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ASSOCIATION BETWEEN CHRONIC KIDNEY DISEASE & NON-ALCOHOLIC FATTY LIVER DISEASE & ITS EFFECT ON EGFR

General Medicine

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ABSTRACT

Background: Although relationship between NAFLD and CKD has been assessed in a number of studies, however, most of the studies have assessed the prevalence of CKD in NAFLD and there are limited studies evaluating the prevalence of NAFLD in CKD patients. Moreover, most of the concerned literature is from overseas and there is lack of evidence from Indian subcontinent. The present study is an attempt to fill that gap. **Material And Method:** After enrolment, demographic information was obtained, personal habits were enquired and presenting signs and symptoms were noted. Subsequent to this, 2 ml blood sample was obtained under aseptic conditions for hematological assessment, liver and kidney function. Estimated glomerular filtration rates (eGFR) were calculated. Urinary samples were analyzed for proteinuria. Liver fibrosis was assessed using FIB-4 score. All the patients thereafter underwent abdominal ultrasound for diagnosis of NAFLD. **Result:** We enrolled 78 patients of previous study and 22 newly diagnosed patients of CKD during this study. Out of 100 patients of CKD, 70 (70.0%) were diagnosed as NAFLD. eGFR levels of NAFLD patients was significantly lower than that of Non-NAFLD patients (46.14±5.98 vs. 49.45±3.96 ml/min/1.73 m³). **Conclusion:** Prevalence of NAFLD was higher in the CKD patients. Mean eGFR of CKD patients with NAFLD were significantly lower compared to that of CKD patients without NAFLD.

KEYWORDS

NAFLD, CKD, eGFR

INTRODUCTION

Despite the availability of substantial evidence between CKD and NAFLD, there is considerable variability in prevalence of NAFLD in CKD patients of different ethnicities showing a possible role of ethnic, geographical, dietary, lifestyle and other factors. Moreover, the correlation between CKD severity and NAFLD stage has also shown a considerable difference across different studies[1-7], hence it is important to study the relationship between CKD and NAFLD in local perspective and to understand as to how ethnic, geographical, dietary, lifestyle and other factors influence the relationship between CKD and NAFLD in our population. A previous study from our department[8] has shown high prevalence of NAFLD in CKD patients. Hence, the present study was planned as a continuation study of this previous work to determine the association between Chronic Kidney disease & non-alcoholic fatty liver disease & its effect on eGFR in a north Indian population.

MATERIAL AND METHOD

This Cohort study was conducted in SRN Hospital, MLN Medical College, Allahabad, U.P. India. All the patients of CKD attending OPD & IPD of Gen. Medicine and Nephrology, diagnosed by suggestive symptoms and confirmed by physical examination and laboratory investigations were included.

Inclusion Criteria

1. Age 18-65 years
2. Either sex with Chronic kidney disease diagnosed by USG, KFT, physical examination and having NAFLD

Exclusion Criteria

1. Patients with known diagnosis of metabolic syndrome, diabetes and/or hypothyroidism.
2. Those on hepatotoxic medication (amiodarone, barbiturates, glucocorticoids, etc.).

The clinical study was started after obtaining Institutional Ethical Committee approval. After enrolment, demographic information was obtained, personal habits were enquired and presenting signs and symptoms were noted. All the patients underwent anti HCV and HBsAg antigen profiling to rule out viral hepatitis. Body weight and height were measured and body mass index was calculated. Blood pressure measurements were done. Subsequent to this, a 2 ml blood sample was obtained under aseptic conditions for hematological assessment, liver function tests, Renal function assessment and HbA_{1c}. Estimated glomerular filtration rates (eGFR) were calculated. Urinary samples were analyzed for proteinuria. Liver fibrosis was assessed using FIB-4 score. All the patients thereafter underwent abdominal ultrasound for diagnosis of NAFLD. Presence and grade of NAFLD was noted. The patients were subsequently followed up at 1, 3 and 6 months intervals. Changes in eGFR and S. creatinine levels were assessed. The data so collected was entered into computer using Microsoft Excel 2013 software and was subjected to statistical analysis.

RESULT

The present study conducted in the Department of Medicine, M.L.N. Medical College & Hospital, Prayagraj was continuation of similar study conducted to study the association of NAFLD and CKD and to find the effect of eGFR on NAFLD. We enrolled 78 patients of previous study and 22 newly diagnosed patients of CKD during this study.

Age of patients enrolled in the study ranged between 36 & 65 years, mean age was 51.12±6.45 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%). Out of 100 patients of CKD, 70 (70.0%) were diagnosed as NAFLD. Grade 2 and Grade 3 NAFLD was observed in 28 patients each (40% each of NAFLD), and rest had Grade 1 NAFLD. At baseline mean eGFR of study population was 47.13±5.65 ml/min/1.73 m^2, while at first, second and third follow up, mean eGFR levels were 46.34±7.26, 46.44±6.16 and 47.22±12.97 ml/min/1.73 m^2 respectively.

eGFR levels of NAFLD patients was significantly lower than that of Non-NAFLD patients (46.14±5.98 vs. 49.45±3.96 ml/min/1.73 m³).FIB-4 score of NAFLD cases was found to be significantly higher than that of Non-NAFLD cases (1.93±0.46 vs. 0.80±0.15).On evaluation in NAFLD and non-NAFLD patients separately, the only significant correlation was observed between baseline FIB-4 and third follow-up eGFR values in NAFLD group (r=-0.343; p=0.004), none of the other correlations were significant statistically (p>0.05).

