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Tobacco chewing and smoking -risk for renal diseases.

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Abstract

Introduction: Tobacco chewing and cigarette smoking is considered to be the most common particular cause of adult death in developed countries. Now days the adverse effects of tobacco chewing and smoking on renal function have gained more attention because it is associated with various diseases.
Methods: The present study included 150 subjects, out of which 50 were controls and 100 were subjects with age group between 30 to 60 years. The analysis of biochemical parameters was done by using standard methods.
Results: Elevated levels of serum urea, urinary microalbumin and hs-C reactive protein but there was no significant change in mean difference of serum creatinine in tobacco chewers and cigarette as compared to controls.
Conclusion: This might offer a new approach to renal disorder prevention in population with tobacco chewing and tobacco smoking.

Keywords: Chronic kidney disease (CKD), Cardiovascular diseases (CVD).

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Introduction

The fight against tobacco chewers and cigarette smokers is a challenging scenario in worldwide. Tobacco is the single greatest cause of preventable death globally. The World Health Organization (WHO) reported that tobacco caused millions deaths over the course of the 20th century [1].

There are several harmful substances found in tobacco and tobacco smoke like nicotine is one of the many substances that may be acquired through active and passive smoking of tobacco [2]. In addition to nicotine, cigarette smoke is primarily composed of many gases, mainly carbon monoxide and tar [3]. Nicotine is commonly consumed via smoking cigarettes, cigars, pipes or chewing. There is some evidence to indicate that tobacco chewing and smoking increases the risk of renal function impairment in general population [4].

Now days the adverse effects of tobacco chewing and smoking on renal function have gained more attention because it is associated with excessive morbidity and mortality in various diseases, most predominantly cardiovascular, lung diseases and cancer [5-7]. In addition to its known cardiovascular consequences, it could accelerate the progression of renal diseases [8]. A tight relationship was seen in between chronic kidney disease (CKD) and cardiovascular diseases (CVD). Chronic kidney disease and its consequences accelerate the risk for CVD; on other side, CVD increases the majority of morbidity and mortality in patients with CKD [8,9].

Tobacco chewing and cigarette smoking is considered to be the most common particular risk factor for the rate of progression of the renal disorders but studies regarding the effect of smoking and tobacco chewing on renal function in subjects without renal disease are uncommon [9]. It is unknown whether chronic smoking and tobacco chewing affects renal function or represents a cause of renal damage in subjects without pre-existing renal diseases, so in this study the renal effects of tobacco chewing and smoking in normal subjects could provide valuable information regarding the relationship between smoking and the progression of renal disease [10,11].

Tobacco chewing and smoking leads the risk of albuminuria in the general population. Micro proteinuria (Micro albuminuria) is defined as, small quantity of protein excreted in urine per day. It is an early indicator for the progressive kidney damage [12]. Intra-individual day-to-day variability of albumin excretion has also albuminuria as a risk factor for cardiovascular disease (CVD) [13].

Tobacco chewing and cigarette smoking produces a systemic inflammatory effect which exacerbates the endothelial injury. Inflammatory biomarkers are strong predictors of future cardiovascular events in cigarette smoking and tobacco chewing [14,15]. In smokers and tobacco chewers alteration of the relevant biochemical parameter may be indicative of onset and progress of renal failure or CVD.

Therefore we decided to identify the biochemical mechanisms and the independent preventable risk factors which help in decreasing the number of patients suffering from chronic

kidney disease and slowing its progression. In view of the above aspects in tobacco chewing and smoking, the aim of present study to find out the effect of tobacco chewing and cigarette smoking on renal function by measuring the levels of urinary micro albumin, serum urea, serum creatinine, and serum hs-C reactive protein, so that their levels will be used as predictive value in the management of tobacco chewers and tobacco smokers.

Materials and Methods

Proposed research work was carried out in Department of Biochemistry, Bharati Vidyapeeth Deemed University Medical College & Hospital, Sangli. The study has been approved by Institute of Ethical Committee Informed consent was obtained from the subjects.

