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ROSUVASTATIN THERAPY FOR PREVENTING CONTRAST-INDUCED ACUTE KIDNEY INJURY IN PATIENTS WITH CHRONIC KIDNEY DISEASE

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Abstract:

Objectives: To evaluate the effectiveness of rosuvastatin in reducing the incidence of contrast-induced acute kidney injury (CI-AKI) in patients with chronic kidney disease (CKD).

Materials and Methods: This Cross sectional study is conducted at multiple centers including Mercy Teaching Hospital Peshawar, Pakistan and Islam Medical College Sialkot, Pakistan in the duration from December, 2023 to May, 2024. A total of 130 patients who met the selection criteria were enrolled in the study, each receiving a unique identification number. Detail clinical and physical examinations were conducted for all participants. Blood samples were collected, and creatinine levels were measured at 48 and 72 hours post-percutaneous coronary intervention (PCI) to assess for contrast-induced nephropathy (CIN) and evaluate the therapy's efficacy according to the operational definition. All procedures were carried out by an experienced surgical team to ensure consistent and reliable patient management and assessment. Data was collected by using a pre-designed questionnaire.

Results: The mean age of the patients was 47.85 ± 8.47 years, with a gender distribution of 75 males (57.7%) and 55 females (42.3%). Mean serum creatinine levels was 0.83 ± 0.18 mg/dL at 48 hours and 0.90 ± 0.21 mg/dL at 72 hours post-contrast exposure. The mean duration of chronic kidney disease was 7.32 ± 1.52 months. Rosuvastatin therapy was effective in 105 (80.8%) patients. On stratification of confounders and effect modifiers in relation to efficacy, no significant differences were observed across age groups (P=0.96), gender (P=0.79), and the duration of CKD (P=0.34). However, a significant difference was found in relation to serum creatinine levels (P=0.04).

Conclusion: It was concluded that rosuvastatin therapy significantly reduces the incidence of CI-AKI in CKD patients, likely due to its anti-inflammatory and antioxidative properties. Further research is needed to optimize dosing and identify which patient subgroups benefit most.

Key words: Rosuvastatin, Acute kidney injury, chronic kidney disease, Contrast induced nephropathy (CIN).

INTRODUCTION:

Contrast-induced acute kidney injury (CI-AKI) is a significant complication associated with the use of contrast media during diagnostic and therapeutic procedures, particularly in patients with chronic kidney disease (CKD).(1) CI-AKI can lead to worsening renal function, increased morbidity, and extended hospital stays, making its prevention a critical concern in clinical practice.(2) Chronic kidney disease patients are especially vulnerable to CI-AKI due to their already compromised renal function, which increases the risk of adverse outcomes following contrast exposure.(1) The incidence of contrast-induced nephropathy (CIN) is approximately 20-20.6% in patients with chronic kidney disease (CKD)(3)

Rosuvastatin, a member of the statin family, primarily functions as a lipid-lowering agent by inhibiting the enzyme HMG-CoA reductase.(4) Statins are commonly prescribed for their cholesterol-lowering effects, which reduce the risk of cardiovascular events.(5, 6) Beyond this, they have pleiotropic properties, including antithrombotic, antioxidative, and anti-inflammatory effects, offering additional therapeutic benefits.(7) In preventing contrast-induced nephropathy (CIN), a potential complication from imaging contrast media, these properties, particularly in reducing inflammation and oxidative stress, show promise in protecting renal function, especially in at-risk patients. The major risk factor for predicting contrast-induced nephropathy (CIN) is preexisting chronic kidney disease (CKD), which has a significantly higher relative risk (11.52) compared to other factors such as diabetes mellitus (1.13), congestive heart failure (1.48), and advanced age (≥ 70 years) (0.84), as identified in multivariable analysis .(8, 9) Several clinical studies have investigated the effectiveness of rosuvastatin in preventing CI-AKI in patients with CKD.(10) One notable study found that patients treated with rosuvastatin had a lower incidence of CI-AKI compared to those who did not receive the medication. (11) This study underscores the potential of rosuvastatin to reduce the risk of CI-AKI, likely due to its antioxidative and anti-inflammatory properties, which may help protect renal function in this high-risk population. Pakistan faces a considerable burden of chronic kidney disease, largely due to the high prevalence of diabetes and hypertension, which are key risk factors for CKD.(12) This underscores the necessity of investigating effective preventive strategies for complications like contrast-induced acute kidney injury (CI-AKI) in this population. So, we conducted the present study to explore these strategies for the at-risk population in Pakistan.

