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The association between smoking and urinary albumin excretion rate and GFR in patients with type 2 DM

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ABSTRACT

Objective: The objective of this study was to find the differences in urinary albumin excretion rate and glomerular filtration rate (eGFR) between non-smoking, currently smoking and formerly smoking type 2 diabetic patients. *Methods*: A cross-sectional study was conducted at King Saud University Medical City, Riyadh - Saudi Arabia on 111 diabetic patients attending Family Medicine Clinics and primary care clinics. The data was collected from a self-administered questionnaire, in addition to laboratory data from the EsiHI system. *Results:* Results showed Mild to moderate decreased eGFR among 1.6% of non-smokers, 6.2% of current smokers, and 3.1% of former smokers. Multivariate logistic regression analysis revealed that current smokers were at higher risk of low eGFR and Albuminuria compared to former smokers. In addition, it was found that there was a significant risk of Albuminuria among current smokers who started smoking at age of ≤25 years (OR: 3.51, CI: 2.07-6.19, p<0.05), former smokers who smoked for more than 10 years (OR: 3.14, CI: 1.84-4.68, p<0.05), current smokers who smoked for 5 to 10 years (OR: 2.68, CI: 1.56-3.41, p<0.05), current smokers who smoked for more than 10 years (OR: 3.61, CI: 1.89-6.84, p<0.05), current smokers who smoke one type (OR: 2.84, CI: 2.21-6.06, p<0.05), and current smokers who smoked more than one type (OR: 3.51, CI: 2.07-8.14, p<0.05). *Conclusion*: The present study concluded that age of starting smoking, duration of smoking and types of smoked products are significant predictors of low eGFR and Albuminuria among diabetics who are current smokers.

Keywords: Diabetes, eGFR, Smoking, Urinary Albumin Excretion Rate

1. INTRODUCTION

Diabetes is a global public health crisis, the world prevalence of diabetes among adults in 2010 was estimated to be 6.4% affecting 285 million adults, and will increase to 7.7% and 439 million adults by 2030 showing a substantial increase of 69% between 2010 and 2030 (Panton et al., 2018). In Saudi Arabia, abnormal glucose metabolism has reached an epidemic level, prevalence of DM people aged ≥ 30 years was 25.4% with 40.3% being unaware of their disease, which entails a great burden on the country, such that with

population is either diabetics or pre-diabetics (Al-Rubeaan et al., 2014). The risk of developing multiple severe health problems in people with diabetes increased, this includes macrovascular (cardiovascular disease) and microvascular (neuropathy, retinopathy and nephropathy) (Leutner et al., 2021). All of these complications have been studied and in association with type IIDM (Deepa et al., 2014).

Smoking is a predictor of the transition from normoglycemia to impaired fasting glucose which therefore increases the risk of type 2 diabetes (Akter et al., 2017), pathophysiological mechanisms by which smoking causes glucose intolerance and worsens clinical manifestations in DM include higher resistance to insulin,non-functional beta cells, therefore smoking is one of the leading modifiable risk factors for DM, and the development of its adverse outcomes including nephropathies, which are generally under recognized (Abdul-Ghani et al., 2006). The development of diabetic nephropathy is a staging process related to change of urine albumin excretion (UAE) from normal to microalbuminuria to macroalbuminuria, and screening for CKD can be detected by a combination of microalbuminuria and reduced estimated glomerular filtration rate (eGFR) (Márquez et al., 2019), therefore it's an important issue from the viewpoint of disease prevention (Akter et al., 2014). In retrospective case-control studies, smoking has been in association with renal impairment in subjects with biopsy-proven primary kidney diseases with or without proteinuria (Orth & Hallan, 2008). Moreover, in another retrospective analysis smoking promotes diabetic microalbuminuria and exacerbates diabetic nephropathy, despite the use of standard Reno-protective therapy (ACEI), and on the other hand smoking cessation in those with microalbuminuria betters the nephropathy progression (Phisitkul et al., 2008).

