without Fatty Liver Disease and 86 participants with Fatty Liver Disease. Among the observers with Fatty Liver Disease, 84 of them have chronic kidney disease, while 2 do not. There was no statistically significant association between Fatty Liver Disease and Chronic Kidney Disease (Chi-Square = 2.911, p = 0.088).

Table 2: Association of fatty liver and chronic kidney disease.

		Chronic Kidney Disease		Total	P-value
		No	Yes		
Fatty Liver Disease	No	0	2	2	0.167
		0.0%	100.0%	100.0%	
	Yes	124	84	208	
		59.6%	40.4%	100.0%	
Total		124	86	210	
		59.0%	41.0%	100.0%	

Table 3 shows the relationship between Fatty Liver Grading and Stages of Chronic Kidney Disease among the 210 participants. 2 had Fatty Liver Grading "0", in Stage 1 of chronic kidney disease. 53 had Fatty Liver Grading "1" in Stage 0, whereas 15 participants in Stage 1, and 1 participant in Stage 2 of chronic kidney disease. Fatty Liver Grading "2", there are 55 participants in Stage 0, 24 participants in Stage 1, and 13 participants in Stage 2 of chronic kidney disease. Fatty Liver Grading "3", there are 17 participants in Stage 0, 17 participants in Stage 1, and 13 participants in Stage 2 of chronic kidney disease. A significant association was found between Fatty Liver Grading and Stages of Chronic Kidney Disease (Chi-Square = 30.309, $p < 0.001$).

Table 3: Association of fatty liver grading and stages of chronic kidney disease.

		Stages of Chronic Kidney Disease			Total	P-Value
		0	1	2		
Fatty Liver Grading	0	0	2	0	2	0.000
		0.0%	100.0%	0.0%	100.0%	
		53	15	1	69	
	1	76.8%	21.7%	1.4%	100.0%	
		55	24	13	92	
		59.8%	26.1%	14.1%	100.0%	
	2	17	17	13	47	
		36.2%	36.2%	27.7%	100.0%	
		125	58	27	210	
Total	59.5%	27.6%	12.9%	100.0%		

In table.4 out of the 106 non-diabetic participants, 74 (69.8%) had stage "0", 24 (22.6%) had stage "1", and 8 (7.5%) had stage "2" chronic kidney disease stage. Similarly, out of the 104 Diabetes participants, 51 (49.0%) had stage "0", 34 (32.7%) had stage "1", and 19 (18.3%) had stage "2" chronic kidney disease stage. A significant association was found between Stages of Chronic Kidney Disease and Diabetes (Chi-Square = 10.420, $p = 0.005$).

Table 4: Associa

		Stages of Chronic Kidney Disease			Total	P-Value
		0	1	2		
Diabetes	No	74	24	8	106	0.005
		69.8%	22.6%	7.5%	100.0%	
	Yes	51	34	19	104	
		49.0%	32.7%	18.3%	100.0%	
Total		125	58	27	210	
		59.5%	27.6%	12.9%	100.0%	

In table 5 out of the 106 non-diabetes participants, 2 (1.9%) had Grade "0", 39 (36.8%) had Grade "1", 48 (45.3%) had Grade "2", and 17 (16.0%) had Grade "3" Fatty Liver. Similarly, out of the 104 Diabetes participants, 30 (28.8%) had Grade "1", 44 of them (42.3%) had Grade "2", 30 (28.8%) had Grade "3" and none of them had Grade "0" Fatty Liver. No significant association was found between Fatty Liver Grading and Diabetes (Chi-Square = 6.925, $p = 0.074$).

Table 5: Association of diabetes with fatty liver grading

		Fatty Liver Grading				Total	P-Value
Diabetes	No	0	1	2	3		0.074
		2	39	48		106	
		1.9%	36.8%	45.3%	16.0%	100.0%	
	Yes	0	30	44	30	104	
		0.0%	28.8%	42.3%	28.8%	100.0%	
		2	69	92		210	
Total		1.0%	32.9%	43.8%	22.4%	100.0%	

In table 6, out of the 116 non-Hypertensive participants, 85 (73.3%) had stage "0", 24 (20.7%) had stage "1", and 7 (6.0%) had stage "2" chronic kidney disease. Similarly, out of the 94 Hypertensive participants 40 (42.6%) had stage "0", 34 (36.2%) had stage "1", and 20 (21.3%) had stage "2". A significant association was found between Stages of Chronic Kidney Disease and Hypertension (Chi-Square = 22.121, $p < 0.001$).

Table 6: Association of Hypertension with stages of chronic kidney disease

		Stages of Chronic Kidney Disease			Total	P-Value
		0	1	2		
Hypertension	No	85	24	7	116	0.000
		73.3%	20.7%	6.0%	100.0%	
	Yes	40	34	20	94	
		42.6%	36.2%	21.3%	100.0%	
		125	58	27	210	
Total		59.5%	27.6%	12.9%	100.0%	

In table 7 out of the 116 non-Hypertensive participants, 2 (1.7%) had Grade "0", 43 (37.1%) had Grade "1", 49 (42.2%) had Grade "2", and 22 (19.0%) had Grade "3" Fatty Liver. Similarly, out of the 94 Hypertensive participants, none of them had Grade "0", 26 (27.7%) had Grade "1", 43 (45.7%) had Grade "2", and 25 (26.6%) had Grade "3" Fatty Liver. No significant association was found between Fatty Liver Grading and Hypertension (Chi-Square = 4.516, $p = 0.211$).

