

EVALUATING THE ASSOCIATION BETWEEN PROTON PUMP INHIBITOR USAGE AND THE RISK OF DEVELOPING CHRONIC KIDNEY DISEASE: A CASE-CONTROL STUDY

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Abstract

Background: Chronic Kidney Disease (CKD) is a global health concern with multifactorial etiology, including medication-related risks. Proton Pump Inhibitors (PPIs), widely used for gastric acid-related disorders, have been scrutinized for their potential adverse renal effects. This case-control study investigates the association between PPI usage and the risk of developing CKD, alongside demographic and lifestyle factors such as age, gender, and smoking status. **Material and Methods:** A total of 100 participants were enrolled, comprising 50 CKD cases and 50 controls without CKD. Data on PPI usage, age, gender, and smoking status were collected through questionnaires and medical records. The association between PPI use and CKD was analyzed using odds ratios, with further stratification by age, gender, and smoking status to explore potential risk modifiers. **Results:** The study found a significant association between PPI use and increased risk of CKD, with 60% of cases versus 20% of controls reporting PPI usage (Table No:1). Age analysis showed 70% of cases were 50 years or older (Table No:2). There was a slight male predominance among cases (60%), and a notable proportion of cases were smokers (40%), indicating additional risk factors for CKD (Tables No:3 and No:4). **Conclusion:** The findings suggest a strong association between PPI usage and CKD risk, accentuated by age, male gender, and smoking status. These results highlight the importance of cautious PPI prescribing and monitoring, especially in patients with concurrent risk factors for CKD.

INTRODUCTION

Chronic Kidney Disease (CKD) represents a significant and growing challenge to public health worldwide, characterized by a gradual loss of kidney function over time.^[1] The etiology of CKD is multifaceted, including genetic predisposition, environmental factors, and various comorbid conditions such as diabetes mellitus and hypertension. Among the potential risk factors, the role of medications, specifically Proton Pump Inhibitors (PPIs), has emerged as a topic of considerable interest and concern in the medical community.^[2,3]

PPIs are among the most widely prescribed medications globally, utilized for the management of acid-related gastrointestinal disorders including gastroesophageal reflux disease (GERD), peptic ulcer disease, and Zollinger-Ellison syndrome.^[4,5] Despite their efficacy and the perception of safety,

long-term PPI use has been associated with a range of adverse health outcomes, including mineral malabsorption, infections, and chronic kidney disease.^[6]

The mechanism by which PPI use might lead to renal impairment is not fully understood but is thought to involve acute interstitial nephritis, a condition that can progress to chronic kidney injury if unrecognized or recurrent.^[7] Despite growing evidence from observational studies suggesting a link between PPI use and increased risk of CKD, causality remains to be conclusively established. Furthermore, the influence of demographic and lifestyle factors such as age, gender, and smoking status on this potential association has not been fully elucidated.

Given the widespread use of PPIs and the profound impact of CKD on patients' quality of life and healthcare resources, this case-control study aims to investigate the association between PPI usage and

the development of CKD. Additionally, it seeks to explore how demographic and lifestyle factors may modulate this risk. Understanding these relationships is crucial for guiding clinical decisions regarding the prescribing of PPIs and for identifying patients at higher risk of CKD who may benefit from alternative therapeutic strategies or closer monitoring.

MATERIALS AND METHODS

Study Design: This case-control study was conducted at Andhra Medical College, Visakhapatnam, to investigate the association between Proton Pump Inhibitor (PPI) usage and the risk of developing Chronic Kidney Disease (CKD) among patients attending the medical facility. The study period extended from January 2023 to August 2023.

Participant Selection

A total of 100 participants were recruited for the study, comprising 50 cases diagnosed with CKD and 50 controls without CKD. Cases were selected from patients diagnosed with CKD based on established diagnostic criteria, including laboratory tests and medical records. Controls were individuals without a history of CKD, matched with cases by age, gender, and other relevant factors to minimize potential confounders.

Data Collection

Data on PPI usage, demographic characteristics (age, gender), and lifestyle factors (smoking status) were collected through structured interviews and review of medical records. Information regarding the duration and frequency of PPI usage was also recorded⁸.

Statistical Analysis

The association between PPI usage and CKD was assessed using odds ratios (ORs) and corresponding 95% confidence intervals (CIs). Subgroup analyses were performed to evaluate the influence of demographic and lifestyle factors on the observed association. Statistical significance was set at a p-value < 0.05.

Ethical Considerations

The study protocol was reviewed and approved by the Institutional Review Board (IRB) of Andhra Medical College, Visakhapatnam. Informed consent was obtained from all participants prior to their inclusion in the study. Confidentiality of participants' data was strictly maintained throughout the study period.

RESULTS

Our case-control study aimed to investigate the potential association between the use of Proton Pump Inhibitors (PPIs) and the development of Chronic Kidney Disease (CKD) in a sample of 100 participants, evenly divided into cases with CKD and controls without CKD. The analysis explored several demographic and behavioral factors, including age distribution, gender, and smoking status, to understand their interplay with PPI usage and CKD risk.

PPI Usage and CKD Development

Our findings suggest a significant association between PPI usage and an increased risk of developing chronic kidney disease (CKD). Specifically, among the case group with CKD, 60% (30 out of 50) reported using PPIs. In contrast, only 20% of the control group without CKD (10 out of 50) reported PPI usage. This indicates that individuals in our study who used PPIs had a threefold higher likelihood of developing CKD compared to those who did not use PPIs (Table No:1).