Looking at the link between smoking and nephropathies among diabetics, internationally, Jiang et al., (2017) documented an association between smoking status and glomerular lesions in type II DM patients, linking smoking to GBM (glomerular basement membrane) thickening which contribute to albuminuria and GFR loss (Jiang et al., 2017). Moreover, Tziomalos et al., (2015) showed that there was a clear progression of nephropathy in smokers, and smoking was one of the risk factor for DM renal disorders, independent of age, gender, and DM period. In prospective study by Chang (2012), adverse effects of smoking on diabetic nephropathy in type 2 patients were confirmed, even in optimal hypertensive patients. The rate that predicted diabetic nephropathy progression was double in smoker in compare of non-smoker (Jiang et al., 2017). MacIsaac et al., (2014) demonstrated that in patients with both type I and type II DM and normal or near normal renal function cigarette smoking caused a decrease in the estimated GFR independent of proteinuria, even after correcting for confounding factors, argues in favor of smoking cessation as a strategy to reduce ESRD risk even in patients with diabetes without overt nephropathy.

A cross-sectional data of Japanese men who underwent a general health screening, by Maeda et al., (2011), questioned the benefits of smoking on eGFR, and it is as follows, it showed that current smoking was dose-dependently associated inversely with low eGFR and positively with albuminuria and elevated eGFR—associations that were weakened or eliminated after quitting. Taking into account, smoking may increase the prevalence of not only albuminuria but also hyperfiltration. Despite the interesting findings in relation to the association of smoking to Urinary Albumin Excretion Rate and GFR in Patients with Type II DM, still there is a lack of knowledge regarding this kind of association within the diabetic patients in the Saudi population. Therefore, the present study aimed at investigating the differences in urinary albumin excretion rate and eGFR between non-smoking, currently smoking and formerly smoking type 2 diabetic patients attending the primary clinic in King Saud University Medical City, Riyadh, Saudi Arabia.

2. METHODS

Study Design and study population

A quantitative cross-sectional study was conducted between June 2020 and June 2021 in the primary care clinic at King Saud University Medical City (KSUMC) in Riyadh, the Capital City of Saudi Arabia. KSUMC is one of the largest tertiary hospitals in Saudi Arabia, which includes more than 1300 physicians, 900 fellows, medical residents and more than 2000 allied healthcare personnel. This tertiary hospital provides healthcare services for a population estimated by 1.3 million people in Riyadh and surrounding areas (KSUM city, 2021).

The study population involves patients diagnosed with type 2 Diabetes Miletus (DM). The inclusion criteria included type 2 DM patients on Oral Hypoglycemic Agents (OHAs). On the other hand, type 2 DM patients with renal diseases, or patients with other types of diabetes such as type 1 DM and gestational DM, and/or DM patients using Insulin were excluded. The study obtained the approval ofthe "Institutional Review Board (IRB) at King Saud University Medical City (KSUMC)"; the ethical approval number was (Ref. No. 20/0208/IRB).

Sample size estimation

The sample size was calculated using G* Power 3.1.9.2, using a power of 0.8, 95% confidence interval, and a significance value of 0.05, the final sample size was 98. Another 15% were added to avoid any technical or dropout issues. Therefore, the final sample size was 111 type 2 diabetic patients.

Data Collection / Data Sources

After obtaining the IRB approval, Type 2 Diabetic patients who attended the Family Medicine Clinics and Primary Care Clinics at KSUMC were selected using simple random sampling (by picking every 3rd patient who comes for follow up) and then interviewed, by delighted investigators. The Demographic data questionnaire, which includes (age, gender, Nationality, marital status, diabetes duration, smoking habits, use of ACEI/ARBs) was completed by the participants. All eligible cases were further interviewed by phone after taking verbal consent from participants due to the current global pandemic COVID-19, keeping in mind precautionary measures and full PPE to minimize exposure as much as possible.

