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Association of Oxidative Stress with Renal Function in Cigarette Smokers

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ABSTRACT

Background and aim: Cigarette smoking is known to be associated with increased oxidative stress and renal function, both known to be associated with cardiovascular disease. The present study aimed to associate oxidative stress with kidney function in cigarette smokers.

Material and methods: The present study was carried out in the department of biochemistry, Santosh medical college, Ghaziabad, National Capital Region (NCR), India. In this study, 280 subjects were enrolled, out of which 140 were smokers, and 140 were non-smokers healthy individuals. The subjects who had been smoking for two or more than two years were included. All the subjects were in 20 – 60 years of age.

Results: The mean levels of blood urea (p=0.019), serum creatinine (p=0.013), urinary albumin (p<0.0001), urinary albumin creatinine ratio (uACR) (p<0.0001), Cystatin C (p=0.01) and Malondialdehyde (MDA) (p<0.0001) were increased in smokers as compared to non-smokers while the concentration of serum uric acid (p=0.02), urinary creatinine (p=0.01) and estimated glomerular filtration rate (eGFR) (p<0.0001) levels were decreased in smokers as compared to non-smokers. Malondialdehyde was negatively and significantly correlated estimated glomerular filtration rate (r=-.442, p<0.05) and positively and significantly correlated with uACR (r=0.536, p<0.01) and Cystatin C (r=0.428, p<0.05).

Conclusions: The present study concluded that Smoking increases renal parameters and oxidative stress and a significant association between oxidative stress and renal parameters in smokers.

1. Introduction

The rising global prevalence of chronic kidney disease, as well as a significant increase in the number of patients in the later stages, has prompted health systems to devote greater resources to identifying possibly modifiable preventative factors. Chronic kidney disease has a large social and economic cost, and it necessitates a set of coordinated criteria among health professionals to guarantee the best possible prevention, diagnosis, and treatment. Furthermore, recognizing renal illness as a cardiovascular risk factor and the significant morbidity and mortality rates associated with it emphasize the need for preventative interventions for potentially avoidable variables like cigarette smoking.[1] Tobacco use may also be a risk factor for chronic renal disease on its own. Cardiovascular and renal illnesses are strongly related, and there is ample evidence that smoking hastens the onset of severe cardiovascular outcomes.[2] Smoking is a prominent cause of avoidable deaths worldwide, and it raises the risk of chronic renal diseases. Longer smoking periods were linked to an increased risk of chronic renal disease development, especially in individuals with an estimated glomerular filtration rate of less than 45 ml/min/1.73 m^2 and proteinuria of less than 1.0 g/g. On the other hand, former smokers had a lower chance of unfavorable renal outcomes as they went longer without Smoking.[3, 4] According to a study published in 2016, smoking is linked to a high glomerular filtration rate and a high prevalence of proteinuria, implying a hyper-filtration mechanism that could lead to chronic kidney disease.[5] Because of the growing number of patients, the high risk of progression to end-stage renal disease, and the poor prognosis in terms of morbidity and mortality, chronic kidney diseases are a significant burden on the healthcare system.[6] Chronic renal diseases are caused by two key controllable factors: sleep and smoking.[7] Every element of physiology is influenced by sleep due to the increased availability of artificial indoor lights, smartphones, and daily life activities. According to a population-based survey, 22.3 percent of males and 28.9 percent of women aged 16 reported to their doctors that they were having problems sleeping.[8]

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2. Material and methods

The present study was carried out in the Department of Biochemistry Santosh Medical College, Ghaziabad, from September 2019 to April 2021. This study was approved by Institutional Ethical Committee [F.No. SU/2020/536(48)] informed consent was taken from all the patients prior to the study. All the subjects were divided into two groups. The participants in the first group were non-smokers and patients in the second group were smokers.

Inclusion and exclusion criteria

In this study, we included all the subjects who had been smoking for two or more years, all the participants were male, and their age was 20-60 years. Patients with Diabetes Mellitus, Subjects with Hypertension, Chronic Diseases, known hepatitis B, C, or HIV/AIDS, and Patients consuming Alcohol and other Drugs were excluded from the study.