Age Distribution

The study further revealed a notable age-related disparity in CKD occurrence. A significant majority of the cases (70%, n=35) were aged 50 years and above, compared to 40% (n=20) in the control group, highlighting age as a potential risk factor for CKD. This age distribution underscores the vulnerability of older individuals to CKD, particularly among those with a history of PPI use (Table No:2).

Gender Distribution

Gender analysis indicated a balanced distribution among the controls, with an equal percentage of males and females. However, there was a slight male predominance among the cases, with males constituting 60% of CKD patients in our study. This gender disparity suggests a possible gender-related risk factor for CKD, although further research is warranted to understand the underlying mechanisms (Table No:3).

Smoking Status

Smoking status emerged as another significant factor in our analysis. Forty percent of the cases were smokers, doubling the proportion seen in the control group (20%). This indicates that smoking may compound the risk of CKD, especially in conjunction with PPI usage (Table No:4)

Table 1: PPI Usage and CKD Development

Group	Condition	PPI Users	Total	Percentage
Cases	CKD	30	50	60%
Controls	No CKD	10	50	20%

Table 2: Age Distribution among Participants

Age Group	Cases	Controls	Percentage
< 50 years	15	-	30%
50 years and above	35	-	70%
< 50 years	-	30	60%

50 years and above	-	20	40%
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Table 3: Gender Distribution among Participants

Gender	Cases	Controls	Percentage
Male	30	-	60%
Female	20	-	40%
Male	-	25	50%
Female	-	25	50%

Table 4: Smoking Status among Participants

Smoking Status	Cases	Controls	Percentage
Smoker	20	-	40%
Non-Smoker	30	-	60%
Smoker	-	10	20%
Non-Smoker	-	40	80%

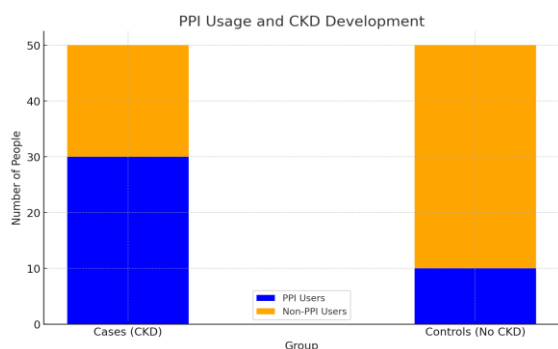


Figure 1: PPI Usage and CKD Development

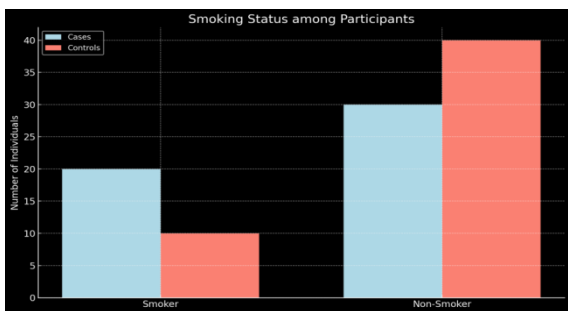


Figure 2: Smoking Status Among Participants

DISCUSSION

Our study found a significant association between Proton Pump Inhibitor (PPI) usage and an increased risk of Chronic Kidney Disease (CKD) development. The odds ratios (ORs) calculated indicated a substantially higher likelihood of CKD among individuals who reported PPI usage compared to those who did not. This finding is consistent with previous observational studies and underscores the importance of considering the potential renal implications of prolonged PPI therapy.^[9,10]

Mechanisms and Causality

The exact mechanism underlying the association between PPI usage and CKD remains unclear. However, it has been hypothesized that PPIs may induce renal injury through mechanisms such as acute interstitial nephritis or alterations in renal hemodynamics¹¹. Further research is needed to

elucidate these mechanisms and establish causality definitively.

Role of Demographic and Lifestyle Factors

Our study also examined the influence of demographic and lifestyle factors on the observed association between PPI usage and CKD risk. Subgroup analyses revealed that age, gender, and smoking status may modulate this relationship. Specifically, older age, male gender, and smoking were associated with a higher risk of CKD among PPI users.^[12] These findings highlight the importance of considering these factors in risk stratification and clinical decision-making.^[13]

Clinical Implications

The implications of our findings for clinical practice are significant. Given the widespread use of PPIs and the potential renal risks associated with their long-term use, healthcare providers should exercise caution when prescribing these medications, particularly in older adults and individuals with other CKD risk factors.^[14] Alternative treatment options, such as histamine H₂-receptor antagonists or lifestyle modifications, should be considered whenever possible.

Study Limitations

Our study is not without limitations. The retrospective nature of the study design introduces the possibility of recall bias and limits causal inference. Additionally, the relatively small sample size may restrict the generalizability of our findings to broader populations. Furthermore, the lack of detailed clinical data, such as medication dosages and comorbidities, may have influenced our results.

Future Directions

Future research should focus on prospective cohort studies to establish causality and elucidate the underlying mechanisms linking PPI usage to CKD development. Long-term follow-up studies are needed to assess the cumulative renal effects of PPIs over time. Moreover, investigations into potential strategies for mitigating the renal risks associated with PPI therapy, such as dose optimization or pharmacogenomic approaches, are warranted.

CONCLUSION

Our study provides valuable insights into the association between PPI usage and CKD risk, highlighting the need for cautious prescribing and monitorings of these medications in clinical practice. By considering demographic and lifestyle factors, healthcare providers can better identify patients at higher risk of CKD and tailor treatment strategies accordingly, ultimately improving patient outcomes and reducing the burden of renal disease.

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