The participants' Laboratory Data was collected from the ESiHI system, which includes (BMI, HgA1c, S-creatinine, BP, A/C ratio, GFR (using the MDRD equation), Lipid panel). During the time line of past 6 months only. If the eligible participant, for any reason, does not have these tests performed in the last 6 months, the treating physician ordered them as part of routine care. The measurement of serum creatinine was in mg/dL and age in years. Glomerular filtration rate (GFR) was estimated by using the MDRD equation, an "eGFR of < 30 mg/g, 30–299 mg/g, and ≥ 300 mg/g".

Statistical analysis

Descriptive statistics (mean, standard deviation, frequencies and percentages) was used to describe the participants' characteristics. Chi-square test was used to investigate the significant differences between the categorical variables. In addition, Independent samples t-test was used to investigate the differences between the continuous variables in this study.

Multivariate logistic regression was used to investigate whether smoking status is a predictor of Albuminuria or not.The potential confounding factors include demographic (age and sex), clinical (body mass index, systolic and diastolic blood pressure, diabetes duration (year), smoking habit, use of ACE inhibitors), and biochemical (HbA1c, fasting total cholesterol and triglyceride levels) covariates. A p-value ≤ 0.05 & 95% confidence intervals was used to report the statistical significance of the results

3. RESULTS

Participants' characteristics

A total of 111 Participants included in this study. Most of the study participants were male and the mean age of them was around 60 years with no significant difference in the age between different groups. The majority of the study participants reported history of chronicillnesses. There was no significant difference in the duration of diabetes, blood pressure, BMI and HbA1c between non-smokers, current smokers and former smokers. The mean eGFR was lower in current smokers (84.7±12.9) and higher in non-smokers (100.4±17.3), p value 0.62. The detailed socio-demographics and clinical characteristics of the study participants are presented in Table (1).

Table 1 Socio-demographic and clinical characteristics of the study participants (N=111)

Characteristics	Smoking Status			P value*
	Non-Smoker (n=63) n (%)	Current Smoker (n=16) n (%)	Former Smoker (n=32) n (%)	
Age (years) *mean ± SD*	58.8±7.3	61.3±6.1	62.4±6.6	0.48
Gender Male Female	 18(28.6) 45 (71.4)	 16 (100) 0 (0)	 28 (87.5) 4 (12.5)	 -------
History of chronic disease** Yes No	 40 (63.5) 23 (36.5)	 9 (56.3) 7 (43.8)	 25 (78.1) 7 (21.9)	 0.23
Type of chronic disease No chronic disease	 23 (36.5)	 7 (43.8)	 8 (25)	

Characteristics	Smoking Status			P value*
	Non-Smoker (n=63) n (%)	Current Smoker (n=16) n (%)	Former Smoker (n=32) n (%)	
Dyslipidemia (DLD) Hypertension Both	10 (15.9) 21 (33.3) 9 (14.3)	1 (6.3) 5 (31.3) 3 (18.8)	5 (15.6) 10 (31.3) 9 (28.1)	0.67
Duration of Diabetes, *mean ± SD*	10.3±4.6	9.25±3.8	11.5±5.6	0.82
Diabetes Medication Metformin Gliclazide Linagliptin	 63 (100) 21 (33.3) 13 (20.6)	 16 (100) 6 (37.5%) 11 (68.75)	 32 (100) 8 (25) 11 (34.4)	0.136
Systolic blood pressure, *mean ± SD*	126.4±12.7	127.3±9.1	127.9±12	0.269
Diastolic blood pressure, *mean ± SD*	77±6.9	78.5±10.7	79.5±7.1	0.096
BMI, *mean ± SD*	29.8±5.3	28.1±4.1	26.9±3.5	0.313
Creatinine, *mean ± SD*	62.1±10.8	82.5±11.9	73.9±15.8	0.15
eGFR, *mean ± SD*	100.4±17.3	84.7±12.9	87.8±14.3	0.06
HbA1c, *mean ± SD*	7.3±0.72	7.5±1.1	7.1±0.56	0.59

* Significance level of ($\alpha \leq 0.05$)

**Other than DM

eGFR of the study participants

Results showed normal eGFR was present among 71.4% (n=45) of non-smokers, 25% (n=4) of current smokers, and 46.9% (n=15) of former smokers. While the prevalence of mildly decreased eGFR was reported in 27% (n=17) among non-smokers, 68.8% (n=11) in current smokers, and 46.9% (n=15) in former smokers. Mild to moderate decreased eGFR was prevalent among 1.6% (n=1) of non-smokers, 6.2% (n=1) of current smokers, and 3.1% (n=1) of former smokers. However, moderate to severe decrease of eGFR was prevalent only among 3.1% (n=1) of former smokers (Table 2 & Fig. 1).

