

## ORIGINAL ARTICLE

# Association of Fatty Liver (Non-Alcoholic), Metabolic Syndrome and Subclinical Inflammation on Mild Renal Inadequacy

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## ABSTRACT

**Background:** Non-alcoholic liver disease causes liver damage and influences the insulin production, metabolic and inflammatory pathways and renal sufficiency.

**Aim:** To find an association of fatty liver, metabolic syndrome and subclinical inflammation on mild renal inadequacy.

**Study design:** Comparative analytical study

**Place and duration of study:** Department of Medicine, Bolan Medical College Quetta from 1<sup>st</sup> January 2020 to 30<sup>th</sup> June 2021.

**Methodology:** One hundred and twenty patients were enrolled. They were divided in two groups; 60 controls and 60 non-alcoholic fatty liver disease patients age between 30-55 years of age included. Their demographic, ultrasonography, anthropometric measurements and biochemical details were recorded.

**Results:** There were 34 men out of 60 having NA fatty liver with a mean age of 45±5.8 years. Mild renal inadequacy was seen in 21, metabolic syndrome in 27, hypertension in 18 and diabetes in 8 of non-alcoholic fatty liver patients with a mean raised CRP as 1.5±0.8mg/L.

**Conclusion:** Non-alcoholic fatty liver presence in addition to metabolic syndrome and subclinical inflammation effect on mild renal inadequacy

**Key words:** Fatty liver, Metabolic syndrome, Subclinical inflammation, Mild renal inadequacy

## INTRODUCTION

The global inclination in hyper tension and diabetes has resulted in high prevalence of chronic renal diseases as these factors are major high risk associated with impaired kidney function.<sup>1</sup> Chronic renal disease (CRD) has become a major threat worldwide with increasing economical burden on developing countries like Pakistan. CRD also ascend the risk of cardiovascular diseases beside itself being a high risk factor of mortality.<sup>2</sup> Cardiovascular diseases, metabolic syndrome aggravated the chances of mild renal insufficiency.<sup>3</sup> Early stage detection of the CRD can attribute to better chances of survival.<sup>4</sup>

Fatty liver diseases which are not due to alcohol consumption can be progressed into cirrhotic, cancerous liver if untreated. It has also being linked with the cardio-metabolic risk, obesity and diabetes. Non-alcoholic fatty liver has been reported for its association with CRD and cardiovascular diseases development.<sup>4,5</sup>

The risk of type 2 diabetes mellitus, CRD and cardiovascular diseases accelerates in cases with metabolic syndrome.<sup>6</sup> The causative agent can be their common pathophysiology showing an association of chronic inflammation, insulin resistance and also oxidative stress. These all variables are interlinked as liver metabolizes glucose and insulin resistance causes oxidative stress.<sup>7</sup> Subclinical inflammations can cause CRD as well as cardiovascular disease formation.<sup>8</sup> C-reactive proteins (CRP) can identify the subclinical inflammation.<sup>9</sup>

The present study was designed to compare the effect of non-alcoholic fatty liver disease, subclinical inflammation, and metabolic syndrome on mild renal insufficiency.

## MATERIALS AND METHODS

It was a comparative analytical study including 120 patients which were further divided into two groups after permission from IRB. Sixty were healthy individuals with no fatty liver, metabolic syndrome or subclinical inflammation, whereas the other group had 60 individuals with non-alcoholic (NA) fatty liver, metabolic syndrome and subclinical inflammation in them. The age between 30-55 years adults from both genders were included. Patient consuming alcohol/any other addictive drugs or having liver

damage due to carcinoma/cirrhosis were excluded from the study. After attaining an informed consent each patient complete data profile was entered on a questionnaire. Each participant was diagnosed for fatty liver by ultrasonography and 5cc fasting blood was withdrawn for serum and whole blood formation. Biochemical testing of complete lipid profile, CRP, creatinine, Liver function test (LFT) and HbA1c levels were performed on each participant. The weight, height and blood pressure of each individual was measured for analyzing BMI and hypertension. All the biochemical analysis was done through ELISA bioscience, Germany kits and anthropometric measurements were conducted by using digital weight and height measurement machines and also using sphygmomanometer for BP measurements.

Ejection glomerular fraction rate (eGFR) was calculated by MDRD formula:  $eGFR = 175 \times \text{serum creatinine}^{-1.154} \times \text{age}^{-0.203} \times 0.742$  (for females) where Mild renal inefficiency is if eGFR value is  $\geq 60$  and also  $<90 \text{ mL/min/1.73 m}^2$ .<sup>10,11</sup>

The data was analyzed by using statistical package SPSS-23.0 where quantitative variable were analyzed by t test and categorical data was analyzed through Chi-square. p value less than 0.05 was considered as significant.

