Smoking — A Renal Risk Factor

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Abstract
Smoking has adverse effects on health, causing ischemic heart disease, stroke, chronic obstructive lung disease and cancers of the respiratory, gastrointestinal, pancreas, kidney and urinary tract. Smoking causes an acute increase in mean arterial pressure and heart rate. Chronic smoking reduces the renal plasma flow. There is clinical evidence that smoking has adverse effects on renal outcome in essential hypertension, diabetic nephropathy, primary glomerular diseases, systemic diseases involving the kidney and renal allograft recipients.

INTRODUCTION
Smoking is a major health hazard. In recent years, it has become apparent that cigarette smoking is associated with excessive morbidity and mortality in various diseases, most prominently cardiovascular and lung diseases. Recently, however, the adverse effects of smoking on renal function have gained more attention, mainly through investigations in diabetic patients.

RENAL EFFECTS OF SMOKING IN HEALTHY INDIVIDUALS
Beat to beat recording of blood pressure showed that smoking causes a transient acute increase, with rise in systolic blood pressure reaching 20 mmHg. Ritz et al observed that in healthy volunteers, smoking increased renovascular resistance and caused a significant reduction of GFR, filtration fraction and renal plasma flow.

Smoking increases the risk of albuminuria/proteinuria in the general population. There is some evidence to indicate that smoking increases the risk of renal function impairment in general population, particularly in men and in the elderly.

Data from the large population based studies, including 40619 individuals of 28-75 years age, 7476 non-diabetic subjects and 28409 healthy volunteers, has shown that smoking had a dose-dependent increase in albumin excretion and abnormal renal function. Cessation of smoking seems to reverse the change in renal function and, to a lesser extent, albuminuria.

Data from the prospective Multiple Risk Factor Intervention Trial (MRFIT) of 332,544 men indicated that smoking also increases the risk of renal failure in general population. Also the retrospective case control study of 4142 non-diabetic elderly subjects showed that cigarette smoking was found to be highly associated with an increase in serum creatinine.

RENAL EFFECTS OF SMOKING IN ESSENTIAL HYPERTENSION
Smoking is considered a renal risk factor in hypertensives in view of its proven effects on albuminuria/proteinuria. In a study of lean subjects with essential hypertension, prevalence of microalbuminuria was almost double in smokers as compared to non-smokers. In another study of 63300 urine samples, proteinuria was more common in smokers as compared to nonsmokers and was more prominent in heavy smokers.

Since, urinary albumin is a sensitive marker of glomerular injury, it is conceivable that the relationship of smoking to albuminuria indicates direct or indirect renal damage induced by smoking.

The effect of smoking on the rate of progression in primary hypertension remains controversial. Regalado et al in a prospective study, including 51 patients with essential hypertension with a mean follow-up of 35.5 months, showed for the first time that smoking is an independent risk factor for renal function decline in patients with severe essential hypertension. On the contrary, in a large prospective study from U.S. including 5730 black and 6182 non-black hypertensive males there was no relation between smoking and the risk of end-stage renal failure during a minimum of 13.9 years of follow-up.

RENAL EFFECTS OF SMOKING IN DIABETIC NEPHROPATHY
In diabetic patients, smoking increases mortality two to
three-folds mainly by cardiovascular complications. This risk is particularly high in patients of diabetic nephropathy with end-stage renal disease. Various studies, both in type 1 and type 2 diabetes mellitus, have shown that smokers have a higher risk to develop diabetic nephropathy as compared to nonsmokers. The data shows that:

* Smoking increases the prevalence of microalbuminuria by 2.8 folds.
* Shortens the time interval between onset of diabetes and onset of albuminuria or proteinuria.
* Accelerates the progression from stage of microalbuminuria to the stage of overt proteinuria.
* Accelerates the rate of progression to end stage renal disease.
* Smoking might be aggravating the risk of ischemic nephropathy in diabetics.

### Renal effects of smoking in non-diabetic renal disease

There is evidence that smoking is a major risk factor for progression in primary renal disease e.g. autosomal dominant polycystic kidney disease, IgA nephropathy. This effect was dose-dependent and was seen in males and elderly.

There is no documented evidence that the risk of developing primary or secondary glomerular disease is higher in smokers.

### Smoking and atherosclerotic renal artery stenosis/ischemic nephropathy

Atherosclerotic peripheral vascular disease is common in smokers. Smokers have a higher risk of atherosclerotic renal artery stenosis and ischemic nephropathy in elderly patients (> 65 years of age).

There are no reports comparing the rate of progression of renal artery stenosis between smokers and non-smokers. However, smoking is a known factor for cholesterol micro-embolism and it is likely that smoking accelerates the course of ischemic nephropathy.

### Adverse Effects of Smoking in Renal Allograft Recipients

Contrary to the earlier reports, recent prospective studies have shown smoking to affect the graft function adversely. In a multivariate analysis, pre-transplant smoking was associated with a relative risk of 2.3 for graft loss. In a retrospective study, current smoking was documented to be a risk factor for decreased graft survival in elderly (> 60 years) renal transplant recipient.

The adverse effect of smoking in renal transplant has been shown to depend upon the etiology of basic disease. There was substantial higher loss of graft function in smokers of patients of lupus nephritis.

The adverse effect of smoking in renal donors on the graft survival was found to be statistically insignificant.

### Smoking and renal pathology

There is some experimental data to suggest a more severe glomerulosclerosis and tubulointerstitial fibrosis related to smoking. Clinical data did not show any association of smoking and severity of glomerulosclerosis. However, compared to non-smokers, smokers did exhibit more severe myointimal hyperplasia in elderly male patients.

### Potential mechanisms of smoking-induced renal damage

The exact mechanisms of nephrotoxic effects of smoking are not well understood. The various postulated mechanisms include the acute effects, particularly sympathetic activation (influencing blood pressure and renal hemodynamics) and the chronic effects, particularly endothelial cell dysfunction (diminished nitric oxide availability, diminished endothelial-dependent vasodilatation, and intimal cell hyperplasia).

### Conclusion

Smoking is one of the most important remediable renal risk factor. It has negative impact on the renal function both in the healthy individuals as well as the patients with different types of renal diseases. Smoking is a recognized risk factor for progression of renal damage in diabetic patients but its relationship to other renal diseases is less clear. The present data do not allow the drawing of a definite conclusion about the magnitude of renal benefit derived from smoking cessation. In view of the data showing clear negative impact of smoking on the course of renal disease, it is rational to conclude that cessation of smoking may help to retard the progression of renal failure.

### References


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**Announcement**

10th Annual Conference Association of Physicians of India West Bengal Branch to be held on 1st and 2nd November, 2003, at Park Hotel, Kolkata.

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