The present study included 150 subjects, out of which 50 were controls and 100 were subjects with age group between 30 to 60 years. The controls were age and sex matched to study subjects. Upon the inclusion of the subjects, a record was made containing current history, diet along with laboratory investigations. The subjects who are willing to participate with informed consent were included in the present study. The subjects afflicted by any systemic or metabolic disease, subjects of vascular diseases like cardiovascular, renal artery stenosis, alcoholics and those who were taking any medication, pregnant female excluded from this study.

5 ml venous blood sample was collected under aseptic precautions in plain bulb. The sample was allowed to clot at room temperature for 20-30 minutes and serum was separated for analysis of biochemical parameters. Fresh urine sample was collected in sterile container. The analysis of biochemical parameters was done by using standard analytical grade reagents and chemicals. Blood urea [16] and serum creatinine [17] were assayed by colorimetric methods. Urinary microalbumin [18] was assayed by turbid metric immunoassay and high-Sensitivity CRP (hsCRP) levels were measured by turbid metric method [19] and values were expressed as mg/dl.

Statistical analysis

All graphics and statistical comparisons were performed with spreadsheet software (Excel, Microsoft). The statistical analysis was carried out by using SPSS software, version 22. The statistical analysis was done using the ANOVA and "t" test. All results were calculated as Mean ± SD and "p" value of <0.05 was considered statistically significant. Mean values were compared using the paired't' test. Bivariate correlation is obtained to check the relationship between urinary micro albumin, serum urea, serum creatinine, and hs-C reactive protein in tobacco chewers ,smokers and controls.

Results

Table 1 shows statistical comparison between concentration of serum urea, serum creatinine, urinary micro albumin and serum Hs-CRP in tobacco chewers, smokers and controls. There is highly statistically significant difference in means of serum urea, urinary micro albumin and hs-C reactive protein in tobacco chewers and smokers as compared to controls (P=0.00) but there was no significant change in mean difference of serum creatinine in tobacco chewers and cigarette smokers (P> 0.05) as compared to controls (P= 0.151,0.208).

Table1. The mean values of biochemical analytes in tobacco chewers, tobacco smokers and controls subjects.

Name of Parameter	Group N=50	Mean mg/dl + Std. Devation	Std error mean	Significance
Serum Urea	Tobacco Chewers	30.58 ± 7.23***	1.02	t=6.099, P=0.00
	Tobacco Smokers	30.37 ± 7.30***	1.04	t = 5.831, P =0.00
	Controls	23.32 ± 4.31	0.61	
Serum Creatinine	Tobacco Chewers	1.06 ± 0.16*	0.02	t =1.447, P=0.151
	Tobacco Smokers	1.05 ± 0.15*	0.02	t = 1.267, P =0.208
	Controls	1.01 ± 0.14	0.02	
Urinary Microalbumin	Tobacco Chewers	200.00 ± 97.51***	13.79	t=13.443, P =0.00
	Tobacco Smokers	234.54 ±117.32***	16.59	t = 13.257, P = 0.00
	Controls	55.48 ± 3.70	0.52	
Serum Hs-CRP	Tobacco Chewers	3.62 ± 0.84***	0.12	t =10.385, P = 0.00
	Tobacco Smokers	3.75 ± 0.80***	0.11	t = 11.346, p = 0.00
	Controls	1.74 ± 0.97	0.14	

The statistical method used to compare data was unpaired 't' test

*P>0.05 ------ Not Significant

**P<0.05 ----- Significant

***P<0.001 ----- Highly significant

Discussion

Tobacco consumption is a major cause of mortality and morbidity in India. Adverse impact of tobacco products on health has been well established for more than 50 years. Apart from the direct tobacco smoke, exposure to second-hand tobacco smoke (Passive route) causes illness, disability, and death from a wide range of diseases [20], tobacco use is the leading cause of preventable disorder and premature death and the principle risk factor for oral cancer. Approximately half of all smokers will die of a smoking-related disorder [21,22].