## RESULTS

The mean age of control group was 41.5±6.5 years while of patients was 45±5.8 years. More percentage of men (n=34), BMI and blood pressure values was noticed in NA fatty liver group than controls. Table 1

The comparison of lipid profile between the two groups showed that mean cholesterol, Low density lipids (LDL) and triglycerides were higher in NA fatty liver group than the controls. Further the high density lipid (HDL) also known as good cholesterol was higher in controls than NA fatty liver disease patients. The mean glycated haemoglobin A1C (HbA1C) level also showed an increased prediabetic/diabetic trend in NA fatty liver group of patients (Table 2).

This study also compared the LFT, creatinine, hsCRP and eGFR between two groups and found mean increase in their levels in NA fatty liver group than controls (Table 3).

This study elaborated that out of the total cases NA fatty liver disease patients had a significant association with mild renal dysfunction, metabolic syndrome and diabetes being presented in 35%, 45% and 13.3% of patients respectively (Fig. 1).

Received on 19-06-2021

Accepted on 28-11-2021

Table 1: Comparison of demographics and anthropometric measurements between controls and NA fatty liver groups

Variable	Controls	NA fatty liver	P value
Age (years)	41.5±6.5	45±5.8	0.018
Gender (male)	22 (36.6%)	34 (56.6%)	<0.001
BMI (kg/m <sup>2</sup> )	22.3±2.1	25.4±2.7	<0.001
Systolic BP (mmHg)	117±10.1	123±10.2	<0.001
Diastolic BP (mmHg)	76±6.2	8.4±9.1	<0.001

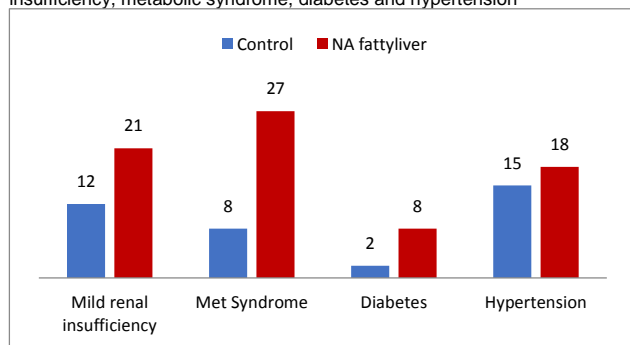
Table 2: Comparison of lipid profile and HbA1C between controls and NA fatty liver groups (n=120)

Variable	Controls	NA fatty liver	P value
Total cholesterol (mg/dL)	156±20	210±19.1	0.007
Triglyceride (mg/dL)	82±19.1	148±45.3	<0.001
HDL-C (mg/dL)	57±7.1	42±5.5	<0.001
LDL-C (mg/dL)	116±25	125±27	<0.001
HbA1c (%)	5.3±0.3	5.8±0.9	<0.001

Table 3: Comparison of LFT, creatinine, hsCRP and eGFR values between controls and NA fatty liver groups (n=120)

Variable	Controls	NA fatty liver	P value
AST (IU/L)	24±5.0	28±6.1	<0.001
ALT (IU/L)	18±5.2	27.5±9.7	<0.001
hsCRP (mg/dL)	0.6±0.4	1.5±0.8	<0.001
Creatinine (mg/dL)	0.7±0.1	0.8±0.1	<0.001
eGFR (mL/min/1.73 m <sup>2</sup> )	103±11.1	86.5±9.2	<0.001

Fig 1: Number of NA fatty liver cases and controls having mild renal insufficiency, metabolic syndrome, diabetes and hypertension



## DISCUSSION

The mean age of patients were 45±5.8 years with 56.6% being males having fatty liver diseases. Most men in Pakistan have an outdoor working hours making them eat more oily foods and sit for long day working activities thus making them more disposed towards fatty liver disease than women<sup>12,13</sup>.

Non-alcoholic fatty liver also increases the chance of obesity as well as raised lipid profile as observed in the present study. In females having NA fatty liver the risk increases with menopausal or pre menopause age. Similar results have been reported in studies elsewhere<sup>14,15</sup>.

This study also elaborates that there was a strong association of hypertension and metabolic syndrome with NA fatty liver infection as well as subclinical inflammation. The similar findings have been suggested in other researches in which a significant relation between these variables and NA fatty liver<sup>16-18</sup>.

Finally mild renal insufficiency was also seen in 35% of NA fatty liver disease patients. The results correlate with data reported from other part of the globe showing mild renal insufficiency in 22-28% of NA fatty liver disease patients<sup>19,20</sup>.

## CONCLUSION

There is a significant association of fatty liver (non-alcoholic), metabolic syndrome and subclinical inflammation on mild renal inadequacy in comparison with control groups.

