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RESEARCH ARTICLE

CROSSTALK BETWEEN NAFLD AND CKD AND ITS EFFECT ON EGFR

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Abstract

Introduction:- NAFLD and CKD are associated with poor outcomes and high costs; they have become major public health problems owing to their increasing prevalence and incidence. The present study is determined to establish the association between NAFLD and CKD by studying the effect of NAFLD on eGFR.

Material and Methods:- This prospective observational study was conducted at MLN Medical College, SRN hospital, Prayagraj and Tejas Microdiagnostics. A total of 800 newly diagnosed CKD patients were enrolled. Among CKD patients NAFLD was diagnosed by USG whole abdomen, degree of steatosis, and severity was accessed by FIB-4 score. Renal function of the CKD patients was examined at the beginning of the study and six monthly follow up of serum creatinine was done. Study was completed after 18 months.

Results:- Out of 800 CKD patients, 600 patients were diagnosed with NAFLD while 200 patients did not show any symptom of NAFLD. These 200 patients were taken as control. A significant increase in serum creatinine and significant decline of eGFR was noted. CKD patients with NAFLD have significantly higher FIB-4 score than patients without NAFLD. Patients with high FIB-4 score (> 1.1) had significant decline of eGFR while in patients without NAFLD, decline of eGFR was not statistically significant.

Conclusion:- The findings of the study clearly establish a high prevalence of NAFLD in CKD patients and their impact on the renal functions. After excluding the other causes of CKD and Fatty liver disease, NAFLD can be considered as an independent risk factor of CKD.

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Introduction:-

Liver and kidney are vital organs that maintain homeostasis and injury to either of them triggers pathogenic pathways affecting the other. For example, non-alcoholic fatty liver disease (NAFLD) promotes the progression of chronic kidney disease (CKD), vice versa acute kidney injury (AKI) endorses the induction and progression of liver dysfunction (Sharma N et al., 2020). Indeed, NAFLD affects up to ~25–30% (Bellentani, 2017; Coresh J et al., 2007) and CKD affects up to ~10–15% of the general adult population in many parts of the world (Couser et al., 2011; Eckardt et al., 2013).

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It is well established that CKD is also a major risk factor for cardiovascular disease (CVD) and all stages of CKD are associated with an increased risk of cardiovascular morbidity, premature mortality and decreased quality of life (Hill et al., 2016). Recently, it has also been shown that NAFLD is an independent risk factor for CVD, regardless of the coexistence of cardio metabolic risk factors, such as obesity, hypertension, type 2 diabetes mellitus (T2DM) or metabolic syndrome (MetS) (Targher et al., 2016; Wild et al., 2018). Therefore, since NAFLD and CKD often occur with features of the MetS that adversely affect the kidney, elucidating the relative impact of NAFLD on the risk of incident CKD presents a substantial challenge to investigators working in this field of research (Byrne and Targher, 2020). The present study is determined to establish the association between NAFLD and CKD by studying the effect of NAFLD on eGFR.

Material And Methods:-

This was a prospective study conducted in Nephrology OPD, S.R.N. Hospital, M.L.N. Medical College, Prayagraj and Tejas Microdiagnostics, Prayagraj from March 2019 to August 2021. A total no of 800 Newly diagnosed cases of CKD with age between 35 to 65 years were included in the study while patients with diabetes, hypothyroidism, alcoholics (greater than one drink per day in women or two drinks per day in men) or patients were on hepatotoxic medications like Methotrexate, Azacytidine, HAART, Amiodarone, high dose oestrogen, glucocorticoids within 6 months were excluded from the study.

Figure 1:- FIB-4 Score

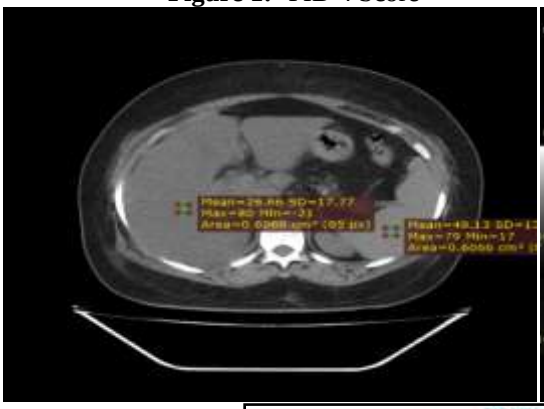

Figure 2:- USG.