Objective: To evaluate the effectiveness of rosuvastatin in reducing the incidence of contrast-induced acute kidney injury (CI-AKI) in patients with chronic kidney disease (CKD).

MATERIALS AND METHODS:

Study Design: Cross sectional study.

Study setting: This Cross sectional study is conducted at multiple centers including Mercy Teaching Hospital Peshawar, Pakistan and Islam Medical College Sialkot, Pakistan. December, 2023 to May, 2024

Duration of the study: The study duration was 6 month December, 2023 to May, 2024

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Inclusion Criteria:

- Patients with a confirmed diagnosis of CKD with duration of CKD >3 months.
- Both male and female patients.
- Patients of aged 18 to 60 years.

Exclusion Criteria:

- Patients with severe liver impairment, such as cirrhosis or marked abnormalities in liver enzymes.

- Patients with current or recent AKI.
- Patients having history of hypersensitivity or allergic reactions to statins.
- Patients with poorly controlled diabetes mellitus or hypertension.
- Pregnant and breastfeeding patients.

Methods:
This Cross sectional study is conducted at multiple centers including Mercy Teaching Hospital Peshawar, Pakistan and Islam Medical College Sialkot, Pakistan in the duration from December, 2023 to May, 2024. A total of 130 patients who met the selection criteria were enrolled in the study. Each and every patients were given unique identification number. Complete clinical and physical examination of all the patients were done. Blood samples and creatinine levels were taken 48 hours and 72 hours post-percutaneous coronary intervention (PCI) to assess for contrast-induced nephropathy (CIN) and evaluate the efficacy of the therapy as per the operational definition. All procedures were performed by an experienced surgical team, ensuring consistent and reliable patient management and assessment. Data was collected using a pre-designed questionnaire. Statistical analysis was performed using SPSS Version 26.

Results:
The mean age of all enrolled patients was 47.85±8.47years. Out of total patients 75 males (57.7%) and 55 females (42.3%). The age distribution was as follows: 3.8% were aged 18-30 years, 13.1% were aged 31-40 years, 38.5% were aged 41-50 years, and 44.6% were aged 50-60 years. The means serum creatinine levels were 0.83 ± 0.18 mg/dL at 48 hours and 0.90 ± 0.21 mg/dL at 72 hours post-contrast exposure. The mean duration of chronic kidney disease (CKD) among participants was 7.32 ± 1.52 months. The efficacy was found in 105(80.8%) patients, while 25 (19.2%) patients did not respond to the treatment. Among males, 60 (57.1%) demonstrated efficacy, while 15 (60.0%) did not. In contrast, among females, 45 (42.9%) showed efficacy compared to 10 (40.0%) who did not, with a p-value of 0.79. Efficacy rates across age groups were 3.8% for 18-30 years, 12.4% for 31-40 years, 39.0% for 41-50 years, and 44.8% for 50-60 years, with non-efficacy rates of 4.0%, 16.0%, 36.0%, and 44.0%, respectively, and a p-value of 0.96. For creatinine levels at 48 hours, patients with levels between 0.1–1 had a 93.3% efficacy rate, while those with levels above 1 had a 6.7% efficacy rate, showing a significant p-value of 0.04. Concerning the duration of CKD, patients with a duration of 4-8 months showed a 49.5% efficacy rate, compared to 50.5% for those with CKD lasting more than 8 months, with a p-value of 0.34.

