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Role of Smoking as a Modifiable Risk Factor in Diabetic Nephropathy and Nondiabetic Nephropathy

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***Abstract**: **Objective**: To study the effect of smoking on development and progression of nephropathy in type II diabetic and non diabetic patients and to compare the effect of smoking on progression of nephropathy in above two groups.*

***Material and methods** - It was a cross sectional study done over a period of 2 years on total 120 subjects which were divided in 4 groups of 30 subjects each, Diabetic smokers, diabetic non smokers, non diabetic smokers and non diabetic non smokers. The main parameters assayed were: blood urea, serum creatinine, urine albumin creatinine ratio (ACR) , glomerular filtration rate (GFR) , fasting plasma glucose (FPG) and serum lipid profile. The parameters assayed in the different groups were compared .Logistic regression analysis was done to study the effect of smoking on renal function.*

***Results:** Mean difference of blood urea, serum creatinine, urinary ACR excretion between diabetic smokers and diabetic non smokers and also between non diabetic smokers and non diabetic non smokers was found to be statistically significant. As the number of pack years increased , mean ACR level also increased in both diabetic and non diabetic smokers. Mean difference of total cholesterol, triglycerides, HDL, LDL, and VLDL excretion between diabetic smokers and diabetic non smokers and also between non diabetic smokers and non diabetic non smokers was found to be statistically significant. On stepwise logistic regression analysis, overall derangement in renal function due to smoking in diabetics and in non diabetics came out to be 50.2%. and 49% respectively .*

***Conclusion**: Smoking increases risk of proteinuria and renalfunction deterioration in both diabetics as well as non diabetics. So, smoking is an independent risk factor in development and progression of diabetic as well as non diabetic nephropathy.*

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I. Introduction

Chronic kidney disease is a major growing worldwide health problem because of its detrimental clinical outcome including end stage renal disease and cardiovascular morbidity and mortality. Patients with TypeII diabetes mellitus are especially at increased risk of developing chronic kidney disease leading to end stage renal failure. About 20-40% patients with type 2 diabetes mellitus develop diabetic nephropathy.(1) Smoking has emerged as an important modifiable and independent risk factor for kidney dysfunction in diabetic as well as in non diabetic patients. The main approach towards prevention and management of nephropathy in both diabetics and non diabetics has always been focussed on treatment of hyperglycemia, hypertension, obesity and other factors. Consequently, role of smoking cessation in prevention and management of nephropathy has always been neglected. The consequences of smoking for patients with nephropathy in both diabetes and non

diabetes could be detrimental. Therefore the study of impact of smoking on the development and rate of progression of nephropathy in diabetics and non diabetics is of utmost importance.[2]

Diabetic nephropathy is considered to be one of the major complications of diabetes mellitus and its prevalence is continuously increasing worldwide.[1] Progression of this disease is further accelerated by various factors, such as hypertension, chewing tobacco, alcoholism and smoking .Smoking has been shown to promote the progression of all stages of diabetic nephropathy. It increases the risk for the development of microalbuminuria and macroalbuminuria resulting in end stage renal failure.[2]

The pathophysiological mechanisms underlying the effects of smoking on diabetic and non diabetic nephropathy are quite complex. Smoking leads to glomerular hypertrophy, glomerulosclerosis, tubulointerstitial fibrosis and messangial cell expansion, followed by albuminuria and progressive reduction in the glomerular filtration rate[3,4]. Smoking may induce proteinuria and derange renal function through formation of advanced glycation end products. Advanced glycation end products (AGE'S) are cross linked moieties formed from the reaction of reducing sugars and the amino groups of plasma proteins, lipids and nucleic acids. AGE'S are responsible for enhanced vascular permeability, thereby leading to increased vasculopathy leading to end stage renal disease[5].Smoking leads to increased oxidative stress which plays key role in development of nephropathy. Nicotine (an active constituent of cigarette and bidi) increases lipid peroxidation in liver and decreases superoxide dismutase activity in liver leading to oxidative stress. The oxidative stress upregulates the expression of transforming growth factor-β (TGF-β), a prosclerotic and profibrogenic cytokine leading to nephropathy.[6,7] Hyperlipidemia is considered another major risk factor implicated in the progression of diabetic nephropathy. Nicotine causes an impairment of lipoprotein lipase (LPL), an enzyme involved in the hydrolysis and clearance of triglyceride (TG) from the circulation, and thus causes hypertriglyceridemia.[8] Nicotine also stimulates sympathetic adrenal system leading to increased secretion of catecholamines. Catecholamines increase the activity of hormone sensitive lipase resulting in increased lipolysis and increased free fatty acids, thus causing hyperlipidemia[9].Furthermore, smoking accelerates atherosclerosis of renal arteries and arterioles leading to increased glomerular pressure resulting in impairment of renal function. Mediators released by nicotine lead to vasoconstriction causing further decrease in GFR. Nicotine also increases blood pressure and heart rate promoting progression of both diabetic and non diabetic nephropathy.[10]

