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Cigarette smoking and its effect on glomerular filtration rate (GFR) in apparently healthy individuals: A prospective study from heart of India

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Abstract
Background: Early-stage diabetic kidney disease (ESDKD) can predict future renal failure. ESDKD is usually accompanied by glomerular hyper filtration and albuminuria. Several cross sectional studies across the world reported cigarette smoking and its association with elevated GFR in apparently healthy individuals.
Aims and Objective: To evaluate the relationship between cigarette smoking and alteration in GFR and urinary albumin excretion in apparently healthy male subjects.
Material and methods: Two hundred and thirty subjects were studied after dividing them in to Group S (n=115; smokers) and Group NS (n=115; non smokers) in the Department of Medicine, Gandhi Medical College and Hamidia Hospital, Bhopal from January 2015 to February 2016. A detailed history including age, clinical evaluation including systolic and diastolic blood pressure and laboratory investigation including hemoglobin, serum creatinine and GFR were performed in all the subjects.
Results: The present study included 100 smokers and 100 non smokers. The mean age of the studied patients was 39.85 ±8.15 among smokers and 39.80±7.28 among non-smokers. Among smokers 49% smokers have proteinuria. Proteinuria was significantly associated with pack years among current smokers (p=0.011). Smokers with >40 pack years were found to be significantly associated with proteinuria. Among smokers 67% have high gfr. As compared to non-smokers, current smokers have high GFR (mean=120.06±18.53) High GFR was significantly correlated in smokers with pack year>40 (p=0.025). The average GFR in current smokers is 120.06±18.53.
Conclusion: Current smokers have altered glomerular filtration rate and proteinuria as compared to non smokers. Glomerular filtration rate, proteinuria, high SBP and high DBP significantly correlated with pack years.

Keywords: smokers, apparently healthy individuals, glomerular filtration rate, proteinuria

Introduction

Smoking has emerged as one of the major risk factor of renal injury but has not been extensively studied in Indian population. Although smoking is related to ESRD in the long term, the effect of cigarette smoking on renal function in early-stage kidney disease is unclear [1].

Chronic kidney disease (CKD) causes a large number of morbidity and mortality, cardiovascular disease (CVD) being the most common cause of mortality among them.

This rise is expected to continue, particularly in developing countries like India, where smoking and other cardiovascular risk factors are increasing substantially [2, 3], and will be paralleled by rising CKD-and ESRD-related costs [4, 5].

Detailed investigation has not been done, how smoking affects the kidney. In recent years, it has become apparent that smoking has a negative impact on renal function, being one of the most important remediable renal risk factors [6]. In this study, we examined the effects of cigarette smoking on renal function and albuminuria in apparently healthy participants.

Material and Methods

A prospective study was performed on 230 subjects after dividing them in to Group S (n=115; smokers) and Group NS (n=115; non smokers) in the Department of Medicine, Gandhi Medical College and Hamidia Hospital, Bhopal from January 2015 to February 2016. Institutional Ethics Committee approval and written informed consent was obtained from each patient.

Subjects having age between 20-50 years, current smokers, having normal liver functions and were non hypertensive non diabetic were included in present study. Diabetic, hypertensive, patients with pulmonary disease and primary renal disorder at the time of presentation or diagnose later in the study were excluded from the study.

Clinical examination including medical history, physical examination measurement like height and weight. Self-reported questionnaire on life style characteristics such as smoking habit frequency of alcohol drinking were recorded in pre-approved proforma.

Blood sampling for the measurement of RFT, LFT, CBC, FBS, PPBS sand urinalysis r/m and dipstick urinalysis. Early morning blood samples were drawn. Serum creatinine was estimated by jaffe method. We calculated estimated GFR by using Gault Cock and Croft equation. Urine samples were collected as clean catch mid-stream, early morning specimens. The result of dipstick urinalysis was interpreted as +1, +2, and

+3. After 5 minutes of rest BP was measured in a sitting room. BP was measured in supine position right arm with a standard sphygmomanometer.

A pre-approved questionnaire about the smoking habit consisted of smoking status, average number of cigarettes smoked per day and duration of cigarette smoking for current smokers, and years since quitting for past smokers were recorded in excel sheet. The number of pack-years of exposure (that is, the number of packs of cigarettes smoked per day multiplied by the number of years smoked) was calculated to see the long-term adverse effect of smoking on renal function. GFR was calculated and proteinuria was estimated. Glomerular hyper filtration was diagnosed if estimated GFR was more 120 ml/min per 1.73 m2. Proteinuria was defined as 1+ or higher (30 mg/dl or higher) for dipstick examination.

All the data analysis was done using IBM SPSS ver. 20 software. Frequency distribution and cross tabulation was used to prepare tables. The quantitative data was expressed as mean ± standard deviation (SD) where qualitative data were expressed in percentage. The data was analyzed by using chi square test and the difference in means were analyzed by using student T Test. Significance level for tests was set at 5%.

Results

All the subjects in both the groups were male. The mean age of subject in Group S and Group NS was 42.95 ±6.12 and 41.82±6.21 respectively. Most of the subjects belong to age group of 41 -50. In Group S, 52% had proteinuria and in Group NS only 6.5%% had proteinuria. Proteinuria was significantly associated with pack years among Group S (p=0.011). Subjects in Group S with >40 pack years were found to be significantly associated with proteinuria (p=0.001). Most of the subjects of Group S (69%) have high GFR.

As compared to subjects of Group NS, subjects of Group S have high GFR (mean=126.26±18.53). High GFR was significantly higher in group S with pack year>40 (p=0.025). The average GFR in Group S was 126.26±18.53. High systolic and diastolic blood pressure is found among Group S subjects as compared to Group NS (p>0.05).