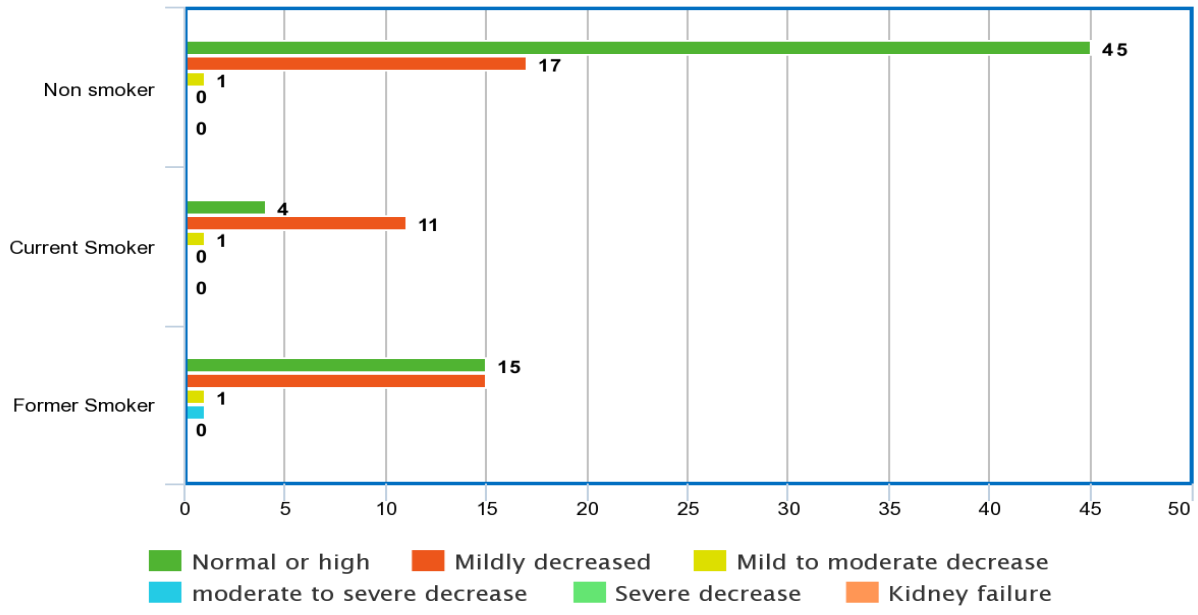

Figure 1 Prevalence of low, moderate and elevated eGFR among study participants

Table 2 Prevalence of low, moderate and elevated eGFR among study participants

eGFR	Non-Smoker (n=63)	Current Smoker (n=16)	Former Smoker (n=32)
≥90 (Normal or high)	45 (71.4%)	4 (25%)	15 (46.9%)
60 – 89.9 (Mildly decreased)	17 (27%)	11 (68.8%)	15 (46.9%)
45 – 59.9 (Mild to moderate decrease)	1 (1.6%)	1 (6.2%)	1 (3.1%)
30 – 44.9 (moderate to severe decrease)	0	0	1 (3.1%)
15 – 29.9 (Severe decrease)	0	0	0
≤15 (Kidney failure)	0	0	0
Total	63	16	32

Smoking status as a predictor of low eGFR

Table 3 showed In model one, which was adjusted for age and duration of DM, it was found that there was a significant risk of low eGFR among current smokers with smoking durations of 5 to 10 years (OR: 2.44, CI: 1.17-3.01, p=0.000), 10 years or more (OR: 2.68, CI: 1.79-3.37, p=0.000) and current smokers who smoke more than one type (OR: 2.49, CI: 1.21-3.64, p=0.000).