Therefore, after taking all the factors into consideration, it could be undoubtedly suggested that smoking could induce and worsen diabetic as well as non diabetic nephropathy. So screening for development of nephropathy should be started early in smokers. As smoking is a modifiable risk factor in development of nephropathy, so smoking cessation can be one of the single most effective measures to retard progression of renal failure. Therefore, this study was done to find out the effect of smoking on development of nephropathy in diabetic and non diabetic patients.

Aims and Objectives

- To study the effect of smoking on development and progression of nephropathy in type II diabetic patients.
- To study the effect of smoking on development and progression of nephropathy in non diabetic patients.
- To compare the effect of smoking on progression of nephropathy in above two groups.

II. Material and Methods

Type of Study: Cross Sectional Study

Source of Data : The main source of data for the study were type II diabetic patients, non diabetic patients, smokers and non smokers presenting to outpatient or inpatient, Department of Medicine, Rajindra Hospital, Patiala.

Inclusion criterion:

1. Type II diabetes mellitus patients of age 30-65 years.
2. Smokers who smoked atleast 1 cigarette/ bidi per day for a minimum of two years of age 30-65 years.
3. Age Matched non diabetics.
4. Age Matched non smokers.

Exclusion criterion

1. Patients with history of preexisting primary renal disease.
2. Age less than 30 and more than 65 years.
3. Type 1 diabetes mellitus patients.
4. Known hypertensives (SBP$\geq$140 And DBP$\geq$90)

Method: Detailed history with a structured questionnaire which included age, history of diabetes, hypertension, kidney disease, other comorbidities, duration of diabetes and detailed smoking history was taken. Detailed physical examination including Blood Pressure, BMI and relevant investigations were also undertaken. 120 subjects were divided into 4 groups of 30 subjects each.

Group A-Type 2 diabetic smokers.

Group B- Type 2 diabetic non smokers.

Group C-Non diabetic smokers

Group D-Non diabetic non smokers

All groups were subjected to detailed investigations. Urine albumin creatinine ratio, blood urea, serum creatinine, GFR were the main parameters for assessing nephropathy. Smokers were divided in 3 groups according to number of pack years: < 10 pack years, 10-20 pack years and > 20 pack years. Group A was compared with group B, group C was compared with group D, also group A was compared with group C. Patients with FPG >126 mg/dl after 8 hours of fasting were considered as diabetics .

Statistical Analysis: The parameters assayed in the different groups were compared. Data were analyzed using computer software, Statistical Package for Social Sciences (SPSS). To elucidate the associations and comparisons between different parameters, ANOVA test was used. For all statistical evaluations, p value of < 0.05 was considered significant and p value ≤0.001 was considered highly significant. Stepwise logistic regression analysis was done to study the effect of smoking on renal function.

III. Results

Majority of patients were in age group of 41- 50 years. Overall mean age of subjects under study was 48.2± 7.18 years. Overall male to female ratio in our study came out to be 3:1. Mean pack years in diabetic smokers group and in non diabetic smokers group were 10.57± 4.85 and 10.17±4.89 respectively . In group A (diabetic smoker group), mean duration of type 2 DM was 4.33 ± 0.96 years. Similarly, in group B (diabetic non smoker group), mean duration of Type 2 DM was 4.27 ± 0.87 years .Mean fasting plasma glucose (FPG) in group A came out to be 166.93±13.65 mg/dl while in group B came out to be 161.87±11.61, the difference of mean pack years in smokers, mean duration of type 2 diabetes and mean FPG in diabetic smokers and non diabetic smokers were comparable to each other, the difference between them being statistically non significant.