Table 1: Showing different parameters in study cohort

Parameters	Group S	Group NS	P value
Age (years)	42.95 ±6.12	41.82±6.21	NS
Hemoglobin (gm %)	12.42±1.33	11.74 ±0.67	NS
Serum Creatinine	0.62±0.12	0.66±0.13	0.012
GFR	126.26±18.53	113.26±16.52	<0.001
SBP (mmHg)	131.21±4.52	128.23±5.62	NS
DBP (mmHg)	76.52±2.24	74.26±2.42	NS

Data is expressed as mean± SD, NS; not significant, SBP; systolic blood pressure, DBP; diastolic blood pressure, GFR; glomerular filtration rate.

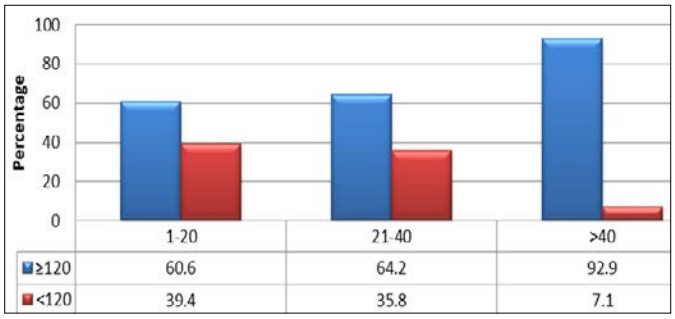

Fig 1: Comparing pack year with glomerular filtration rate

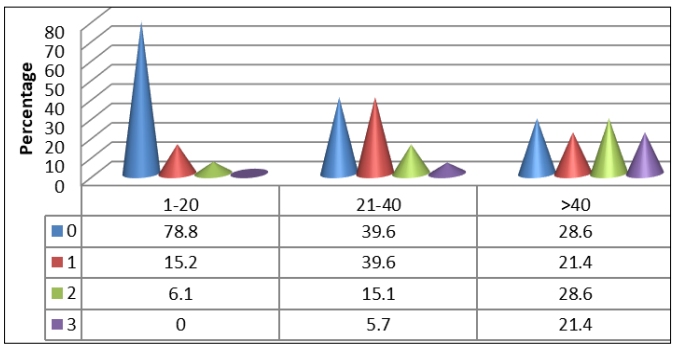

Fig 2: Comparing pack year (as 0, 1, 2 and 3) and urine albumin level

Discussion

All the patients were male in Group S whose age range from 20-50 years and mean age was 42.95 ±6.12 year, had high GFR (69%) which was significantly correlated with pack years (p<0.01) compared to Group NS. In agreement to present study Ekberg *et al.* [7] who reported a significantly higher prevalence of glomerular hyper filtration (41% vs. 18%) in the smokers compared to non-smokers.

In present study, among these current smokers, high GFR was significantly more common among smokers with pack year ≥40. (p=0.025) these result were also shown in the study done by Ishizaka N *et al.* [8]. Cross-sectional in 7,078 Japanese male participants in whom they found high eGFR (>90.73ml/min/1.73 m^2) current smokers consuming 20-39 cigarettes per day.

Among 100 current smokers, GFR was found to highest among 41 to 50 age group smokers and age was insignificantly correlated with GFR (p=0.61). There was significantly higher prevalence of glomerular hyperfilterarion among current smokers than in the non smokers, and is related to amount of cigarette smoking. Pintosiestsma *et al.* [9]. Cross sectional study, in 7476 adults in a dutch community found elevated e GFR (>Mean±2SD) in current smokers consuming up to 20 cigarettes per day and in those consuming more vs. never smokers was 1.82 (1.31~2.53) and 1.84 (1.12~3.02) respectively adjusted for age, gender, BMI, BP, PG and alcohol. Similar results were obtained by Yoon HJ *et al.* [10]. n a study including 35,228 Korean participants in a health

screening program mean eGFR was significantly higher in current smokers than in former and never smokers.

Several mechanisms may have played a role in contributing this association. Hyper filtration is supposed to be an early manifestation of kidney disease. The nicotine induced increase in blood pressure and heart rate via sympathetic activation and vasopressin release probably explains this. Cadnapaphornchai *et al.* [11] reported that nicotine increases vasopressin release by altering cervical parasympathetic tone.

Another key finding in our study was the relationship between cigarette smoking and proteinuria. We found that out of total current smoker 52 % have proteinuria, which is in agreement with results obtained by Zhang L *et al.* [12] which reported that higher albuminuria in current smokers than the nonsmokers ($p<0.001$). We found that proteinuria was significantly more in current smokers with pack year ≥40 ($P=0.03$). Out of total current smokers 10% have proteinuria with pack year≥40 and is significantly correlated with pack years 32% of current smokers have proteinuria with pack years ranging between21-40. This relationship was concordant with Ishizaka N *et al*. [8] A Cross-sectional study including 7,078 Japanese male participants in health screening (III) OR for albuminuria (≥ 30 mg/girl) in current smokers consuming 20-39 cigarettes per day and those consuming more was 1.56 (1.17~2.08) and 1.88 (0.99~3.55) respectively in comparison with never smokers adjusted for age, BP and FPG.

Cross sectional nature was the main limitation of the present study; a large randomized clinical trial is needed to strengthen the present study results.

Conclusion

In our study it was found that current smokers have glomerular hyperfilteration and proteinuria as compared to nonsmokers. Proteinuria and increased GFR can be considered as surrogate marker of chronic kidney disease in smokers. Thus, Even if ESRF is reached, smoking should be discontinued. Patients should be motivated to quit smoking, because it is the most effective and beneficial strategy against the whole spectrum of CKD.

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