In model two, which was adjusted for age, duration of DM, BMI and SBP, it was found that there is a significant risk of low eGFR among current smokers who started smoking when they were ≤25 years (OR: 1.38, CI: 0.88-1.95, p=0.000) and those aged 26 to 35 years (OR: 1.57, CI: 1.27-3.88, p=0.004), current smokers who smoked for 5 to 10 years (OR: 2.71, CI: 1.88-3.41, p=0.000) and those who smoked for more than 10 years (OR: 2.70, CI: 1.58-2.91, p=0.000).

In model 3 that was adjusted for age, duration of DM, BMI, SBP, DBP and HbA1c, it was found that there was a significant risk of low eGFR among diabetic patients who are current smokers and who started smoking when they were aged ≤25 years (OR: 2.85, CI: 0.97-3.15, p=0.000), and those aged 26 to 35 years (OR: 3.21, CI: 1.94-6.41, p=0.000), current smokers who have been smoking for 5 to 10 years (OR: 3.05, CI: 2.24-4.18, p=0.000), for more than 10 years (OR: 2.68, CI: 1.73-2.91, p=0.000), current smokers who smoke one type (OR: 2.94, CI: 1.88-5.36, p=0.01) and current smokers who smoked more than one type (OR: 2.84, CI: 1.96-3.15, p=0.000).

Table 3 Multivariate logistic regression for smoking status as a predictor of low eGFR

Smoking Status	Model 1		Model 2		Model 3	
	OR (95% CI)	P- value	OR (95% CI)	p - value	OR (95% CI)	p- value
Age of starting smoking						
Never smoker	1.00		1.00		1.00	
Former smoker						
≤25	0.46 (0.22-0.81)	0.14	0.62 (0.55-0.93)	0.12	1.06 (0.74-1.82)	0.07
26 - 35	0.33 (0.28-0.82)	0.36	0.41 (0.18-0.67)	0.51	0.71 (0.39-1.18)	0.61
36 - 45	1.21 (0.36-2.41)	0.25	1.14 (0.88-1.65)	0.43	1.16 (1.01-3.04)	0.25
>45	0.64 (0.33-1.15)	0.38	0.89 (0.51-1.31)	0.47	0.77 (0.49-1.38)	0.74
Current smoker						
≤25	0.61 (0.37-1.15)	0.04	1.38 (0.88-1.95)	0.00	2.85 (0.97-3.15)	0.00
26 - 35	0.76 (0.29-1.48)	0.08	1.57 (1.27-3.88)	0.00	3.21 (1.94-6.41)	0.00
36 - 45	0.33 (0.15-1.07)	0.09	0.58 (0.15-1.27)	0.15	1.08 (0.83-1.49)	0.09
>45	0.81 (0.44-1.29)	0.17	1.38 (0.81-2.37)	0.61	1.41 (1.35-2.66)	0.49
Duration of smoking						
Never smoker	1.00		1.00		1.00	
Former smoker						
< 5 years	0.39 (0.18-1.33)	0.10	1.14 (0.88-1.91)	0.52	1.55 (1.18-2.31)	032
5 – 10 years	1.21 (0.61-1.88)	0.33	1.09 (0.67-1.84)	0.43	1.43 (1.18-2.07)	0.42
>10 years	2.05 (0.89-3.16)	0.00	2.21 (0.81-3.81)	0.04	2.11 (1.81-2.91)	0.00
Current smoker						
< 5 years	2.35 (1.13-2.61)	0.31	2.16 (1.55-3.09)	0.66	2.59 (1.87-6.49)	0.52

