Original Research Article

The Effect of Chronic Cigarette Smoking on some Kidney Function Markers

ABSTRACT

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. 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. 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 ($p > 0.05$). In conclusion, smokers experience negative effects on their renal function.

Keywords: Albuminuria, Tobacco Use, Kidney, Urea, Creatinine, and (GFR) Glomerular Filtration Rate

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 Tobacum) has been farmed in Africa. Smokeless tobacco consumption is currently on the rise in the United States of America (USA) [2] and is extremely common in the Far East, Middle East, and Europe [1]. 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. Native Americans grew tobacco for use in beverages, but they mostly smoked it through pipes to consume it. Tobacco has been used as an antiseptic and to prevent minor bleeding in addition to being a frequent cure for insect bites and stings since it kills numerous microorganisms. It was occasionally administered as an enema for therapeutic purposes, but the significant likelihood of overdose rendered this practice far too risky. As a result, the only way for shamans to have visions was to smoke. Additionally, chewing and snorting are used. Finally, since tobacco is easily absorbed via the skin, some users have been known to snuff between their toes to blend in. After the Civil War, cigarette sales soared, which contributed to the growth of cigarette smoking. By the 20th century, cigarette smoking had exponentially increased among all socioeconomic groups and both men and women.

The end of the pipe is where the tobacco is burned, and before the smoke reaches the mouth, it is dragged via a long tube and filtered through water. In Asia, the Mediterranean region, and North Africa, water pipelines are widely used. Native Americans in North and South America have long held pipe ceremonies to commemorate important religious and communal holidays. Sacred pipes are still regularly utilized for traditional Native American ceremonies today, according to Britinicana [3]. Additionally, pipe smoking occurs after a deal or contract was finalized.

A cigarette is paper-wrapped tobacco. Cigarette smoking is the most popular way to consume tobacco now and for the majority of the 20th century. The switch from chewing tobacco, snuff, and pipe smoking to cigarette smoking after the Civil War represented a significant change in the production and consumption of tobacco. The first cigarettes, which were wrapped in cornhusks, were created in the seventeenth century. One of the earliest businesses to mass-make cigarettes was Duke & Company, established in Durham, North Carolina, after the Civil War.

Cigars can't be mass-produced as quickly as cigarettes. Due to their higher cost and less widespread marketing than other tobacco products, cigars require more effort to manufacture since the tobacco leaves are manually rolled. These come in a variety of shapes and sizes and are constructed of air-cured and fermented tobacco with a tobacco wrapper.

Cheap cigarettes called "Bidis" are flavored with flavors like strawberry, vanilla, and chocolate and made from subpar tobacco. Bidis originate in Asia, especially in India, where they are exceedingly well-liked.

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[4]. 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[5]. Our nation's leaders ought to be concerned.

It is well known that smoking raises the levels of liver enzymes responsible for breaking down medicines and poisons. That implies that these medications are removed by these enzymes more quickly in smokers, which could lead to the treatments' ineffectiveness. In particular, CYP1A2 and CYP2A6 levels are increased. Substrates for CYP1A2 include valproic acid, an anticonvulsant, and tricyclic antidepressants like amitriptyline.

Smoking cigarettes can have both immediate and long-term impacts. In the short term, smoking causes tachycardia and elevated blood pressure by activating the sympathetic nervous system more. 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 [6]. 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 [7].

Furthermore, K. Yamagata's [8] 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 [9].

The incidence and progression of CKD may be influenced by smoking, regardless of the underlying disease, according to a recent meta-analysis [10] based on 15 prospective cohorts and including more than 65.000 incident CKD patients. However, interestingly, there was no correlation between smoking and proteinuria.

Tobacco powder is eaten orally or breathed through the nasal canal to make dry snuff. Tobacco was commonly chewed and used by medicine men in various Native American tribes for its therapeutic effects. Throughout Europe and the United States in the seventeenth and eighteenth centuries, snuff was widely used. Fine-ground smokeless tobacco is generally referred to as snuff

[11]. A wet tobacco paste known as dipped snuff is held between the gums and cheeks to allow the nicotine to be absorbed there.

Chewing tobacco was the most popular method of tobacco use for a long time. Native Americans chewed tobacco leaves, often combined with lime, in both North and South America. The first type of chewing tobacco is the "twist." Three premium tobacco leaves are twisted into a rope, braided together, and dried. It is still available in several shops in the Appalachian region. Before, during, and after the Civil War, troops and farmers in the North and the South enjoyed chewing tobacco. Spittoons were commonplace in both urban and rural American public buildings. Spittoons are now considered antiques. People who chew tobacco are more likely to get periodontal disease and oral cancer.