Collection of blood sample

A 5 ml venous blood sample was collected from the medial cubital from each participant into a plain vial. After centrifugation at 1500 rpm for 3 minutes, the serum was assayed. All the parameters were measured by the enzymatic method by using an automated analyzer (Beckman Coulter- AU-480). Homocysteine levels were analyzed by enzymatic assay on a full autoanalyzer, and its reference range was 4.44-13.56 µmol/L.For the screening of urinary albumin and urinary Creatinine concentration, a first-morning void (timed) Quantitative midstream urine sample was taken. Urinary albumin (Bromocresol Green Method) and urinary creatinine (Jaffe's Method) were measured by using a fully automated analyzer (Beckman Coulter- AU-480), Cystatin c was analyzed by quantitative turbidimetric immunoassay, and glomerular filtration rate was estimated by Modification of Diet in Renal Disease (MDRD) equation.[9]

Statistical analysis

Statistical analysis was performed using SPSS software, version 16. A two-sided P-value <0.05 was considered statistically significant. The statistical differences between the groups were determined by student independent sample t-test.

3. Results

The mean and standard deviation of all the biochemical parameters is depicted in Table 1. The mean levels of urea (p=0.019), serum creatinine (p=0.013), urinary albumin (p<0.0001), urinary albumin creatinine ratio (p<0.0001), Cystatin C (p=0.01), and malondialdehyde (p<0.0001) were found to be increased significantly in smokers as compared to non-smokers. While the mean levels of serum uric acid (p=0.02), estimated glomerular filtration rate (p<0.0001), and urinary creatinine (p=0.01) were found to be decreased significantly in smokers as compared to non-smokers. Fig. 1 represent the co-efficient correlation analysis. A positive and significant association was observed between malondialdehyde and Cystatin C (Fig. 1) and malondialdehyde and urinary albumin creatinine ratio (Fig. 2), while a significant negative correlation was observed between malondialdehyde and estimated glomerular filtration rate (Fig. 3).

Table:1 Showed biochemical parameters of studied subjects.

Parameters	Non-Smokers	Smokers	P-value
Blood Urea (mg/dl)	34.77 ± 19.54	41.37 ± 26.67	=0.019
Serum Creatinine (mg/dl)	0.92 ± 0.51	1.09 ± 0.63	=0.013
Serum Uric Acid (mg/dl)	5.05 ± 1.98	4.54 ± 1.71	=0.02
Urinary Albumin (mg/day)	18.69 ± 2.27	37.54 ± 13.52	<0.0001
Urinary Creatinine (mg/day)	963.83 ± 326.24	874.46 ± 245.26	=0.01
Urinary Albumin Creatinine Ratio (uACR*) (mg/gm)	19.36 ± 15.24	43.38 ± 30.63	<0.0001
e-GFR (mL/Min/1.72m^2)**	102.28 ± 31.45	78.37 ± 28.74	<0.0001
Cystatin C (mg/L)	0.79 ± 0.26	0.87 ± 0.29	=0.01
Malondialdehyde (MDA) (nmol/mL)	1.56 ± 1.01	2.81 ± 1.76	<0.0001

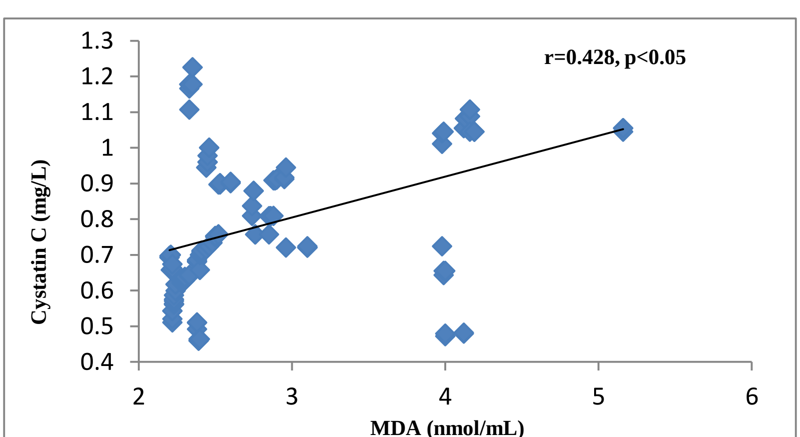

Fig. 1. Correlation between MDA and cystatin C in cigarette smokers.