The addictive liability and pharmacological effects of tobacco chewing and smoking are primarily mediated by the major tobacco alkaloid nicotine. High stress jobs enhance the repeated episodes of tobacco chewing and smoking and further reinforce addictive behaviours [23].

Among the health hazards of tobacco chewing and smoking carcinogenesis, cardiovascular disease and lung disease have attracted considerable attention but the potential impact of smoking on renal function and renal disease have remained largely unnoticed. Tobacco chewing and smoking was recently proven to play an important role in renal disorders [24]. This study aims to investigate the relationship between tobacco chewing and cigarette smoking and chronic kidney disease, and its effects on renal function.

As regards urea being an indicator for kidney disorder, the mean difference of urea significantly elevated ($P<0.001$) but there was a no significant change in mean difference of serum creatinine in tobacco chewers and cigarette smokers ($P>0.05$) as compared to controls. High levels of serum urea and creatinine is said to be a predictable component of either post-renal obstruction or pre-renal uremia superimposed on renal disease. It is known however, that elevated serum urea and creatinine level is associated with abnormal renal function, especially glomerular function. As regards urea and creatinine being an indicator for kidney disorder, the elevated values in the test groups, suggests that tobacco may contain some toxic components that are nephrotoxic which, according to Varely et al. (1987), can be linked with the fact that the presence of toxic compounds increases blood urea and decreases plasma protein [25].

Earlier studies reported that a progressive kidney failure can be associated with a gradual decrease of renal and non-renal elimination of nicotine, and this increases the rate of nephrotoxicity [26]. Also, the effects of heavy metals in tobacco like Cadmium (Cd), Mercury (Hg) and Lead (Pb), might be another possible mechanism for tobacco-induced renal damage [27]. However, the mechanism by which tobacco chewing and smoking induces renal damage may be through enhancing the synthesis of free radicals may lead to alter the glomerular function leading to elevated the levels of urea and creatinine in tobacco chewers and smokers [28].

The term micro albuminuria describes small amounts of albumin in urine. Micro albuminuria may be due to various pathophysiological, mechanisms in tobacco chewers and smokers. In present study there was highly significant elevation of urinary micro albumin in tobacco chewers and smokers as compared to controls ($P<0.001$). Earlier studies remarked that nephropathies are accelerated by nicotine with an increased incidence of micro albuminuria progressing to proteinuria, followed by type-1diabetes mellitus induced renal failure [29].

Nicotine increases mesangial cell proliferation through activation of nicotinic receptors. Tobacco chewing and smoking may be responsible to decrease in renal plasma flow and glomerular filtration rate. These small and frequent episodes of acute renal hypoperfusion may damage some glomeruli which may result in hyperfiltration, together with capillary albumin leakage [30]. It is well known that urinary albumin is a responsive marker of glomerular injury and there is a relationship between tobacco chewing and smoking with albuminuria indicates direct or indirect renal damage induced by tobacco chewing or smoking [31,32].

One of the underlying mechanisms by which tobacco chewing or smoking induces albuminuria and abnormalities in renal function is through advanced glycation end products (AGEPs). AGEPs are cross-linking moieties formed from the no enzymatically reaction of reducing sugars and the amino groups of plasma proteins, lipids and nucleic acids [33]. AGEPs which may be responsible for enhanced vascular permeability causes of albuminuria. Cerami et al., [34] have shown that both aqueous extracts of tobacco and cigarette smoke contain glycotoxins, highly reactive glycation products that can rapidly induce AGEP formation on proteins. It is reasonable to expect that the AGEPs formed by the reaction of glycotoxins from cigarette smoke with serum and tissue proteins will have the same effect on the renal functions.

Recent study also documented that cigarette smoking contains carbon monoxide which has affinity towards the hemoglobin and forms carboxyhemoglobin. Smoking causes generation of high amounts of carboxyhemoglobin and decrease oxygen delivery to tissue lead to hypoxia causes ischemia in renal glomeruli and basement membrane. This damage might be the cause of microalbumin in urine [35-37].