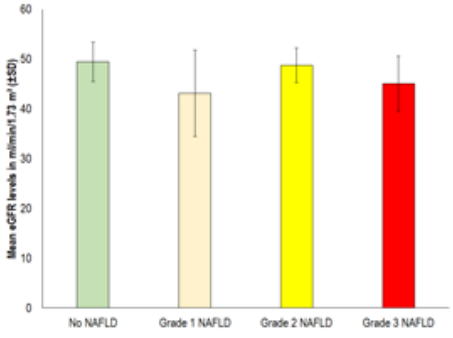

Fig.1: Association of Severity of NAFLD with eGFR

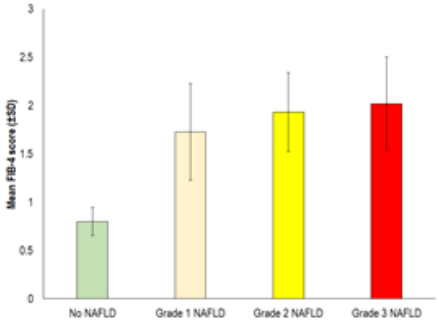

Fig.2: Association of NAFLD Severity with FIB-4 in CKD Patients

DISCUSSION

In the past, non-alcoholic fatty liver disease, a liver disease sharing multiple risk factors with CKD has been shown to affect a large proportion of CKD patients and vice versa, thus indicating the existence of a relationship between the two disorders. Hence, the present study was planned to study the association between Chronic Kidney disease and non-alcoholic fatty liver disease in terms of prevalence of NAFLD in CKD patients and to correlate the prevalence and severity of NAFLD with renal functions in terms of eGFR.

In the present study, prevalence of NAFLD was 70%. A high prevalence of NAFLD has been reported to be a characteristic feature of CKD in different previous studies. Compared to the present study, where a total of 70% CKD patients were found to have NAFLD too, a number of other studies reported it to be higher than 70% (78.69% to 87.9%)[9,10,11,12,13,14,15]. There are studies that have reported the prevalence of NAFLD to be as high as 96% in CKD patients[16]. However, there are a few studies that report it to be in 25-50% range[17]. There are some other studies that report it to be even <25%[18,19,20,21].In general, most of the studies report a high prevalence of NAFLD in CKD patients as observed in the present study. As far as reports of low prevalence of NAFLD in CKD patients in some studies it might be owing to use of strict criteria. Differences in prevalence of NAFLD in different studies could also be attributable to difference in patient profile and design of the study.[14,18,19].

In the present study, among NAFLD patients, Grade 1, 2 and 3 NAFLD was seen in 20%, 40% and 40% cases respectively. Mean FIB-4 was 1.59±0.65. Compared to findings of the present study, Rajender et al.[14] in their study had a dominance of Grade 2 NAFLD (55.64%) and had only 13.5% patients with Grade 3 NAFLD. Most of the other studies did not assess the severity of NAFLD in terms of grade.

In the present study, mean eGFR scores of CKD patients with NAFLD were significantly lower while mean serum creatinine levels were significantly higher as compared to that of CKD patients without NAFLD at baseline and all the three follow-up intervals. Further, there was a significant but non-linear relationship of NAFLD and its grades with eGFR and serum creatinine levels. However, Choe et al.[20] in one of their two subgroups found lower creatinine and higher eGFR to be significantly associated with NAFLD whereas in the other subgroup, they did not find a significant difference between two groups with respect to serum creatinine but found higher eGFR to be significantly associated with NAFLD. In the study of Jang et al.[22] and Chinnadurai et al.[19]too CKD patients with NAFLD had significantly higher eGFR and significantly lower serum creatinine / proteinuria. Adrian et al.[21] too failed to find out a significant association of kidney function with the prevalence of moderate-to-severe hepatic steatosis. Contrary to this, Kasim et al.[15] in their study found a significant association of NAFLD with higher grades of CKD (lower eGFR) and higher prevalence of A3 grade of proteinuria. In a more recent study, Behairy et al.[23] too observed a significant association of NAFLD and its severity with decreased glomerular function and an increased CKD stage as observed in the present study.

The findings of present study and their comparison with previous studies shows that although there is high prevalence of NAFLD in CKD patients yet except for the metabolic factors the association of other factors in determining this relationship is not homogeneous. Moreover, the impact of NAFLD on renal function (eGFR) is also a matter of scrutiny. The interactions of NAFLD with CKD and corresponding renal function parameters is still a matter of controversy with variable results in different studies.

There were several limitations of the present study such as absence of retrospective data related with the duration of CKD and information related with other co-morbid conditions, personal habits, metabolic profile, lipid levels and inflammatory markers which could also have a determining role. Moreover, in the present study we could not establish whether CKD was the primary disease or NAFLD was the primary disease. Hence, further longitudinal studies in newly diagnosed CKD patients are recommended to evaluate the prevalence of NAFLD at baseline and subsequently at different long-term follow-up intervals with inclusion of exhaustive medical history, personal and dietary habits, metabolic profile and other hematological and biochemical parameters that could play the role as a risk factor in determining the clinical course of CKD as well as in the occurrence of incident cases of NAFLD in these patients.

CONCLUSION

Prevalence of NAFLD was higher in the CKD patients. Mean eGFR of CKD patients with NAFLD were significantly lower compared to that of CKD patients without NAFLD. There was a significant but non-linear relationship of NAFLD and its grades with eGFR and serum creatinine levels.

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