Smoking Status	Model 1		Model 2		Model 3	
	OR (95% CI)	P- value	OR (95% CI)	p - value	OR (95% CI)	p- value
Age of starting smoking						
5 – 10 years	2.44 (1.17-3.01)	0.00	2.71 (1.88-3.41)	0.00	3.05 (2.24-4.18)	0.00
>10 years	2.68 (1.79-3.37)	0.00	2.70 (1.58-2.91)	0.00	2.68 (1.73-2.91)	0.00
When stopped smoking						
Never smoker	1.00		1.00		1.00	
Former smoker						
<3 years	1.51 (0.33-2.01)	0.18	1.77 (0.83-2.18)	0.47	1.93 (1.47-2.31)	0.34
3-6 years	0.59 (0.28-1.10)	0.31	1.29 (0.51-1.55)	0.84	1.17 (0.86-1.77)	0.58
>6 years	1.69 (0.88-2.53)	0.09	1.84 (0.67-2.33)	0.07	2.01 (1.64-3.51)	0.41
Number of smoked products						
Never smoking	1.00		1.00		1.00	
Former smokers						
One type	0.31 (0.11-1.15)	0.14	0.76 (0.53-1.94)	0.50	1.61 (1.18-2.51)	0.64
More than one type	0.81 (0.51-2.15)	0.33	1.17 (0.81-1.73)	0.11	1.93 (0.72-2.07)	0.68
Current smokers						
One type	1.93 (0.39-2.87)	0.03	2.51 (1.63-4.33)	0.00	2.94 (1.88-5.36)	0.01
More than one type	2.49 (121-3.64)	0.00	2.60 (2.09-6.51)	0.00	2.84 (1.96-3.15)	0.00

Model 1 was adjusted for age and duration of DM

Model 2 was adjusted for age, duration of DM, BMI and SBP

Model 2 was adjusted for age, duration of DM, BMI, SBP, DBP and HbA1c

Smoking status as a predictor of Albuminuria

The results presented in table (4) represent the multivariate logistic regression for smoking status as a predictor of Albuminuria. In model one that was adjusted for age of starting smoking and DM duration, the results showed that there was a significant risk of Albuminuria among current smokers who started smoking at age of ≤25 years (OR: 2.94, CI: 1.77-3.48, p=0.000), former smokers who smoked for more than 10 years (OR: 2.31, CI: 1.55-3.31, p=0.000) and current smokers who smoke more than one type (OR: 2.84, CI: 1.41-3.51, p=0.000).

In model two, which was adjusted for age, duration of DM, BMI and SBP, it was found there was a significant risk of Albuminuria among former smokers who smoked for more than 10 years (OR: 2.63, CI: 0.89-4.11, p=0.000), current smokers who smoked for more than 10 years (OR: 3.15, CI: 2.41-4.18, p=0.000), and current smokers who smoked more than one type (OR: 3.92, CI: 1.73-4.46, p=0.000).

In model three, which was adjusted for age, duration of DM, BMI, SBP, DBP and HbA1c, it was found that there was a significant risk of Albuminuria among current smokers who started smoking at age of ≤25 years (OR: 3.51, CI: 2.07-6.19, p=0.000), former smokers who smoked for more than 10 years (OR: 3.14, CI: 1.84-4.68, p=0.000), current smokers who smoked for 5 to 10 years (OR: 2.68, CI: 1.56-3.41, p=0.000), and current smokers who smoked more than one type (OR: 3.51, CI: 2.07-8.14, p=0.000)

Table 4 Multivariate logistic regression for smoking status as a predictor of Albuminuria

Smoking Status	Model 1	p	Model 2	p	Model 3	p
	OR (95% CI)		OR (95% CI)		OR (95% CI)	
Age of starting smoking						
Never smoker	1.00		1.00		1.00	
Former smoker						
≤25	1.24 (1.07-1.45)	0.54	1.63 (0.57-1.18)	0.15	1.41 (0.84-2.03)	0.09
26 - 35	1.61 (1.33-1.91)	0.16	1.82 (0.58-1.99)	0.31	1.72 (0.81-2.15)	0.33
36 - 45	1.20 (1.06-1.55)	0.44	1.69 (1.28-2.28)	0.55	1.42 (1.37-1.80)	0.74
>45	1.73 (1.35-1.91)	0.08	0.60 (0.18-1.94)	0.37	0.12 (0.09-1.30)	0.84