Table 7: Hypertensive participants

		Fatty Liver Grading				Total
Hypertension	No	1.00	1.00	2.00	3.00	
		2	43	49	22	116
	Yes	1.7%	37.1%	42.2%	19.0%	100.0%
		0	26	43	25	94
		0.0%	27.7%	45.7%	26.6%	100.0%
Total		2	69	92	47	210
		1.0%	32.9%	43.8%	22.4%	100.0%
Chi-Square Tests						
		Value	df	Asymp. Sig. (2-sided)		
Pearson Chi-Square		4.516 ^a	3	.211		
Likelihood Ratio		5.279 ^a	3	.152		
N of Valid Cases		210				

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)
Pearson Chi-Square	4.516 ^a	3	.211
Likelihood Ratio	5.279	3	.152
N of Valid Cases	210		

In table 8 out of 101 Non-Obese participants, 65 (64.4%) had Stages "0", 24 (23.8%) had Stages "1", and 12 (11.9%) had Stages "2" Chronic Kidney Disease. Similarly, out of 109 Obese participants, 60 (55.0%) had Stages "0", 34 (31.2%) had Stages "1", and 15 (13.8%) had Stages "2" chronic kidney disease. No significant association was found between Stages of Chronic Kidney Disease and Obesity/Non-Obesity (Chi-Square = 1.956, $p = 0.376$).

Table 8: Association of obesity with stages of chronic kidney disease

		Stages of Chronic Kidney Disease		P-Value
		1.00	2.00	
Non-obese	65	24	12	0.376
	64.4%	23.8%	11.9%	
Obese	60	34	15	
	55.0%	31.2%	13.8%	

In table 9 out of the 101 non-Obese participants, 2 (2.0%) had Grade "0", 53 (52.5%) had Grade "1", 35 (34.7%) had Grade "2", and 11 (10.9%) had Grade "3" Fatty Liver. Similarly, out of 109 Obese participants,

none of them had Grade "0", 16 (14.7%) had Grade "1", 57 (52.3%) had Grade "2", and 36 (33.0%) had Grade "3" Fatty Liver. A significant association was found between Fatty Liver Grading and Obesity/Non-Obesity (Chi-Square = 40.153, $p < 0.001$).

Table 9: Association of obesity with fatty liver disease

	Fatty Liver Grading				P-Value
	.00	1.00	2.00	3.00	
Non-obese	2 2.0%	53 52.5%	35 34.7%	11 10.9%	0.000
Obese	0 0.0%	16 14.7%	57 52.3%	36 33.0%	

DISCUSSION

The present study aimed to investigate the sonographic association of non-alcoholic fatty liver disease (NAFLD) and chronic kidney disease (CKD) with metabolic syndrome. The study involved a cohort of 210 participants, and various demographic and clinical characteristics were examined to understand the relationships between these conditions.

The distribution of participants based on diabetes status revealed that nearly half of the participants were diabetic (49.5%). This finding aligns with the global prevalence of diabetes and its strong association with metabolic syndrome [9]. Furthermore, the association between diabetes and CKD has been well-established, as observed in previous studies [10]. Our results corroborate these findings, showing a significant association between stages of CKD and diabetes status (Chi-Square = 10.420, $p = 0.005$), highlighting the impact of metabolic disturbances on renal health.

Hypertension, another hallmark of metabolic syndrome, was observed in 44.8% of participants. This prevalence is consistent with the known link between hypertension and metabolic syndrome, emphasizing the role of elevated blood pressure in the development of various metabolic and organ-related disorders [11]. Our study demonstrated a significant association between stages of CKD and hypertension (Chi-Square = 22.121, $p < 0.001$), underscoring the close relationship between these conditions.

The study also evaluated the influence of obesity on metabolic and organ-related health. Approximately 51.9% of participants were obese, which mirrors the global trend of increasing obesity rates and its strong association with metabolic syndrome [12]. Our results indicated a significant association between fatty liver grading and obesity/non-obesity (Chi-Square = 40.153, $p < 0.001$), confirming the intricate link between obesity and NAFLD.

Interestingly, the relationship between fatty liver grading and diabetes did not reach statistical significance

(Chi-Square = 6.925, $p = 0.074$). This finding contrasts with some previous studies that have reported a stronger association between diabetes and NAFLD [13]. However, the complex interplay of genetic, environmental, and metabolic factors may contribute to variations in these associations across different populations.

Intriguingly, our study unveiled a notable association between fatty liver grading and stages of CKD (Chi-Square = 30.309, $p < 0.001$). This finding highlights a potential shared pathophysiology underlying NAFLD and CKD, possibly related to systemic inflammation, oxidative stress, and insulin resistance[14][15]. These results align with prior research that has also suggested a significant association between NAFLD and CKD[16].