**Conflict of interest:** Nil

## REFERENCES

- Musso G, Gambino R, Tabibian JH. Association of non-alcoholic fatty liver disease with chronic kidney disease: a systematic review and meta-analysis. *PLoS Med* 2014; 11(7): e1001680.
- Kim SH, Jo MW, Go DS, Ryu DR, Park J. Economic burden of chronic kidney disease in Korea using national sample cohort. *J Nephrol* 2017;30(6):787-93.
- Oh SW, Baek SH, Kim YC, Goo HS, Heo NJ, Na KY, et al. Mild decrease in estimated glomerular filtration rate and proteinuria are associated with all-cause and cardiovascular mortality in the general population. *Nephrol Dialysis Transplantation* 2012;27(6):2284-90.
- James MT, Hemmelgarn BR, Tonelli M. Early recognition and prevention of chronic kidney disease. *Lancet* 2010;375(9722):1296-1309.
- Chacko KR, Reinus J. Extrahepatic complications of nonalcoholic fatty liver disease. *Clin Liver Dis* 2016;20(2):387-401.
- Lee JI, Kim MC, Moon BS, Song YS, Han EN, Lee HS, et al. The relationship between 10-year cardiovascular risk calculated using the pooled cohort equation and the severity of non-alcoholic fatty liver disease. *Endocrinol Metabol* 2016; 31(1):86-92.
- Yang T, Chu CH, Hsu CH, Hsieh PC, Chung TC, Bai CH, et al. Impact of metabolic syndrome on the incidence of chronic kidney disease: a Chinese cohort study. *Nephrology* 2012; 17(6):532-8.
- Jing C, Xu S, Ming J, Cai J, Zhang R, Shen H, et al. Insulin resistance is not independently associated with chronic kidney disease in Chinese population: a population-based cross-sectional study. *Clinica Chimica Acta* 2015;448:232-7.
- Nam GE, Hwang SY, Chung HS, Choi JH, Lee HJ, Kim NH, et al. Implication of nonalcoholic fatty liver disease, metabolic syndrome, and subclinical inflammation on mild renal insufficiency. *Int J Endocrinol* 2018; 2018: 1835486.
- Levey AS, Coresh J, Greene T, Stevens LA, Zhang YL, Hendriksen S, et al. Using standardized serum creatinine values in the modification of diet in renal disease study equation for estimating glomerular filtration rate. *Ann Int Med* 2006;145(4):247-254.
- 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 Int Med* 2003;139(2):137-47.
- Lonardo A, Nascimbeni F, Ballestri S, Fairweather D, Win S, Than TA, et al. Sex differences in nonalcoholic fatty liver disease: state of the art and identification of research gaps. *Hepatology* 2019;70(4):1457-69.
- Long MT, Pedley A, Massaro JM, Hoffmann U, Ma J, Looma R, Chung RT, et al. A simple clinical model predicts incident hepatic steatosis in a community-based cohort: The Framingham Heart Study. *Liver Int* 2018; 38(8): 1495-1503.
- Depner CM, Stothard ER, Wright KP Jr. Metabolic consequences of sleep and circadian disorders. *Curr Diab Rep* 2014; 14(7):507.
- Sarwar R, Pierce N, Koppe S. Obesity and nonalcoholic fatty liver disease: current perspectives. *Diabetes Metab Syndr Obes* 2018;11:533-42.
- Petrović G, Bjelaković G, Benedeto-Stojanov D, Nagorni A, Brzački V, Marković-Živković B, et al. Obesity and metabolic syndrome as risk factors for the development of non-alcoholic fatty liver disease as diagnosed by ultrasound. *Vojnosanit Pregl* 2016 73(10):910-20.
- Oikonomou D, Georgiopoulos G, Katsi V, Kourek C, Tsioufis C, Alexopoulou A, Koutli E, Tousoulis D. Non-alcoholic fatty liver disease and hypertension: coprevalent or correlated? *Eur J Gastroenterol Hepatol* 2018;30(9):979-85.
- Streba LA, Vere CC, Rogoveanu I, Streba CT. Nonalcoholic fatty liver disease, metabolic risk factors, and hepatocellular carcinoma: an open question. *World J Gastroenterol* 2015;21(14): 4103-10.
- Le MH, Yeo YH, Henry L, Nguyen MH. Nonalcoholic fatty liver disease and renal function impairment: a cross-sectional population-based study on its relationship from 1999 to 2016. *Hepatology Communications*, 2019; 3(10):1334-46.
- Nampoothiri RV, Duseja A, Rath M, Agrawal S, Sachdeva N, Mehta M, Dhaliwal HS, Dhiman RK, Chawla Y. Renal dysfunction in patients with nonalcoholic fatty liver disease is related to the presence of diabetes mellitus and severity of liver disease. *J Clin Exp Hepatol* 2019;9(1):22-8.