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The Effect of Chronic Cigarette Smoking on Some Kidney Function Markers

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Background / Aim: One of the organs that are negatively impacted by smoking is the kidney. The purpose of this study is to compare the mean serum levels of urea and creatinine, microalbumin, albumin-creatinine ratio, and estimated glomerular filtration rate of smokers to non-smokers and their implications to ascertain the impact of chronic cigarette smoking on some kidney function markers.
Methodology: This investigation was conducted in and around Anambra State's Nnewi Metropolis. Two hundred participants, ranging in age from 20 to 40, were chosen at random and involved in the study. They were divided into two groups: the control group, which consisted of 100 healthy males, and the smoker's group, which consisted of 100 male smokers who smoked at least seven sticks a day. All subjects had blood drawn, and spectrophotometric techniques were used to determine the levels of microalbumin, uric acid, serum urea, and creatinine. Each individual filled out questionnaires on their personal information, medical history, and drug use. The participant was permitted to observe 10 minutes of sat resting to allow fluid shifts to equilibrate, reducing variability in a pre-analytical variable.
Results: Analysis of the data revealed that, as compared to the control patients, smokers had significantly higher mean levels of urea, creatinine, urine albumin (malb), albumin-creatinine ratio, and estimated glomerular filtration rate ($p < 0.05$). When compared to the control group, the serum urea and creatinine levels in the smoking group were considerably higher ($p > 0.05$).
Conclusion: Smokers experience negative effects on their renal function. Renal function was negatively impacted in the smoker's group, they experience elevated serum creatinine and urea

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level. Since there is a decline in the filtration rate in the glomerular, an increase was observed in the urea ad creatinine level as a result of the decline. Nicotine usage does have several systemic effects mostly in connection with creatinine and urea in renal illness.

Keywords: Albuminuria; creatinine; Glomerular Filtration Rate (GFR); kidney; tobacco use; urea.

1. INTRODUCTION

Smoke from tobacco products, including tobacco, contains a variety of dangerous chemicals. One of these compounds that can be obtained through both active and passive smoking is nicotine. Smoking's addictive potential and physiological consequences are principally mediated by nicotine, the main tobacco alkaloid. Repeated smoking is encouraged by stressful professions, which also support addictive habits.

For many years, tobacco (Nicotiana Tabacum) has been farmed in Africa. Smokeless tobacco consumption is currently on the rise in the United States of America (USA) [1] and is extremely common in the Far East, Middle East, and Europe [2]. But in Nigeria, potash is added as an ingredient to the powdered form known as "tobacco snuff." It can either be applied topically or inhaled (sniffed) through the nose. There are two types of tobacco: chewing tobacco and tobacco snuff. Tobacco can be consumed in a variety of ways.

The most prevalent form of tobacco usage is cigarette smoking. If the current pattern holds by 2030, smoking will result in the yearly death toll exceeding 9 million. According to the Minister of Health, Prof. Isaac Adewole, smoking is a growing public health issue, particularly in emerging nations like Nigeria. In recent years, it has been clear that smoking is linked to excessive morbidity and mortality in several illnesses, most notably lung and cardiovascular diseases [3]. In addition, the kidney is a key target organ for smoking-related harm, and 4.5 million people in Nigeria smoke 20 billion sticks of tobacco annually. The World Health Organization (WHO) reported in May 2017 that tobacco kills more than 7 million people a year, 6 million of whom die directly from using it and the remaining 200,000 through being exposed to smoking [4]. Our nation's leaders ought to be concerned.

Catecholamine circulation is stimulated by increased sympathetic nervous system activity. Vasoconstriction results from this in the vascular system. Vascular resistance rises by 11% in the Renovascular bed. This results in a 15% decrease in the glomerular filtration rate and an 18% decrease in the filtration fraction [5]. Less is known about the long-term impact of smoking on renal health. There is proof that chronic smokers have lower renal plasma flow, which is associated with a little increase in endothelin. Functioning problems are brought on by endothelin through vaso-constriction.

Only a small number of studies examined the effects of smoking on kidney function, and they did so only in a few specific population groups, including those with diabetes mellitus, primary kidney diseases like polycystic kidney disease, glomerulonephritis, and lupus nephritis, or, more recently, those with atherosclerotic renal artery stenosis [6].