Table 1: Comparison of mean values of Blood Urea, Serum creatinine , Urinary ACR and GFR in four groups .

Parameter	Group A (n=30)	Group B (n=30)	Group C (n=30)	Group D(n=30)
Blood urea (mg/dl)	40.30±4.18	31.47 ± 3.58	31.27±4.54	24.33±4.52
Serum creatinine (mg/dl)	1.30±0.19	1.18±0.16	1.15±0.10	0.97±0.15
Urine ACR (µg/mg)	129.13±73.38	31.23±8.96	92.80±47.88	20.07±2.94
GFR (ml/min. /1.73 m^2)	77.79±9.30	80.75±11.49	86.33±11.66	90.18±9.14

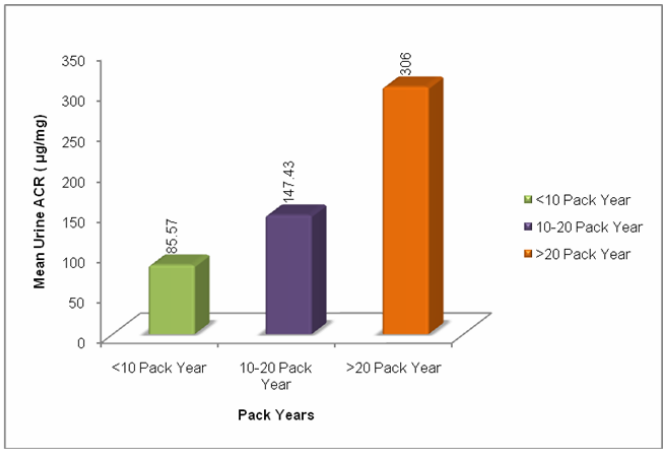
As shown in table above, mean blood urea concentration, serum creatinine and urine ACR values were higher in group A as compared to group B and also in group C as compared to group D . On statistical analysis, mean difference of blood urea between group A and B , between group C and D and also between group A and C came out to be statistically highly significant (p value < 0.001). Mean difference of serum creatinine levels between group A and B , between group C and D and also between group A and C was statistically significant (p value <0.05) .Mean difference of urinary ACR between group A and B , between group C and D came out to be statistically highly significant (p value <0.001) and between group A and C came out to be significant. (p value 0.027). Mean GFR was lower in group A as compared to group B and also in group C as compared to group D but mean difference of GFR in group A vs B came out to be statistically non significant. (p value 0.277). Similarly , mean difference of GFR in group C vs D also came out to be statistically non significant (p value 0. 159) but mean difference of GFR in group A vs C came out to be statistically significant. (p value 0.003)

Table 2: Comparison Of Urinary ACR in Diabetic and non diabetic smokers According To Pack Years .

Pack Year	MEAN ACR Group A (diabetic smokers)	MEAN ACR Group C (non diabetic smokers)
<10 Pack Year	85.57±42.19	60.13± 27.29
10-20 Pack Year	147.43±54.89	118.71±33.38
>20 Pack Year	306.00± 2.83	220.00
Total	129.13±73.38	92.80±47.88

This table shows that as severity of smoking (number of pack years) increased, mean ACR levels also increased in diabetic smokers and non diabetic smokers, the difference being statistically highly significant. (p value 0.001)