Hookahs are tall water pipes that have been used for smoking for millennia throughout South Asia and the Middle East. Recently, they have become more well-liked among college students in America. Tobacco for hookah is soaked in molasses and blended with fruit pulp, including mint, mango, and apples. With disposable mouthpieces, it is smoked in groups. The idea that using a water pipe is safer than using a cigarette is still widespread among some people. It's possible that smoking from a hookah is riskier than other types of smoking. In addition to possibly containing heavy metals, tobacco has higher levels of tar and nicotine than cigarettes. In addition, because charcoal is used to heat tobacco, hookah smoke contains more carbon monoxide than cigarette smoke.

More than 4,000 substances, including 400 additional poisons and 43 recognized carcinogens, are found in cigarette smoke. These include formaldehyde, ammonia, hydrogen cyanide, arsenic, DDT, benzene, lead, cadmium, nitrosamines, polycyclic aromatic hydrocarbons, as well as nicotine, tar, and carbon monoxide (PAHs). The tobacco leaves used to create cigarettes and cigars contain radioactive substances. The amount of tobacco relies on the type of soil the plants were grown in and the fertilizers used because these components come from the soil and fertilizer used to grow the tobacco leaves. 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 [12].

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 [13]. 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. Based on these, it becomes required to conduct a study on the assessment of the levels of microalbumin, albumin-creatinine ratio, urea, uric acid, creatinine, and glomerular filtration rate in chronic smokers.

The degradation of either exogenous (dietary) or endogenous (tissue) proteins produces urea, a metabolic product, in the following order:

Protein ——————> acid, amino ——————-> ammonia ——————-> Urea

Nearly half of the blood's nitrogen which is not a protein is made up of urea. It makes up the majority of the nitrogen-containing compounds produced by protein degradation in humans and is responsible for more than 70% of the non-protein that is subsequently excreted. Urea is synthesized in the liver and then delivered by the plasma to the kidney, where the glomerulus easily separates it from the plasma. [14] 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. Renal perfusion, food protein content, and the amount of protein catabolism that takes place all have a significant impact on the quantity of urea in the plasma.

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 [15]. It is subsequently transferred to various tissues, including muscle and the brain, where it is changed into the highly energetic molecule phosphocreatine. Under physiological circumstances, creatine and creatine phosphate naturally lose water and phosphoric acid, respectively, to create their anhydride creatinine, which is then expelled into the plasma.

Muscle naturally and irreversibly transforms some of its free creatine (between 2% and 1% each day) to creatine anhydride. As a result, creatinine is released into the bloodstream at a rather consistent rate that has been determined to be a function of the person's muscle mass. It is eliminated in the urine after being removed from the bloodstream by glomerular filtration. In the renal tubules, small amounts may also be reabsorbed, particularly at low flow rates.

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) [16]. 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. However, even in the early stages of renal illness, albumin can be found in the urine. To check for kidney disease, the urine albumin test (formerly known as the microalbumin test) finds and quantifies the amount of 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 [17]. 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[18].

A person's kidneys start to lose their capacity to preserve albumin and other proteins if they become ill or damaged. The presence of more protein in the urine, a sign of worsening renal failure, is typically observed in chronic conditions such as diabetes and hypertension.

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 [19]. 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.

METHOD AND MATERIALS

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.

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. 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).

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.

RESULTS

The variation of the Mean values of serum creatinine, urea, uric acid, MALB, ACR, and eGFR in smokers and non-smokers in **table 1.1**

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 1.2 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 1.1 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)	p-value
Creatinine(µmol/l)	74.80±24.713	132.33±68.10	-6.023	0.000
Urea(mmol/l)	4.45±1.64	6.50±2.97	-2.996	0.003
Uric acid	339.81±135.22	377.80±174.30	-0.760	0.447
Malb (mg/l)	47.19±25.38	59.91±46.80	-0.429	0.001
Acr (mg/mmol)	7.94±6.62	11.15±7.13	-2.420	0.016
eGFR(mL/min)	133.23±30.63	81.50±27.56	-6.092	0.000

Table 1.2 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

DISCUSSIONS

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 [20] 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) [21]. The decline in GFR will cause the distal tubular flow rate to decline, which will enhance urea reabsorption [22]. Serum creatinine was much greater in smokers than in non-smokers, according to Halimi's study from 1998 [23], which demonstrated that smoking increases creatinine levels. Additionally, this research partially supports a study by Pittilo et al. [24] that found smokers had higher creatinine clearance (ml/min/1.73m2) than nonsmokers. [25] 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 [26]. 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 [27]. 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 [28]. 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 [29].

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 [30–32]. Catecholamines, arginine, vasopressin, and endothelin-1 are among the vasoconstrictors whose plasma levels are increased by nicotine [21,33]. [24] Smoke from cigarettes harms endothelium cells, and nicotine promotes the growth of smooth muscle cells. [32] 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 [34] 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.

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.

Aware Consent

Before the study, the subjects' informed consent was obtained.

Ethics-related matters

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

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