Furthermore, K. Yamagata's [7] epidemiologic study from 2007 demonstrated a link between smoking and a higher risk of chronic renal disease development and kidney failure in people with diabetes and high blood pressure.

In patients with type 2 diabetes, researchers recently found a dose- and time-dependent relationship between smoking and an increase in the prevalence of chronic kidney disease (CKD) and the urinary albumin-creatinine ratio [8].

The incidence and progression of CKD may be influenced by smoking, regardless of the underlying disease, according to a recent meta-analysis [9] based on 15 prospective cohorts and including more than 65.000 incident CKD patients. However, interestingly, there was no correlation between smoking and proteinuria.

When tobacco is burned, radioactive substances are released into the air, which smokers breathe into their lungs. This could be another important risk factor for lung cancer in smokers [10]. The hazardous and cancer-causing substances in cigar smoke are largely the same as those in cigarette smoke, albeit some of them are present to varying degrees. Cigar tobacco has high levels of several nitrogen compounds as a result of the aging (fermentation) process used to create cigars (nitrates and nitrites). These chemicals release numerous tobacco-specific nitrosamines

(TSNAs), some of the most potent cancer-causing agents known when the fermented cigar tobacco is smoked [11]. The tobacco doesn't burn as completely in a cigar because the wrapper is less porous than a cigarette wrapper. Higher levels of tar, nitrogen oxides, ammonia, carbon monoxide, and other toxic compounds are produced as a result.

However, there is currently limited knowledge regarding how smoking affects glomerular filtration rate, non-protein nitrogen (NPN) metabolites (creatinine and urea), uric acid, microalbumin, albumin-creatinine ratio, and overall kidney function. As they are used to assess renal function integrity, renal function tests are crucial components in the laboratory diagnosis and prognosis of renal dysfunction as well as in the monitoring of therapy response in medicine, particularly in renal pathology.

Urea is synthesized in the liver and then delivered by the plasma to the kidney, where the glomerulus easily separates it from the plasma. [12] Although up to 40% of the urea in the glomerulus is reabsorbed by passive diffusion as the filtrate travels through the renal tubules, the majority of urea in the glomerulus is expelled in the urine. The amount that is reabsorbed is influenced by hydration level and urine flow rate. Urea is eliminated by the kidneys in greater than 90% of cases, with the remaining 10% passing through the GI tract and skin.

In muscles, creatine phosphate is broken down into creatinine. Utilizing two enzymatic processes, arginine, glycine, and methionine are converted into creatine in the kidneys, liver, and pancreas [13]. It is subsequently transferred to various tissues, including muscle and the brain, where it is changed into the highly energetic molecule phosphocreatine.

The urine protein albumin is now known to be the kidney and the heart's initial indicator of arterial injury. The occurrence of albuminuria has been known for more than 200 years, and Richard Bright's ground-breaking discoveries in 1827 are what first linked it to kidney illness. The protein the body utilizes for growth and repair is called albumin. However, when the kidneys aren't functioning properly, albumin leaks into the urine (a medical disease known as albuminuria) [14]. A significant protein called albumin is often found in the blood, but when the kidneys are working correctly, there is essentially no albumin in the urine.

The majority of the time, an albumin-to-creatinine ratio (ACR) is determined after tests for albumin and creatinine are performed on a urine sample that was randomly obtained (not timed). To give a more precise indication of how much albumin is being released into the urine, this is done. The amount of creatinine in the urine, which is a consequence of muscle metabolism and a reliable indicator of urine concentration, is typically delivered into the body at a consistent rate. When measuring albumin in a random urine sample, this feature of creatinine enables its measurement to be used to adjust urine concentration.

A minor amount of albumin in the urine may be a sign of renal disease at an early stage [15]. Urine microalbumin or microalbuminuria are terms used to describe a trace amount of albumin in the urine. The term "albuminuria," which refers to any elevation of albumin in the urine, is gradually replacing "microalbuminuria."