Group A – DIABETIC SMOKERS



GROUP C- NON DIABETIC SMOKERS

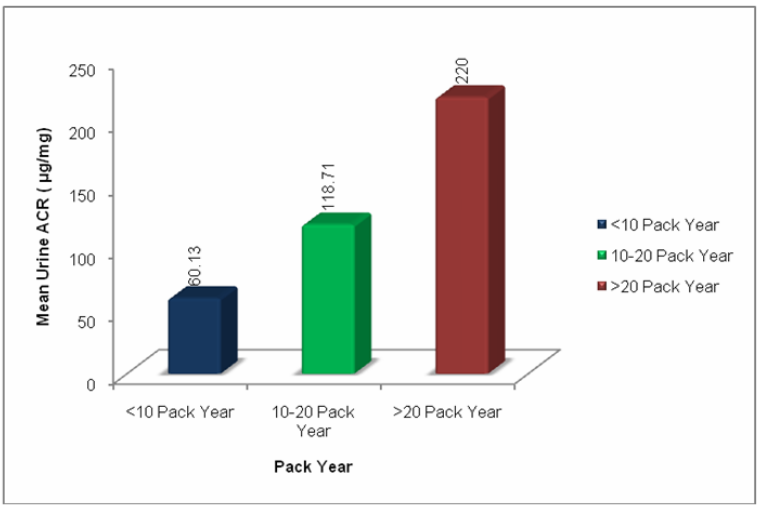


Table 3: **Comparison of SBP, DBP, lipid profile and BMI in four groups.**

Variable	Group A	Group B	Group C	Group D
SBP	132.13 ± 3.99	129.73 ± 2.61	129.53 ± 4.32	126.00 ± 3.40
DBP	86.00±1.39	84.13±2.03	83.60±2.37	81.33±1.52
TG	150.07±2.63	126.10±3.53	128.53±6.77	93.40±6.05
LDL	175.33±7.33	130.40±3.92	135.10±4.79	100.13±3.26
CHOLESTROL	243.37±9.03	199.43±8.45	200.07±10.66	165.07±6.70
HDL	31.13±1.66	32.33±1.70	32.37±2.66	34.47±3.83
VLDL	26.87±2.75	25.33±2.32	24.93±3.69	22.40±3.40
BMI	25.45±1.31	25.16±1.21	24.07±0.99	24.37±1.31

The mean difference of serum trigycerides, cholesterol , LDL, HDL and VLDL between group A and B, between group C and D and also between group A and C was found to be statistically significant. (p value < 0.05). On statistical analysis, mean difference of BMI between group A and B came out to be non significant (p value 0.378). Similarly, mean difference of BMI between group C and D also came out to be non significant (p value 0.319) but , difference of BMI between group A and C came out to be significant (p value (0.001). **Step wise logistic regression analysis:** Step wise logistic regression analysis was done to see the individual contribution by various variables on the parameters of renal function which were significantly deranged in smokers as compared to non smokers as seen previously on ANOVA. i.e. blood urea, serum creatinine and urine ACR .**In group A vs B** (diabetic smokers vs diabetic non smokers)**Blood urea**- The

variables that significantly affected blood urea were smoking, SBP, DBP, Serum triglycerides and serum LDL. Derangement in blood urea in group A as compared to group B due to smoking came out to34.6% . **Serum creatinine** -The variables that significantly affected serum creatinine were smoking and SBP. Derangement in serum creatinine in group A as compared to group B due to smoking came out to be 77.4%. **Urine ACR** - The variables that significantly affected urine ACR were smoking, SBP, DBP, Serum triglycerides and serum LDL . Overall derangement in urine ACR due to smoking came out to38.7% . Overall derangement in renal function in diabetics due to smoking came out to be 50.2% .**In group C vs D (non diabetic smokers vs non diabetic non smokers) Blood urea**- The variables that significantly affected blood urea were smoking, serum triglycerides , serum LDL and serum cholesterol . Overall derangement in blood urea due to smoking came out to be 42.1.% . **Serum creatinine** - The variables that significantly affected serum creatinine were smoking and SBP. Derangement in serum creatinine due to smoking came out to be 80.8 %. **Urine ACR** - The variables that significantly affected urinary ACR were smoking, SBP, Serum triglycerides, serum HDL, serum LDL and serum cholesterol . Overall derangement in urine ACR due to smoking came out to23.8 % . Overall derangement in renal function in non diabetics due to smoking came out to be 49 %.