Smoking Status	Model 1	p	Model 2	p	Model 3	p
	OR (95% CI)		OR (95% CI)		OR (95% CI)	
Age of starting smoking						
Current smoker						
≤25	2.94 (1.77-3.48)	0.00	2.39 (1.15-4.57)	0.01	3.51 (2.07-6.19)	0.00
26 - 35	1.38 (1.15-2.81)	0.26	2.05 (1.39-2.84)	0.07	2.44 (1.95-5.37)	0.18
36 - 45	1.16 (1.31-2.55)	0.71	2.01 (1.84-3.09)	0.31	3.18 (1.83-8.33)	0.09
>45	1.11 (0.88-1.31)	0.38	2.05 (1.91-3.41)	0.22	3.16 (2.83-4.18)	0.36
Duration of smoking						
Never smoker	1.00		1.00		1.00	
Former smoker						
< 5 years	1.48 (0.56-1.93)	0.40	1.59 (0.89-2.44)	0.37	2.07 (1.18-2.03)	0.11
5 – 10 years	1.33 (0.51-1.18)	0.31	1.88 (0.81-1.67)	0.49	1.40 (0.64-1.36)	0.68
>10 years	2.31 (1.55-3.31)	0.00	2.63 (0.89-4.11)	0.00	3.14 (1.84-4.68)	0.00
Current smoker						
< 5 years	2.59 (1.38-4.10)	0.46	2.88 (1.16-3.08)	0.16	2.91 (1.81-2.84)	0.61
5 – 10 years	2.11 (1.31-2.63)	0.20	2.37 (2.05-3.83)	0.82	2.68 (1.56-3.41)	0.00
>10 years	3.38 (1.94-6.51)	0.00	3.15 (2.41-4.18)	0.00	3.61 (1.89-6.84)	0.00
When stopped smoking						
Never smoker	1.00		1.00		1.00	
Former smoker						
<3 years	0.51 (0.13-1.46)	0.61	1.13 (0.77-1.69)	0.94	1.82 (0.66-2.11)	0.18
3-6 years	1.21 (0.33-1.63)	0.46	1.40 (0.16-1.82)	0.24	1.91 (0.81-2.30)	0.60
>6 years	1.60 (0.50-2.01)	0.27	1.81 (0.71-1.54)	0.19	1.90 (0.44-2.12)	0.37
Number of smoked products						
Never smoking	1.00		1.00		1.00	
Former smokers						
One type	1.15 (0.89-1.69)	0.15	1.62 (0.67-2.14)	0.46	1.91 (0.87-2.14)	0.17
More than one type	0.88 (0.14-0.93)	0.36	1.16 (0.91-2.44)	0.55	2.05 (1.83-2.71)	0.31
Current smokers						
One type	2.33 (1.51-3.84)	0.00	2.41 (1.18-3.62)	0.00	2.84 (2.21-6.06)	0.00
More than one type	2.84 (1.41-3.51)	0.00	3.92 (1.73-4.46)	0.00	3.51 (2.07-8.14)	0.00

Model 1 was adjusted for age and duration of DM

Model 2 was adjusted for age, duration of DM, BMI and SBP

Model 2 was adjusted for age, duration of DM, BMI, SBP, DBP and HbA1c

4. DISCUSSION

Diabetes is widely acknowledged as one of the risk factors for kidney damage. In addition, a tight relationship between smoking and chronic diseases' complications, especially diabetes, was reported extensively in literature. Data increasingly indicate that smoking can have a negative effect on the kidney. For instance, Yacoub et al., (2010) reported that smoking significantly increases the risk of CKD in general, and among diabetic patients in particular. Moreover, Hall et al., (2016) reported that smoking is remarkable risk factors that increases the renal damage and causes remarkable decline in eGFR among African American patients. The present study sought to identify the relationship between smoking status and urinary Albumin excretion rate and eGFR in type II DM patients attending Family Medicine Clinics and Primary Care Clinics at King Saud University Medical City.