Blood's liquid component, plasma, is made up of a variety of proteins, including albumin. Plasma protein preservation is one of the kidneys' many jobs to prevent waste products and plasma proteins from being discharged together when urine is made. Normal protein absorption into urine is prevented by two mechanisms:

The kidney's glomeruli are specialized structures made up of loops of specialized capillaries that filter blood and enable small particles to pass through toward the urine while acting as a barrier to keep the majority of big plasma proteins inside the blood vessels.

Smaller proteins that do get through the glomeruli are almost totally reabsorbed by tubes (tubules) that have numerous sections that collect the fluid and molecules.

Most frequently, kidney injury to either the glomeruli or tubules results in protein in the urine (proteinuria). Protein can leak into the urine at increasing levels due to glomeruli inflammation and/or scarring. Protein absorption can be impeded by tubule damage [16]. One of the first proteins to be found in urine with kidney injury is albumin. People who persistently have trace levels of albumin in their urine (albuminuria) are more likely to eventually develop cardiovascular disease and progressive kidney failure.

The National Renal Foundation advises the estimation of GFR for use in the diagnosis, care,

and prevention of chronic kidney disease. It is regarded as the top general indication of renal health [17]. Numerous people with impaired renal function cannot be identified by serum creatinine alone. As an illustration, senior citizens may lose 50% of their kidney function before their serum creatinine level exceeds the normal limit. The National Kidney Foundation.

This study compares the mean serum levels and evaluates the impact of chronic cigarette smoking on a few kidney function measures. The purpose of this analysis was to assess the association between cigarette smoking and albuminuria in an adult male population sample with normal basal kidney function due to the lack of information regarding the effect of cigarette smoking, in the general population, on the risk to develop subclinical kidney damage, such as the increase of albuminuria.

2. METHODS AND MATERIALS

2.1 Study Design

Between the ages of 20 and 40, this study included 100 male cigarette smokers (test) and 100 male non-smokers (control). Smokers and non-smokers were divided into two groups. The smokers in this category have been routinely smoking for at least 4 years, averaging at least 7 cigarettes each day. The study analyzed the average serum levels of urea and creatinine in smokers and non-smokers to look for any potential links between smoking and renal function markers, as well as any consequences. For this study, 200 adult respondents in the Anambra state metropolises of Okofia and Nnewi, ranging in age from 20 to 40, were chosen at random.

For all subjects, a screening questionnaire containing questions about health history, drug use, and personal information was created. For this project, materials including a tourniquet, a 5ml syringe, heparinized blood containers, plain plastic containers, cotton wool, swabs, a spectrophotometer, a refrigerator, and a centrifuge will be used. 40g/l sodium dodecyl sulfate (sodium lauryl sulfate), pH 12.8, phosphate buffer Diacetyl monoxime, 60 percent v/v Acetic acid, reagent for picric acid, and reagent for urea acid.

2.2 Criteria for Inclusion/Exclusion

100 people (smokers) who have been smoking for at least five years and consistently consume at least 7 cigarettes a day and 100 people (non-smokers) who have never touched a cigarette. Exclusion criteria for this study included those with a history of salicylates, thiophenylpyrazolidine, atophan, probenecid, or allopurinol over-the-counter drugs, as well as those with diabetes, renal, sickle cell, or malignant disease, medical therapy, or vitamin supplement use currently and smokeless tobacco patients. Each participant was permitted to observe 10 minutes of sat resting to allow fluid shifts to equilibrate, reducing variability in a pre-analytical variable. Without letting the tourniquet remain on for longer than a minute, blood was drawn from the median cubital vein using a clean venipuncture technique to get roughly 5ml of blood. To obtain the serum, blood was diluted into test tubes, allowed to coagulate, and then spun at 3000 rpm for five minutes. A separate, labeled test tube was used to separate the supernatant (based on serial numbers on the sample).

2.3 Analytical Statistics

Using SPSS, the statistical analysis will be carried out (Statistical Package for the Social Sciences). P values of <0.05 and <0.01 will be considered significant values. The spearman's correlation coefficient will be used to assess the relationship between the parameters and the severity of the condition.