IV. Discussion

Mean age of subjects of our study was 48.2 ± 7.18 years. The mean age of our study was comparable to study by Yakoub R et al [11] where mean age was 45.36 ± 15.95 years and to study by Alagavenkatesan et al[12] where mean age was 47.27 years. In our study, majority of the patients were males (75 %). Females comprised (25 %) . Overall male: female ratio in the study was 3: 1 Similarly, in studies by Gupta RK et al[13] and Tojawa M et al[14], majority of subjects were males, male to female ratio being 2.24:1 and 1.7:1 respectively.

TABLE 4: Comparison Of Blood Urea .

Blood urea (mg/dl)	Diabetic smokers	Diabetic non smokers	Non Diabetic smokers	Non Diabetic non smokers
Present study	40.30±4.18	31.46 ± 3.58	31.27±4.54	24.33±4.52
Jose MJ et al[2]	39.45± 12.1	29.72± 5.01	30.7±.4.13	25.8± 6.14
Mustafa I et al [15]	_	_	28.35 ± 4.27	27.52 ± 4.56
Ahmed M et al [16]	_	_	30.63 ± 3.69	25.13 ±5.45
Gupta RK et al[13]	_	_	32.16 ± 5.08	33.83 ± 4.53

Jose MJ et al[2] also found statistically significant higher blood urea concentration in diabetic smokers and non diabetic smokers as compared to diabetic non smokers and non diabetic non smokers respectively. Similarly, Mustafa I et al [15], Ahmed M et al [16]and Gupta RK et al[13] also found statistically significant higher blood urea concentration in smokers as compared to non smokers.

TABLE 5 : Comparison Of Serum Creatinine

Serum creatinine (mg/dl)	Diabetic smokers	Diabetic non smokers	Non Diabetic smokers	Non Diabetic non smokers
Present study	1.30 ± 0.19	1.18±0.16	1.15±0.10	0.97±0.15
Jose MJ et al[2]	1.20 ± 0.5	1.02 ± 0.41	0.96 ± 0.2	0.9 ± 0.14
Mustafa I et al [15]	_	_	1.0 ± 0.13	0.91 ± 0.13
Ahmed M et al [16]	_	_	1.12 ± 0.12	0.81 ± 0.09
Gupta RK et al[13]	_	_	0.86 ± 0.13	0.83 ± 0.11

In present study , mean serum creatinine in diabetic smokers and diabetic non smokers was 1.30 ± 0.19 mg/dl and 1.18± 0.16 mg/dl respectively which were comparable to results obtained in study carried out by Jose MJ et al[2]In present study , mean serum creatinine in non diabetic smokers and non diabetic non smokers was 1.15 ± 0.10 mg/dl and 0.97 ± 0.15 mg/dl respectively The results were comparable to mean serum creatinine in studies by Jose MJ et al[2], Mustafa I et al [15] and Ahmed M et al [16] In these studies also, higher serum creatinine concentration was found in smokers as compared to non smokers.

TABLE 6 : Comparison Of Urinary Albumin Creatinine Ratio (ACR)

urinary ACR (µg/mg)	Diabetic smokers	Diabetic non smokers	Non Diabetic smokers	Non Diabetic non smokers
Present study	129.13±73.38	31.23±8.96	92.80±47.88	20.07±2.94
Gupta RK et al[13]	_	_	93.98 ± 78.68	18.99 ± 6.65
Mustafa I et al [15]	_	_	93.98	18.99 µg/mg
Aggarwal J et al [17]	125	26.38	_	_
Azhari M et al [18]	_	_	42.22 ± 33.9	19.58 ± 3.9