C- reactive protein (CRP) is synthesized in the liver and is one of the first acute-phase proteins to rise in response to inflammatory disease. Normally, there are minimal levels of CRP in blood. A high or increasing amount of CRP suggests an acute infection or inflammation. C-reactive protein (CRP), may be easily and sensitively measured in a variety of clinical situations to monitor disease progression [38,39].

Tobacco chewing and smoking has been shown to have harmful property on different organs of the body and is leading to different diseases. A previous study shows that cigarette smoking is a conventional and major risk factor in the development of cardiovascular disease (CVD) and atherosclerosis. More recently, it has been recognized that CVD contains a component of inflammation and has even been referred to as an inflammatory disease [40-42].

CRP appears to be a central player in the harmful effects of inflammation, and hs-CRP is a widely available, inexpensive screening test to assess inflammation-associated risk. However, values defining elevation of CRP will depend on multiple factors, including baseline cardiovascular risk as determined by traditional and nontraditional risk factors and extent of CVD. Earlier studies also reported that tobacco chewing and smoking is associated with higher polymorphonuclear leukocyte counts, fibrinogen, CRP, and other inflammatory markers [42].

Results from our study demonstrate that tobacco chewing and cigarette smoking results in chronic inflammatory state, evidenced by increased levels of CRP. In present study there is highly statistically significant difference in means of hs-C reactive protein of tobacco chewers and smokers as compared to controls ($P<0.001$). Tobacco chewing and cigarette smoking also activates monocytes and enhances recruitment and adhesion of leukocytes to blood vessel walls, an integral step in

vascular inflammation contributes to atherogenesis because high leukocyte counts and high levels of CRP and fibrinogen are all powerful predictors of future cardiovascular events. Oxidative stress is probably another major inducible factor in the genesis of smoking-induced vascular renal injury [3].

Our result indicates that serum hs-CRP is independent risk factors for renal dysfunction in tobacco chewers and smokers. Proper use of hs-CRP to rule out the renal dysfunction in early stage will help to reduce the renal disorder in tobacco chewers and smokers.

Our study supports the hypothesis that tobacco chewing and smoking, contributes to the development of renal impairment leading to renal disorders. The association was strongest of tobacco chewing and smoking with renal disorders, this is supported by the results. We observed increased levels of microalbumin, serum urea, serum creatinine in tobacco chewers and smokers. Significant correlation of urinary micro albumin with serum urea, serum creatinine and hs-CRP was moderate (table 2), which indicate that tobacco chewing and smoking are strongly associated with renal impairment which may lead to future abnormalities in renal function.

Table 2. *Correlations of serum microalbumin, serum urea, serum creatinine and hs-CRP in tobacco chewers, tobacco smokers and controls.*

		Serum Urea	Serum creatinine	hs-CRP
Urinary mciroalbumin	Pearson Correlation	0.665**	.492**	.691**
	p value	0.00	0.00	0.00
Serum Urea	Pearson Correlation		0.547**	0.480**
	p value		0.00	0.00
Serum creatinine	Pearson Correlation			.342**
	p value			0.00

Significant correlation of urinary microalbumin with serum urea, serum creatinine and hs-CRP was moderate.

Significant correlation of serum urea with serum creatinine and hs-CRP was moderate.

Correlation between serum creatinine and hs-CRP was low.

Consumption of tobacco and smoking may be toxic, which, in the case of the kidney, can alter its renal function. As such, there is a need to draw the attention of consumers to the hazardous effects and subsequent health implications of tobacco chewing and smoking.

To conclude, the overall scenario of tobacco chewing and smoking in India looks severe alarming with increased incidence of chronic renal failure patients. Altered levels of urinary micro albumin, serum urea, serum creatinine, urinary creatinine, creatinine clearance and hs-CRP are associated with increased risk of renal dysfunction, which leads to different renal disorders, and application of these biochemical parameter may serve as important tool for early detection as well as to reduce risk of kidney function deterioration. This might offer a new approach to renal disorder prevention in population with tobacco chewing and tobacco smoking.

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