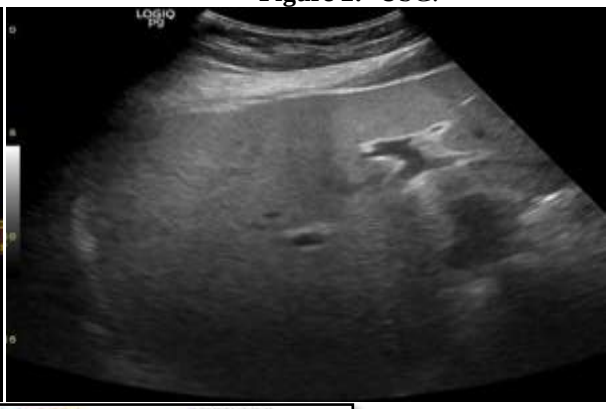

Figure 3:- CT

These CKD patients were suspected for NAFLD on the basis of symptoms and diagnosed by blood investigations, USG of whole abdomen and degree of steatosis. Severity was accessed by FIB-4 score. USG, CT scan and Fibroscan revealing presence of NAFLD is depicted in Fig 1, Fig 2 and Fig 3 respectively. After taking consent, venous blood was drawn and immediately sent to the laboratory for CBC, HbA1C, LFT, KFT, HBsAg, Anti HCV, eGFR, AST, ALT. eGFR was calculated by using MDRD 2009 equation. Requisition was made for USG ABDOMEN and KUB. FIB-4 score was used to access the severity of NAFLD and calculated by using standard formula for it. FIB-4 Score = (Age* x AST) / (Platelets x $\sqrt{}$(ALT)). Cut off value for FIB-4 score >1.100 was used for predicting CKD and NAFLD association.

All the base line investigations of these enrolled patients were examined at the beginning of the study and follow up was done after 6 months and 18 months respectively.

Results:-

Out of 800 CKD patients, 600 patients were diagnosed with NAFLD while 200 patients did not show any symptom of NAFLD and these 200 patients were taken as control. The demographic and physical parameters of CKD patients were revealed in Table 1.

Table 1:- Demographic and physical parameters of CKD patients.

S.N.	Total No. of patients n = 800		p value
	With NAFLD (n=600)	Without NAFLD (n=200)	
Age (in years)	50.13 ± 6.44	53.43 ± 5.95	---
Male	48 (68.6)	18 (60.00)	---
Female	22 (31.4)	12 (40.00)	---
Abdominal Circumference (in cm)	91.48 ± 5.11	91.30 ± 7.21	0.901
BMI	26.00 ± 3.92	22.90 ± 1.98	0.001

Age of CKD patients with NAFLD was recorded between 36 & 65 years, mean age was 50.13 ± 6.44 years, majority of the patients were aged 41-60 years (88.0%). Only 7.0% were aged ≤40 years and 5.0% >60 years of age. Approximately two-third of the study population was male (66.0%), rest were female. BMI of patients enrolled in the study was ranged between 14.7 & 35.8 kg/m^2 mean BMI was 26.00 ± 3.92kg/m^2. Data regarding CKD patients without NAFLD is revealed in the table. Association of NAFLD in CKD patients with different clinical variables were depicted in Table 2.

Table 2:- Association of NAFLD in CKD patients with different clinical variables.

S.N.	Total No. of patients n = 800		Statistical	
	With NAFLD (n=600)	Without NAFLD (n=200)	't' value	'p' value
Hb (g/dl)	10.44 ± 0.87	11.92 ± 1.53	-6.27	0.001
Platelet (lacs/mm^3)	2.26 ± 0.40	3.28 ± 0.44	-11.32	0.001
AST (IU/L)	56.02 ± 21	30.3 ± 5.38	6.16	<0.001
ALT (IU/L)	42.73 ± 20.63	40.15 ± 13.43	0.20	0.602
FIB-4 score	1.92 ± 0.47	0.81 ± 0.13	12.98	<0.001

Range of haemoglobin level of patients enrolled was 8.7 to 14.9 g/dl; mean haemoglobin level was 10.44 ± 0.87g/dl. Range of platelet counts was 1.42-3.94 lacs/cumm respectively, mean values of platelet counts were 2.26 ± 0.40 lac/cumm. Mean AST and ALT levels of patients was 56.02 ± 21 (range: 24-98) IU/L and 42.73 ± 20.63 (range: 16-88) IU/L respectively. FIB-4 levels ranged from 0.54 to 2.89 mean FIB-4 levels were 1.92 ± 0.47. Data regarding CKD patients without NAFLD is revealed in the table. Comparisons of renal functions between NAFLD & non-NAFLD patients at different follow-up intervals were showed in Table 3.