In present study , mean urinary ACR in diabetic smokers and non diabetic smokers was 129.13±73.38 µg/mg and 31.23 ± 8.96 µg/mg respectively w hich was comparable to results obtained in study by Aggarwal J et al [17] Similarly in present study, in non diabetic smokers and non diabetic non smokers mean urinary ACR was 92.80±47.88 µg/mg and 20.07±2.94 µg/mg respectively . The findings were comparable to studies by Gupta RK et al[13] and Mustafa I et al [15]. Azhari M et al[18] also found statistically significant high urinary ACR in non diabetic smokers as compared to non smokers. In present study smokers were sub divided into 3 groups : < 10 pack years , 10 – 20 pack years and > 20 pack years. Mean urinary ACR values in 3 subgroups were60.13 ± 27.29 µg/mg , 118.71 ± 33.38 µg/mg , and 220 µg/mg respectively. Thus, as severity of smoking increased, mean ACR values also increased. The results obtained were similar to study by Gupta RK et al[13] , Alagavenkatesan et al. [12] and Mustafa I et al [15]. In these studies also, mean urinary ACR values increased as severity of smoking increased. Study by Azhari M et al [18] also found a positive corelation between number of cigarettes smoked and urinary ACR in non diabetic smokers. In present study, mean SBP and DBP was found to be higher in diabetic smokers than non smokers. Results obtained were similar to studies by Jose MJ et al[2]and De cosmo S et al[19].Similarly. mean SBP and DBP was found to be higher in non diabetic smokers than non smokers. Jose MJ et al[2], Jeganathan J et al [20] and Halperin RO et al[21]] found higher SBP and DBP in non diabetic smokers as compared to non diabetic non smokers. The mean values of serum triglycerides , total cholesterol , LDL, VLDL , were significantly higher in smokers as compared to non smokers in both diabetics and non diabetics. Mean value of HDL was found to be significantly higher in non smokers as compared to smokers in both diabetics and non diabetics. Results obtained were similar to studies by Jose MJ et al[2] , Neki NS et al[9], Joshi N et al[22] and Kavita et al[23] who also found higher mean values of serum triglycerides , total cholesterol , LDL, VLDL in smokers and lower HDL values in smokers as compared to non smokers. In this study, on step wise logistic regression analysis, smoking was found to be independent risk factor in progression of diabetic nephropathy and non diabetic nephropathy leading to 50.2 % and 49 % derangement in renal function in diabetic smokers and non diabetic smokers respectively. Similarly, studies by Jose MJ et al[2] , Sawicki PT et al[24] , Mehler PS et al[25] , Anan F et al [26] also found smoking to be a independent risk factor in development and progression of diabetic nephropathy. Similarly, study by Yacoub R et al [11] et al also showed that smoking significantly increased the risk of CKD overall and particularly for diabetic nephropathy and hypertensive nephropathy (OR being 2.24 and 2.85 respectively).

V. Conclusion

From this study, it can be concluded that smoking increases risk of proteinuria and renal function deterioration in both diabetics as well as non diabetics. So, smoking is an independent risk factor in development and progression of diabetic as well as non diabetic nephropathy. So, patients whether diabetic or non diabetic and especially people with preexisting renal disease should be advised to stop smoking and also screening for nephropathy should be started early in smokers. So, it is rationale to conclude that smoking cessation is one of the single most effective measures to decrease risk of development or progression of nephropathy.