2.4 Sample Size

The sample size will be calculated using the method described by Charan and Biswas, (2013):

$$N = \frac{(Z^2 p\text{-}q)}{d^2}$$

Where:

N= Desired number of samples when the population of the facility is limited

Z = The standard normal variance where the confidence level is 1.96 at 95%

p = Prevalence rate of cigarette smoking in Anambra Nigeria is 3.1% (Ezekwesili et al, 2016)

q = 1-p

d = 5% i.e degree of precision as desired by the researcher.

Applying the method,

$$N = \frac{Z^2 \times P \times (1-P)}{D^2}$$

$$N = \frac{1.96^2 \times 0.031 \times 1-0.031}{0.0025^2}$$

N=200 ± 10%

3. RESULTS

The variation of the Mean values of serum creatinine, urea, uric acid, MALB, ACR, and eGFR in smokers and non-smokers in Table 1.

There was a significant difference in the mean creatinine, urea, and microalbumin ($p<0.05$). the mean values of creatinine, urea, and microalbumin were higher in the smoker's group than their respective mean values in the non-smoker's group.

There was a significant difference in microalbumin was higher in smokers compared to non-smokers (control).

The mean value of estimated glomerular filtration rate (eGFR) ($p<0.05$) in smokers was lower compared to non-smokers (control).

There was no significant difference in the mean value of uric acid ($p>0.05$). The mean value of uric acid in smokers was higher compared to that of non-smokers.

In Table 2 the correlation of the average amount of cigarette sticks per day with creatinine, urea, uric acid, albumin-creatinine ratio, and estimated glomerular filtration rate and microalbumin in smokers.

There was a strong positive correlation between the levels of urea, creatinine, and uric acid in smokers in comparison with the average amount of cigarette sticks consumed daily.

There was a strong positive correlation between the levels of the albumin-creatinine ratio (ACR) and microalbumin (Malb) of the smokers when compared with the average amount of cigarette sticks consumed daily.

There was a strong negative correlation between the estimated glomerular filtration rate (eGFR) in comparison to the average sticks of cigarettes smoked daily.

Table 1. Shows the mean levels of serum creatinine, urea, uric acid, malb, ACR, and eGFR in chronic smokers and non-smokers (mean±SD)

Parameters	Non-smokers	Smokers	Mann-Whitney (u)	t-value	p-value
Creatinine(µmol/l)	74.80±24.713	132.33±68.10	-6.023	7.9	0.000
Urea(mmol/l)	4.45±1.64	6.50±2.97	-2.996	6.02	0.003
Uric acid	339.81±135.22	377.80±174.30	-0.760	1.7	0.447
Malb (mg/l)	47.19±25.38	59.91±46.80	-0.429	2.4	0.001
Acr (mg/mmol)	7.94±6.62	11.15±7.13	-2.420	3.4	0.016
eGFR(mL/min)	133.23±30.63	81.50±27.56	-6.092	12.6	0.000

Table 2. Shows the Correlation of the average amount of cigarette sticks per day with creatinine, urea, uric acid albumin-creatinine ratio and estimated glomerular filtration rate and microalbumin in smokers

	Parameters	r	p-value
Smokers	Av. Sticks vs Creatinine	0.103	0.528
	Av. Sticks vs Urea	0.044	0.798
	Av. Sticks vs Uric acid	0.125	0.442
	Av. Sticks vs ACR	0.415	0.008
	Av. Sticks vs eGFR	-0.102	0.533
	Av.sticks vs Malb	0.390	0.013

Keywords: ACR = Albumin-Creatinine ratio; eGFR = Estimated Glomerular Filtration Rate; MALB = Microalbumin; SD = Standard Deviation

4. DISCUSSION

One of the organs that are negatively impacted by smoking is the kidney. This study demonstrates how smoking affects renal function as measured by serum urea and creatinine levels. It demonstrates that smokers had significantly higher serum levels of urea and creatinine than non-smokers at (p0.05) and (p0.05), respectively. These results are consistent with those of Yuka [18] and El Sayed et al. (2013). Additionally, they could be brought on by the influence of smoking, which raises renovascular resistance and causes a considerable decline in renal plasma blood, filtration fraction, and glomerular filtration rate (GFR) [19]. The decline in GFR will cause the distal tubular flow rate to decline, which will enhance urea reabsorption [20]. Serum creatinine was much greater in smokers than in non-smokers, according to Halimi's study from 1998 [21], which demonstrated that smoking increases creatinine levels. Additionally, this research partially supports a study by Pittilo et al. [22] that found smokers had higher creatinine clearance (ml/min/1.73m2) than nonsmokers. [23] The study also found that smokers had considerably higher mean urine albumin levels than non-smokers, which is consistent with research was done by R K. Gupta et al. in 2014. Notably, microalbuminuria was more common in smokers.