CONCLUSION

Our findings demonstrate significant associations were found between diabetes and CKD, as well as between hypertension and stages of CKD. However, no significant associations were observed between diabetes and fatty liver grading, hypertension and fatty liver grading, or obesity and stages of CKD. Furthermore, no associations were found between obese/non-obese status and fatty liver disease or chronic kidney disease.

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REFERENCES

1. Younossi ZM, Koenig AB, Abdelatif D, Fazel Y, Henry L, Wymer M. Global epidemiology of non-alcoholic fatty liver disease - Meta-analytic assessment of prevalence, incidence, and outcomes. *Hepatology*. 2016 Jul;64(1):73-84.
2. Hill NR, Fatoba ST, Oke JL, Hirst JA, O'Callaghan CA, Lasserson DS, Hobbs FD. Global prevalence of chronic kidney disease - A systematic review and meta-analysis. *PLoS One*. 2016 Jul 6;11(7):e0158765.
3. Saadeh S, Younossi ZM, Remer EM, Gramlich T, Ong JP, Hurley M, Mullen KD, Cooper JN, Sheridan MJ. The utility of radiological imaging in non-alcoholic fatty liver disease. *Gastroenterology*. 2002 Feb;123(3):745-50.
4. Tuma F, Kidambi S, Rader T, Herman WH, Brauer B, Loomba R. Nonalcoholic fatty liver disease is not associated with a change in cardiovascular or diabetes-related risk factors in youth with type 2 diabetes. *Diabetes Care*. 2019 Apr;42(4):711-718.
5. Chen Y, Li X, Boini KM, Pitzer AL, Gulbins E, Zhang Y, Li PL. Endothelial Nlrp3 inflammasome

- activation associated with lysosomal destabilization during coronary arteritis. *Biochim Biophys Acta Mol Basis Dis.* 2015 Oct;1853(10 Pt A):396-408.
6. Musso G, Gambino R, Tabibian JH, Ekstedt M, Kechagias S, Hamaguchi M, Hultcrantz R, Hagström H, Yoon SK, Charatcharoenwitthaya P, George J, Barrera F, Hafliðadóttir S, Björnsson ES, Armstrong MJ, Hopkins LJ, Gao X, Francque S, Verrijken A, Yilmaz Y, Lindor KD, Charlton M, Machado MV, Cortez-Pinto H, Yasui K, Stein LL, Liddle C, Marchesini G, Brunt EM, Trauner M, Schattenberg JM, Dieterich DT, Anstee QM, Adams LA, Krag A, Alves C, Rinella ME. Association of non-alcoholic fatty liver disease with chronic kidney disease: a systematic review and meta-analysis. *PLoS Med.* 2014 Jul 22;11(7):e1001680.
 7. Ballestri S, Lonardo A, Bonapace S, Byrne CD, Loria P, Targher G. Risk of cardiovascular, cardiac and arrhythmic complications in patients with non-alcoholic fatty liver disease. *World J Gastroenterol.* 2014 Oct 21;20(39):1724-45.
 8. Saadeh S, Younossi ZM, Remer EM, Gramlich T, Ong JP, Hurley M, Mullen KD, Cooper JN, Sheridan MJ. The utility of radiological imaging in nonalcoholic fatty liver disease. *Gastroenterology.* 2002 May 1;123(3):745-50.
 9. International Diabetes Federation (IDF). *IDF Diabetes Atlas*, 9th ed. Brussels, Belgium: IDF; 2019.
 10. KDOQI. *KDOQI Clinical Practice Guidelines and Clinical Practice Recommendations for Diabetes and Chronic Kidney Disease.* *Am J Kidney Dis.* 2007;49(2 Suppl 2):S12-S154.
 11. Reaven GM. The role of insulin resistance in human disease. *Diabetes.* 1988;37(12):1595-1607.
 12. World Health Organization (WHO). *Obesity and overweight. Fact sheet.* Updated February 2020.
 13. Angulo P. Nonalcoholic fatty liver disease. *N Engl J Med.* 2002;346(16):1221-1231.
 14. Targher G, Day CP, Bonora E. Risk of cardiovascular disease in patients with nonalcoholic fatty liver disease. *N Engl J Med.* 2010;363(14):1341-1350.
 15. Targher G, Bertolini L, Rodella S, et al. Nonalcoholic fatty liver disease is independently associated with an increased incidence of cardiovascular events in type 2 diabetic patients. *Diabetes Care.* 2007;30(8):2119-2121.
 16. Musso G, Gambino R, Tabibian JH, et al. Association of non-alcoholic fatty liver disease with chronic kidney disease: a systematic review and meta-analysis. *PLoS Med.* 2014;11(7):e1001680.

Authors Contributions:

Hafiza Aimon Baqar, Muhammad Uzair, Muhammad Abdul Hannan: Substantial contributions to the conception and design of the work.
Sara Sarfraz Iqbal, Muhammad Ahmed Ehsan, Zain ul Abideen: Design of the work and the acquisition. Drafting the work.
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