Table 1: Mean age of all enrolled Patient *(n=130)*

Variables	Mean±SD
Age (Years)	47.85±8.47

Discussion:
The present study aimed to evaluate the efficacy of rosuvastatin therapy in preventing contrast-induced acute kidney injury (CI-AKI) in patients with chronic kidney disease (CKD). When patients already have renal impairment, CI-AKI is a serious complication that can arise from using iodinated contrast media. The illness can cause considerable morbidity and mortality, and there are currently no viable treatments for it, making avoidance of CI-AKI imperative. In the present study, rosuvastatin therapy was found to be effective in 105 (80.8%) of the patients. These findings are consistent with previous research that highlights the pleiotropic effects of statins. These effects, which include anti-inflammatory and antioxidative properties, are believed to play a significant role in providing renal protection and reducing the incidence of contrast-induced acute kidney injury (CI-AKI). Statins' ability to modulate inflammatory responses and oxidative stress may contribute to their protective effects on renal function, particularly in patients undergoing procedures involving iodinated contrast media. This supports the potential use of statins, like rosuvastatin, as a preventive measure for CI-

AKI in clinical settings. Various studies supported our findings, a study conducted by Asadullah et al.(10) stated that efficacy was observed in 97 (77.6%) patients. another study conducted by Leoncini et al.(13) reported an efficacy rate of 69.6% in their study, which aligns with and reinforces our results. This consistency across studies suggests that the therapeutic approach we examined may be broadly effective in similar patient populations. In contrast to our study, where a higher prevalence of efficacy was observed, Abaci et al.(14) reported a lower prevalence of efficacy, with only 29.1% (103 patients) showing a positive response. Similarly, Han et al.(15) found efficacy in 58.6% (878 cases) of their study population, which also differs from our findings.

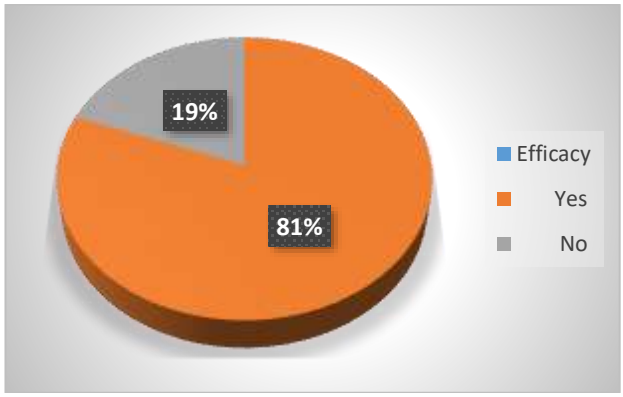

Fig: Frequency of efficacy

Table 2: Characteristics of all enrolled patients *(n=130)*

Variables	**Frequency (%)**
Gender	
Male	75(57.7%)
Female	55(42.3%)
Age Groups	
18-30 years	5(3.8%)
31-40 years	17(13.1%)
41-50 years	50(38.5%)
50-60 years	58(44.6%)
Serum creatinine level at 48 hours	0.83±0.18
Serum creatinine level at 72 hours	0.90±0.21
Duration of CKD (months)	7.32±1.52
Efficacy	
Yes	105(80.8%)
No	25(19.2%)

The results of the present study show that the effectiveness of rosuvastatin medication varies depending on the clinical and demographic category. 50 (57.1%) and 45 (42.9%) of the male and female participants demonstrated efficacy respectiely, with a p-value of 0.79 indicating no significant gender difference in treatment response. Additionally efficacy rates for rosuvastatin therapy varied by age group, with 3.8% efficacy in the 18-30 years group, 12.4% in the 31-40 years group, 39.0% in the 41-50 years group, and 44.8% in the 50-60 years group (p-value 0.96). Patients with creatinine levels between 0.1–1 had a high efficacy rate of 93.3%, while those with levels above 1 had a significantly lower rate of 6.7% (p-value 0.04). The efficacy rate for CKD duration of 4-8 months was 49.5%, compared to 50.5% for more than 8 months (p-value 0.34). These results indicate varying responses to treatment, emphasizing the need for personalized approaches.

In a meta-analysis of five randomized controlled trials, Zhang (16) observed the beneficial effects of preoperative rosuvastatin use in patients with diabetes or chronic kidney disease (CKD). The analysis

highlighted rosuvastatin's potential to reduce the incidence of contrast-induced nephropathy (CIN). Zhang (16) emphasized the need for further research to identify patients who may be at increased risk of developing CIN, to determine the optimal preoperative dosing of rosuvastatin, and to ultimately reduce the incidence of this complication. In a comprehensive meta-analysis and systematic review conducted by Ukaigwe (17), involving 12 randomized controlled trials with a total of 5,564 participants, the efficacy of statins was assessed, particularly focusing on the comparative effectiveness of high versus low doses. The analysis included a detailed subgroup evaluation which revealed that the incidence of contrast-induced acute kidney injury (CIAKI) was not significantly different between patients with diabetes and those with chronic kidney disease (CKD). However, the study found that high-dose statins were notably more effective than low-dose statins or placebo in reducing the occurrence of CIAKI among patients undergoing percutaneous coronary intervention (PCI). This finding suggests a dose-dependent protective effect of statins against CIAKI, emphasizing the potential benefits of administering higher doses in clinical practice, particularly for patients at elevated risk due to underlying conditions like diabetes and CKD.