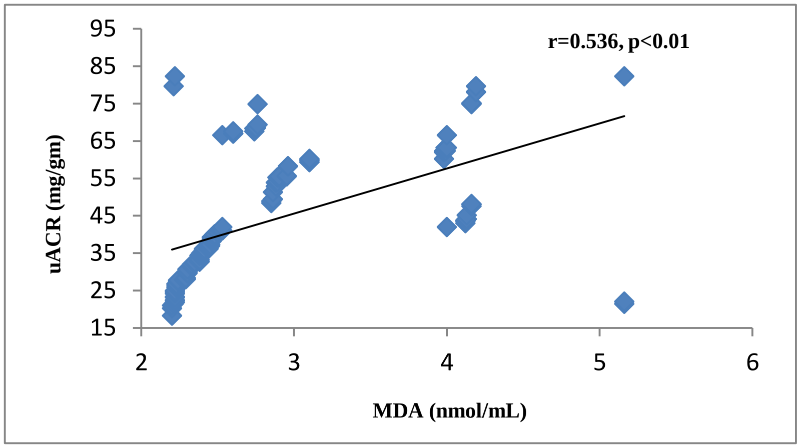

Fig. 2. Correlation between malondialdehyde (MDA) and urinary albumin creatinine ratio (uACR) in smokers.

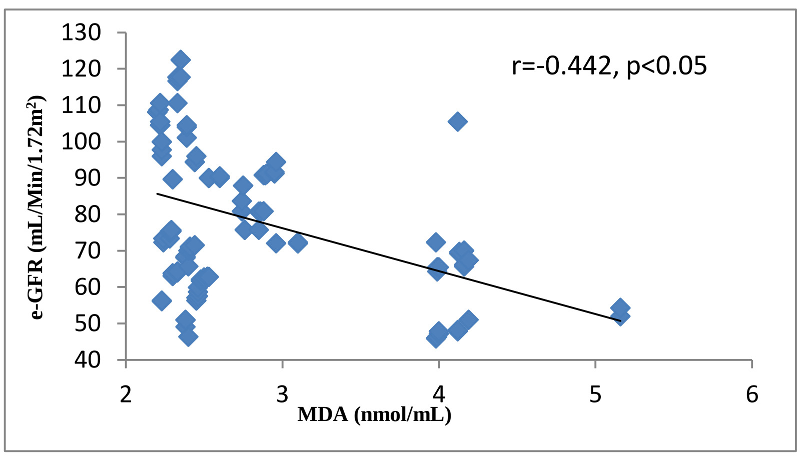

Fig. 3. Correlation between malondialdehyde and estimated glomerular filtration rate in smokers.