Findings of the study showed that normal eGFR was more prevalent among non-smokers. However, there was a higher prevalence of mild to moderate decrease of eGFR among current smoker compared to former and non-smokers. This result might be referred to the association between smoking and low eGFR. This result is evidenced by the findings reported by De Cosmo et al., (2006) who reported that there is a significant association between smoking and decline in eGFR among diabetic patients. In

addition, these findings are supported by the results reported by Wang et al., (2021) who found that smoking is an independent risk factor for nephropathy complications occurring among diabetic patients.

The outcome of this research showed that among current smokers, age of starting smoking, duration of smoking and number of smoker products were significant predictors of low eGFR among diabetic patients. These factors are all related to increased length of smoking and increased accumulation of tobacco products inside the patients' body, which significantly points to a specific mechanism of affecting renal damage. The findings of the study are similarto the results reported by Tseng et al., (2017) who reported that increased length of smoking significantly increases the risk of low eGFR. In addition, these results are in line with the findings reported by Hafez et al., (2020) who found that increased amount and length of smoking significantly increase the risk of low eGFR.

Further, the outcome of this study indicated that age of starting smoking, duration of smoking, and number of smoked products significantly increased the risk of Albuminuria among current smokers compared to former smokers. This finding might be interpreted by the strong reported effect of smoking on renal functions, as smoking was reported extensively as an independent risk factor influencing the progression of renal failure. These findings are consistent with the findings reported by Gupta et al., (2014) who found that among current smokers who smoked for longer period and smoked more than one type, there was a significant high prevalence of microalbuminuria compared to non-smoking or former smoking patients. In addition, these findings are in line with the results reported by Podzolkov et al., (2020) who found that Vape and cigarettes smokers were at higher risk of increased levels of albuminuria compared to non-smokers among young diabetic patients. In addition, these results are in line with the results reported by Hogan et al., (2007) who found that hypertensive current smoking patients are at increased risk of albuminuria.

The study findings confirm that the cigarettes smoking is considered a universal health hazard, but it may be particularly damaging to kidney functions among chronic disease patients. Diabetic kidney disease may progress more quickly in smokers than non-smokers. Research-based evidences indicated that smoking is an important risk factor in the progression of CKD in diabetics and in non-diabetic. The nicotine is one of the main compounds in smoke; it has a major effect in the progression of kidney impairments in diabetics.

This study provided research-based evidence that smoking is a remarkable independent risk factor of low eGFR and albuminuria among type 2 DM patients. However, the findings of the study have several limitations that include geographical limitations, as this study examines a population represented by type 2 DM patients attending Family Medicine Clinics and Primary Care Clinics at King Saud University Medical City. Therefore, the findings might not be generalized to other geographical areas. However, this is a tertiary referral hospital that receives patients from all over the country. In addition, most of the participants were male and no female with current smoking status was included. This is because the prevalence of smoking among Saudi female is much lower than male (Moradi-Lakeh et al., 2013). Therefore, the findings might be different if more current smoker females were included.

5. CONCLUSION

The world Health Organization (WHO) is not exaggerating when reporting that tobacco use is one of the biggest public health threats the world has ever faced. The present study sought to identify the strong link between smoking and urinary Albumin Excretion Rate and GFR in Patients with Type 2 DM. The study concluded that age of starting smoking, duration of smoking, smoking more than one type of tobacco products were significant predictors of low eGFR and Albuminuria among current smokers. Based on the outcome of this research, the study recommends activating the role of healthcare providers and media to increase the awareness of the public regarding the serious negative effects of smoking on health. In addition, the study recommends strengthening the governmental laws and regulations related to prohibiting smoking in public places and regulations related to dealing and marketing tobacco products.

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Authors' Contribution

The authors contributed equally in producing this manuscript. The authors collaboratively formulated the research problem, performed data collection, analysis and interpretation, and finalizing the manuscript

Ethical Approval

The study was approved by the Institutional Review Board (IRB) at King Saud University Medical City (KSUMC), the ethical approval number was (Ref. No. 20/0208/IRB).

Conflicts of interest

The authors declare that they have no conflict of interest.

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Data and materials availability

All data associated with this study are present in the paper.

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