Table 3:- Comparison of renal functions between NAFLD & non-NAFLD patients at different follow-up intervals.

Time Duration	CKD with NAFLD		CKD without NAFLD	
	Creatinine (mg/dl)	eGFR (ml/min/1.73m2)	Creatinine (mg/dl)	eGFR (ml/min/1.73m2)
F0 (Baseline)	1.46 ± 0.12	49.51 ± 4.56	1.44 ± 0.12	50.14 ± 2.75
F1 (Six months)	1.49 ± 0.11	48.29 ± 4.54	1.45± 0.12	49.50 ± 2.68
F2 (Twelve month)	1.52 ± 0.11	47.46 ± 4.55	1.47 ± 0.12	48.97 ± 2.75
F3 (Eighteen month)	1.57 ± 0.18	46.24 ± 4.58	1.48 ± 0.70	48.37 ± 2.76
p value	0.001	0.001	0.665	0.213

At baseline mean eGFR of study population was 49.51 ± 4.56 ml/min/1.73 m^2, while at first, second and third follow up, mean eGFR levels were 48.29 ± 4.54, 47.46 ± 4.55 and 46.24 ± 4.58 ml/min/1.73 m^2 respectively. On comparing the eGFR levels at follow up visits with baseline eGFR levels, change in baseline eGFR was found to be significant.

At baseline mean serum creatinine level was 1.46 ± 0.12 mg/dl. At first, second and third follow up Serum creatinine levels were found to be higher than that at baseline (1.49 ± 0.11 mg/dl; 1.52 ± 0.11 mg/dl and 1.57 ± 0.18 mg/dl). Significant change in Serum creatinine levels were observed on follows up.

Discussion:-

This prospective study enrolled the CKD patients aged 50.13 ± 6.44 years attending nephrology OPD, S.R.N. Hospital, Prayagraj. In this study, NAFLD was an independent risk factor associated with the progression of CKD.

We reported 75% NAFLD in CKD patients based on USG findings like bright hepatic echoes, fatty liver change, vascular blurring of portal and hepatic veins, increased hepatorenal echogenecity and increased renal parenchymal echogenecity and remaining 25% patients had USG evidence related only to medical renal disease. Mikolasevic I et al., 2013, also reported a high prevalence of (85.5%) NAFLD, in our study we observed male dominance with 68.6%. Similarly Choe et al. also reported in two groups of their study a male dominance (55.9% and 65.5% respectively) (Chen PC et al., 2019). Who concluded that as compared to without CKD those with CKD were more male and had lesser platelet count.

FIB-4 score (Mean ± SD) of CKD patients with co existing NAFLD was found to be 1.92 ± 0.47 which was very high with the cut off value of 1.1, while FIB-4 score (Mean ± SD) of patients without NAFLD was found to be 0.812 ± 0.13. This was consistent with findings of study conducted by Xu H W et al., 2016 and a recent study conducted by Sesti G et al., 2014**,** Wijarnpreecha K et al., 2018 and McPherson et al., 2017 reported that, the FIB-4 score has the best diagnostic accuracy for advanced fibrosis.

Renal function of these patients was accessed. The baseline serum creatinine of CKD patients having NAFLD was found higher than those not having NAFLD. Further in the study six monthly evaluation of serum creatinine at 6 months, 12 months and 18 months was done in all the patients. Serial eGFR calculation of the patients was done using MDRD equation. It was found that estimated decline in eGFR was greater in patients with NAFLD (p value = 0.0011) than those without NAFLD (p value = 0.2113) and was found statistically significant, i.e. patients with NAFLD had rapid worsening of renal symptoms than those without NAFLD. This was consistent with finding study conducted by Jang HR et al., 2018. Who found that during follow-up, decline in eGFR was greater in patients with NAFLD (−0.79% per year, 95% CI −1.31%, −0.27%) compared to those without it (0.30%, 95% CI −0.14%, 0.76%; p value= 0.002). Chinnadurai R et al., 2019 also concluded similar results. Chen PC et al., 2019 also concluded that Subjects with NAFLD had a higher proportion of CKD compared to those without NAFLD (24.1% vs. 17.1%, $p < 0.001$).

Conclusion:-

The findings of the present study show a high prevalence of NAFLD in CKD patients and their impact on the renal functions. After excluding the other causes of CKD and Fatty liver disease, NAFLD can be considered as an independent risk factor of CKD.

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