4. Discussion

Nicotine, a primary tobacco alkaloid, has been linked to renal failure in people who smoke. The mechanisms of smoking-related kidney injury remain unknown, but vascular and tubular effects are likely to be involved. Smoking may make the kidney more susceptible to ischemia insults and hasten the transition of acute renal injury to chronic kidney disease.[10] In frequent cigarette smokers, chronic nicotine exposure hastens the onset and progression of kidney disease. As smoking pack–years grew, the chance of unfavorable renal outcomes increased progressively.[11] Nicotine has been proven to increase oxidative stress in the kidneys and lead to kidney failure.[12] Clinical evidence demonstrates that cigarette smoking has a deleterious impact on renal function, kidney dimensions,[13] and the development of chronic kidney disease due to a variety of etiologies, including diabetes and hypertension.[14] One of the most major modifiable renal risk factors is cigarette smoking.[3] This study showed increased levels of serum urea, serum creatinine, urinary albumin, urinary albumin creatinine ratio, and malondialdehyde in smokers compared to non-smokers subject. In contrast, the level of serum uric acid and estimated glomerular filtration rate were found to decrease significantly in smokers compared to non-smokers. Our results are following the previous studies.[2] Smoking can also cause insulin resistance and advanced glycation end products, both of which can lead to kidney damage. Smoking is known to raise blood pressure and urine albumin excretion and influence intrarenal hemodynamic4. Furthermore, nicotine causes podocyte death in vitro by generating reactive oxygen species and signaling through downstream mitogen-activated protein kinase.[15] In animal models, nicotine exacerbates renal injury, resulting in acute kidney injury, diabetes mellitus, acute nephritis, and subtotal nephrectomy. Nicotine encourages mesangial cell growth and hypertrophy. Nicotine causes temporary increases in blood pressure in humans and reductions in eGFR and effective renal plasma flow.[16] In one study, mice exposed to smoke had higher transforming growth factor-beta levels, which is recognized as a key mediator of renal fibrosis. Inflammation, oxidative stress, and endothelial dysfunction are documented pathophysiological effects of smoking. According to studies, smoking enhances superoxide dismutase activity, which causes kidney fibrosis in rats exposed to smoke.[17] A study depicted that the creatinine-based estimated glomerular filtration rate rises as the number of cigarettes consumed rises. In contrast, the cystatin C-based estimated glomerular filtration rate falls and concluded that the creatinine-based estimated glomerular filtration rate is not the best indicator of the relationship between smoking and renal function.[18] In this study increased levels of Cystatin C was observed in smokers as compared to no smokers. It was statistically significant (p=0.01). The principal determinant of serum Cystatin C concentration is glomerular filtration, making Cystatin C an endogenous glomerular filtration rate measure. Cystatin C outperformed serum creatinine as a glomerular filtration rate indicator. Serum cystatin C levels dropped considerably in the current investigation.[19] Cystatin C has been demonstrated to have a strong relationship with blood artery wall flexibility, suggesting that it could be a valuable marker for asymptomatic early arteriosclerosis.[20] Inflammatory cytokine levels, blood pressure, and blood coagulation factor propensity are all said to be substantially associated with cystatin C levels.[21] Furthermore; cystatin C is a biomarker for cardiovascular events that can be used to predict them.[22] This shows that cystatin C is a potent marker of cardiovascular illness and a sensitive early predictor of kidney dysfunction. Funamoto et al. studied 86 subjects who visited the smoking cessation clinic and, after one year follow up, observed that the level of cystatin C was decreased significantly after 3 months of smoking cessation and remained unchanged after 3 months to 1 year.[23] Upon correlation analysis found that malondialdehyde was positively associated with urinary albumin creatinine ratio (r=0.355) and negatively correlated with cystatin C (r= -0.449) and estimated glomerular filtration rate (r= -.520). Many studies showed that smokers of cigarettes responsible for lipid peroxidation increased malondialdehyde levels. As the no. of cigarettes smoked per day increased, the levels of malondialdehyde increased. So the results of the present study revealed that, as the smoked per day increased, the level of estimated glomerular filtration rate and homocysteine increased while the levels of urinary albumin creatinine ratio decreased. Lan et in their study found that the increased oxidative stress in smokers is responsible for the deterioration of renal function.[15] Chen et al., in their cross-sectional study, observed elevated levels of homocysteine. Also, they found an association of smoking with the reduced serum superoxide dismutase (SOD). The elevated homocysteine (Hcy) level is probably associated with changes in metabolism after the damage of the body from oxidation.[24] Another study by Huang et al. observed an association between cigarette smokings with renal function deterioration in hypertensive patients and concluded that this association between cigarette smoking and renal function deterioration was probably mediated by elevated homocysteine.[25] Chai et al., in a meta-analysis, observed elevated levels of serum Cystatin C in patients with Chronic Obstructive Pulmonary Disease (COPD) compared to controls. In their study, serum Cystatin C levels were reversely correlated with FEV1% pre or FEV1/FVC. The results of their study provided an improved understanding of the roles of Cystatin C in Chronic Obstructive Pulmonary Disease development and progression.[26]

5. Conclusions

In conclusion, this study found that smoking is a significant risk factor for developing chronic kidney disease. The renal parameters like serum urea, serum creatinine, cystatin C, urinary albumin creatinine ratio, and malondialdehyde were increased, and uric acid, e-GFR, and urinary creatinine were decreased smokers as compared to non-smokers. The present study showed a positive association between renal function and oxidative stress. Thus, cigarette smokers are more prone to the development of cardiovascular disease.

Conflict of Interest

The authors declared that there is no conflict of interest.

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