Table 3: Stratification of efficacy with respect to different variables (n=130).

	Efficacy		P-Value
	YES	NO	
Gender			
Male	60(57.1%)	15(60.0%)	0.79
Female	45(42.9%)	10(40.0%)	
Age groups			
18-30 years	4(3.8%)	1(4.0%)	
31-40 years	13(12.4%)	4(16.0%)	
41-50 years	41(39.0%)	9(36.0%)	0.96
50-60 years	47(44.8%)	11(44.0%)	
Creatinine level at 48 hours			
0.1–1	97(93.3%)	20(80.0%)	0.04
>1	7(6.7%)	5(20.0%)	
Duration of CKD (Months)			
4-8	52(49.5%)	15(60.0%)	0.34
>8	53(50.5%)	10(40.0%)	

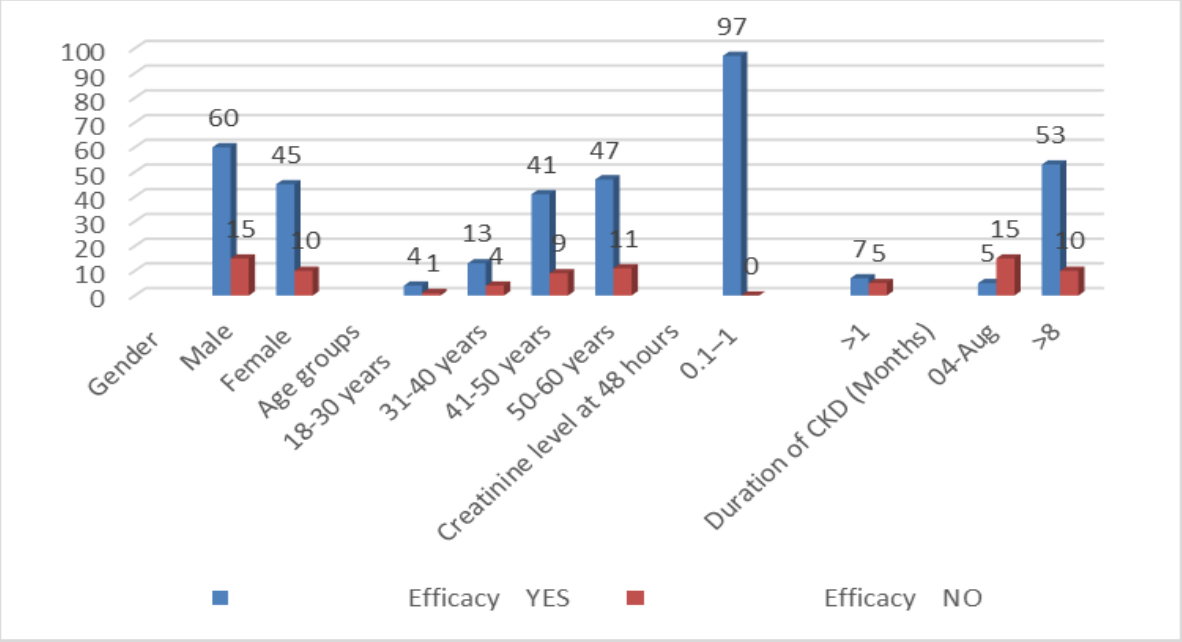

Fig 2: Stratification of efficacy with respect to different variables

Conclusion:

It was concluded that rosuvastatin therapy significantly reduces the incidence of CI-AKI in patients with CKD. The benefits of rosuvastatin are attributed to its pleiotropic effects, including anti-inflammatory and antioxidative properties, which aid in renal protection. Further research is advised to refine dosing strategies and identify specific patient subgroups that may derive the most benefit from this therapy.

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