Smoking was found to be a separate factor in the cardiac outcome preventive evaluation research to determine microalbuminuria [24]. One of the primary mechanisms through which smoking results in albuminuria and decreased renal function is through advanced glycation end products (AGEPs). AGEPs, which are cross-linking moieties, are created when reducing sugars interact with the amino groups of plasma proteins, lipids, and nucleic acids. The aqueous extracts of tobacco and cigarette smoke contain glycotoxins, highly reactive glycation products that can rapidly trigger AGEP formation on proteins in vitro and in vivo, as Cerami et al.,1997 has recently demonstrated [25]. The systemic and renal vasculature are expected to be affected similarly by the AGEPs produced by the reaction of glycotoxins from cigarette smoke with serum and tissue proteins as was previously mentioned. Another mechanism based on the pathophysiological effect of smoking-induced kidney damage is insulin resistance. Numerous researches have found a connection between smoking and insulin resistance in non-diabetic patients [26]. Albuminuria and impairments in renal function have both been linked to insulin resistance. Both procedures lead to endothelial dysfunction by disrupting the balance between the substances the endothelium produces to contract and relax. Smokers have been reported to have greater plasma levels of endothelin 14 than non-smokers, and there is indirect evidence that smoking interferes with endothelin, prostacyclin, or nitric oxide release when prompted [27].

Damage to the vascular system is one of the many harmful health effects of cigarette smoking. Smoking has been linked to arteriosclerosis, which includes the renal arteries. Additionally, it's linked to kidney and other organ thickenings of tiny arteries as well as arteriolar hyalinosis. Vascular injury and renal vasoconstriction may be caused by some processes [28-30]. Catecholamines, arginine, vasopressin, and endothelin-1 are among the vasoconstrictors whose plasma levels are increased by nicotine [19,31]. [22] Smoke from cigarettes harms endothelium cells, and nicotine promotes the growth of smooth muscle cells. [30] Another study linked sympathetic nervous system activation to renovascular resistance. A prior study found that smokers had greater serum levels of cadmium and lead than non-smokers, which suggested that the Lead-linked glomerular dysfunction they experienced may have been the result of more recent exposure to high levels of lead. Seven cigarettes smoked daily result in an estimated 3.6–6.0 Lg of Cd being inhaled, which is cumulatively nephrotoxic.

The nephrotoxicity of cadmium [32] causes changes in proximal tubular function, characterized by increased excretion of beta 2-microglobulin and causing the classic tubular proteinuria, as well as glomerular dysfunction, which is indicated by increased excretion of high molecular weight proteins, increased levels of beta 2-microglobulin and creatinine in plasma, and leading to glomerular type proteinuria. These findings imply that chemicals found in cigarettes can have a serious impact on renal tubule PH and alter the glomerular filtration rate.

5. CONCLUSION

In this work, an effort has been made to identify the biochemical alterations that occur when smoking and reflect renal function. The elevated serum urea and creatinine levels in the smoker group show that renal function is negatively

impacted. The considerable decline in the glomerular filtration rate is what is responsible for the increase in creatinine and urea (GFR). There is evidence that nicotine usage has a variety of systemic consequences, especially in light of the relationship between urea and creatinine in renal illness. The deleterious effects of cigarette smoking on these metabolites appear to be confirmed by the higher mean serum levels of urea and creatinine in active smokers. This analysis also demonstrates that smoking was independently related to the development of greater albuminuria levels over time in a group of male adults without microalbuminuria and with normal kidney function.

CONSENT

Before the study, the subjects' informed consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

Before the study started, the ethics committee for the Faculty of Health Science and Technology granted its clearance for the research.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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