Bibliography

[1]. Alvin C Powers. Harrrison's Principles Of Internal Medicine.(19th)edition 2015; 419: 2424-26. Mc Graw Hill.
[2]. Jose M J ,VipinVarkey. Role of smoking as a modifiable risk factor in diabetic nephropathy. Journal Of Association Of Physicians Of India 2016; Volume 64:34-7.
[3]. Rask-Madsen C, King GL. Mechanisms of Disease: endothelial dysfunction in insulin resistance and diabetes. Nat. Clin. Pract. Endocrinol. Metab. 2007;3:46–56.
[4]. Hua P, Feng W, Ji S, Raij L, Jaimes EA. Nicotine worsens the severity of nephropathy in diabetic mice: implications for the progression of kidney disease in smokers. Am J Physiol Renal Physiol. 2010;299: F732–39.
[5]. Pinto Sietsma SJ, Mulder J. Smoking is related to albuminuria and abnormal renal function in non diabetic persons. Ann Intern Med.2000;133:585-91.
[6]. Esmatjes E, Flores L, Lario S, Clària J, Cases A, Iñigo P et al. Smoking increases serum levels of transforming growth factor-beta in diabetic patients. Diabetes Care 1999;22:1915–16.
[7]. Forbes JM, Coughlan MT, Cooper ME. Oxidative stress as a major culprit in kidney disease in diabetes. Diabetes Care 2008;57:1446–54.
[8]. Mooradian AD. Dyslipidemia in type 2 diabetes mellitus. Nat Clin Pract Endocrinol Metab. 2009;5:150–59.
[9]. N S Neki. Lipid Profile In Chronic Smokers- A clinical study . Journal IACP.2002;3:51-4.
[10]. Orth SR. Smoking and the kidney. J Am SocNephrol 2002;13:1663-72
[11]. Yacoub R, Habib H, Lahdo A, Al Ali R, Varjabedian L, Atalla G, et al. Association between smoking and chronic kidney disease: a case control study. BMC public health. 2010 Dec;10(1):731
[12]. Alagavenkatesan, Anandhi PG, Balamurugan PV, Balajinathan R. A study on the incidence of microalbuminuria in non- diabetic normotensive smokers. International Journal of Information Research and Review. IJIRR. 2017 Jan ; 4,(1) p.3554-57.
[13]. Gupta RK, Gupta R, Maheshwari VD, Mawliya M. Impact of smoking on microalbuminuria and urinary albumin creatinine ratio in non-diabetic normotensive smokers. Indian journal of nephrology. 2014 Mar;24(2):92.
[14]. Tozawa M, Iseki K, Iseki C, Oshiro S, Ikemiya Y, Takishita S. Influence of smoking and obesity on the development of proteinuria. Kidney international. 2002 Sep 1;62(3):956-62.
[15]. Mustafa I, Kumar S, Arora M, Batra J, Sah SP. Effect of Cigarette Smoking on Microalbuminuria and other Kidney Functions in Normotensive Non-Diabetic Smokers. International Journal of Contemporary Medical Research. IJCMR. 2017 Sep; 4(9). 1912-14

[16]. Ahmed M , Jawad A , Osman HM, Shayoub ME. The effect of smoking cigarette on kidney functions among sundaes people. International journal of development research. IJDR. 2005 May;5 (5) 4473-75
[17]. Aggarwal J, Kumar M. Prevalence of microalbuminuria among rural North Indian population with diabetes mellitus and its correlation with glycosylated haemoglobin and smoking. Journal of clinical and diagnostic research: JCDR. 2014 Jul;8(7):CC11.
[18]. Azhari M, Nasr A, Hamdi L. Effect of smoking cigarette in albumin creatinine ratio in Khartoum state .European Academic Research. 2016 Oct ;4 (4) p 6050-55
[19]. De Cosmo S, Lamacchia O, Rauseo A, Viti R, Gesualdo L, Pilotti A, et al. Cigarette smoking is associated with low glomerular filtration rate in male patients with type 2 diabetes. Diabetes Care. 2006 Nov 1;29(11):2467-70.
[20]. Jeganathan J, Chowta N. Study of effect of smoking on blood pressure in normotensive men. International Journal of Medicine and Public Health. 2012;2(4).
[21]. Halperin RO, Michael Gaziano J, Sesso HD. Smoking and the risk of incident hypertension in middle-aged and older men. American journal of hypertension. 2008 Feb 1;21(2):148-52.
[22]. Joshi N, ShahC, Mehta HB . Comparative study of lipid profile on healthy smoker and non-smokers. Int J Med Sci Public Health. 2013 Jul 1;2(3):622-.6
[23]. Kavita , Gohel P , Nanavati MG , Gonsai RN. A Comparative study of Lipid Profile among Smokers and non Smokers. Int J Res Med. 2014; 3(4);76-81
[24]. Sawicki PT, Didjurgeit U, Mühlhauser I, Bender R, Heinemann L, Berger M. Smoking is associated with progression of diabetic nephropathy. Diabetes care. 1994 Feb 1;17(2):126-31.
[25]. Mehler PS, Jeffers BW, Biggerstaff SL, Schrier RW. Smoking as a risk factor for nephropathy in non‐insulin‐dependent diabetics. Journal of general internal medicine. 1998 Dec;13(12):842-5.
[26]. Anan F, Masaki T, Takahashi N, Nakagawa M, Yonemochi H, Eshima N, et al. Smoking is associated with urinary albumin excretion: an evaluation of premenopausal patients with type 2 diabetes mellitus. Metabolism. 2007 Feb 1;56(2):179-84.

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