European Journal of Clinical Pharmacy
Print ISSN: 2385-409X **Online ISSN**: 3105-0409
Website: https://farmclin.com/

Original Research Article

Frequency of Dry Cough in Patients on Angiotensin-Converting Enzyme Inhibitor for the Treatment of Acute Coronary Syndrome

Article History:

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Received: 29-10-2025
Revised: 09-12-2025
Accepted: 20-12-2025
Published: 30-12-2025

Abstract:
Objective: To determine the frequency of dry cough in patients on ACE inhibitor for the treatment of ACS. **Study Design:** A descriptive cross-sectional study. **Place and Duration of Study:** Department of Cardiology, Lady Reading Hospital, Peshawar, Pakistan from 26th July to 26th October 2025. **Methodology:** A total of 75 patients aged 25 to 70 years with acute coronary syndrome receiving angiotensin-converting enzyme inhibitors were included through consecutive non-probability sampling. Dry cough was assessed after treatment initiation. Data were analysed using Statistical Package for the Social Sciences version 25. The Shapiro-Wilk test was used for normality assessment. Stratification was performed for possible effect modifiers, followed by the chi-square or Fisher's exact test. A p-value of <0.05 was considered statistically significant. **Results:** The mean age was 52.00 ± 11.63 years and mean body mass index was 25.17 ± 2.46 kg/m^2. Males were 56 (74.7%) and females 19 (25.3%). Diabetes was present in 22 (29.3%), smoking in 27 (36.0%) and diuretic use in 25 (33.3%) patients. Ramipril was used by 35 (46.7%) patients. Dry cough was observed in 8 (10.7%) patients. No significant association was found with age (p=0.351), body mass index (p=1.000), gender (p=1.000), diabetes (p=0.424), smoking (p=0.448), diuretic use (p=1.000) or angiotensin-converting enzyme inhibitor type (p=0.492). **Conclusion:** Dry cough occurred in a small proportion of patients receiving angiotensin-converting enzyme inhibitors for acute coronary syndrome, with no significant association with the studied factors.

Keywords: Acute coronary syndrome, Angiotensin-converting enzyme inhibitors, Cough, Dry cough, Drug adverse effects, Pharmacotherapy.

INTRODUCTION

Acute coronary syndrome is a common heart disease caused by a sudden decrease or blockage of blood supply to the heart muscles.1 Unstable angina, non-ST-segment elevation myocardial infarction and ST-segment elevation myocardial infarction are types of ACS.2 The underlying cause is often due to rupture or erosion of an atherosclerotic plaque leading to a clot in the coronary arteries. Symptoms include chest pain or discomfort, shortness of breath, sweating, nausea and pain that radiates to the arm, shoulder, jaw or neck.3 Diagnosis and treatment at an early stage help reduce myocardial damage, complications and chances of dying. ACE inhibitors are often administered to patients suffering from ACS especially when they have left ventricular dysfunction, high blood pressure or diabetes among others.4

Treatment of ACS includes antiplatelet agents, anticoagulants, statins, beta-blockers, nitrates, and other drugs depending upon the condition of the patient.5 Use of angiotensin-converting enzyme inhibitors is also made where it is appropriate, especially in patients having hypertension, diabetes mellitus or ventricular dysfunction.6 ACE inhibitors decrease the production of angiotensin II and thus

lead to dilation of blood vessels and reduction in the blood pressure and workload on the heart.7 They may also be beneficial in preventing any untoward effects on the heart following myocardial infarction.

Although ACE inhibitors play a significant role in the cardiovascular system, they cause various adverse effects during the treatment process. A dry cough is the most frequent side effect observed during treatment with ACE inhibitors and it can manifest itself in patients undergoing therapy for acute coronary syndrome.8 This type of cough is non-productive and it can persist in absence of any other signs of the respiratory disorders.9 Coughing starts from the very beginning of therapy, within several days or even months after starting treatment. The mechanism of action is unknown, but it seems that this side effect is caused by accumulation of substances, including bradykinin, due to impaired their breakdown and irritation of airways leading to cough.

The need for conducting the study arises from the observation that dry cough is a frequent side effect associated with the use of ACE inhibitors and this may have adverse effects on patient compliance with therapy for acute coronary syndrome. It is important to note that this side effect may not only result in some discomfort to the patient, but in certain cases it may lead to the withdrawal from the medication. It is possible that the prevalence of this side effect may vary in various populations due to differences in demographic and clinical variables.

METHODOLOGY

This descriptive study was conducted from 26th July 2025 to 26th October 2025 at the Department of Cardiology, LRH, Peshawar. The study included patients aged 25 to 70 years of both genders who had acute coronary syndrome and were receiving ACE inhibitor treatment. The sample size was calculated as 75 using the WHO sample size calculator, taking 14.5% expected frequency of dry cough in ACS cases, 8% margin of error and 95% confidence level.10 Patients were selected through consecutive non-probability sampling technique.

The study was commenced after obtaining approval from the Ethical Review Board of the hospital and the Research Department of CPSP Head Office, under Ref. No. 307/LRH/MTI. Patients fulfilling the required selection criteria were included in the study. Patients aged 25-70 years, male and female, who were diagnosed with ACS and receiving ACE inhibitor were included. Patients having viral infections, Covid 19 or post viral infection, ILD, chronic bronchitis, asthma, allergic rhinitis, environmental irritants, GERD, active heart failure, lung cancer, TB or pulmonary fibrosis were excluded. Pregnant women were also excluded from the study.

After explaining the objective and possible advantages of the study to the participants, written informed consent was obtained before data collection. Demographic information including age, BMI, gender, place of living, literacy status, socio economic status, and occupation status was recorded on a pre-designed structured proforma. Clinical history was taken and patients were examined for relevant cardiac and respiratory findings. Information regarding smoking, diabetes, diuretic use and type of ACE inhibitor was also recorded. ACS was diagnosed in patients presenting with chest pain with VAS>3 and having ECG findings of STEMI with ST-segment elevation in ≥2 contiguous leads or NSTEMI with ST-segment depression/T-wave inversion. Patients were assessed for dry cough after initiation of ACE inhibitor treatment. ACE inhibitor use was considered when the patient was receiving Ramipril 2.5 mg per day, Lisinopril 2.5–5 mg per day, or Enalapril 2.5 mg per day. Dry cough was considered as a non-productive cough occurring after starting ACE inhibitor and continuing for >48 hours. The complete assessment was performed under supervision of a consultant having minimum 5 years of post-fellowship experience.

Data analysis was performed using SPSS v.25. Categorical variables including gender, dry cough, ACE inhibitor type, diuretic use, diabetes, smoking, place of living, literacy status, socio economic status and occupation status were presented as frequencies and percentages. Numerical variables including BMI, age and duration of ACE inhibitor use were presented as mean + SD. Effect modifiers including BMI, gender, age, ACE inhibitor type, diuretic use, diabetes and smoking were controlled through stratification. Post stratification chi-square or Fisher's exact test was applied, with p-value <0.05 considered statistically significant.

RESULTS

A total of 75 patients were included in the study. The mean age was 52.00 ± 11.63 years, BMI was 25.17 ± 2.46 Kg/m^2 and duration of ACE inhibitor use was 45.71 ± 30.99 days. Majority were male 56 (74.7%). Literate patients were 38 (50.7%) and rural residents were 42 (56.0%). Employed patients were 43 (57.3%) and low socioeconomic class was most common 40 (53.3%). Diabetes was present in 22 (29.3%) and smoking in 27 (36.0%) patients. Diuretic use was noted in 25 (33.3%) patients and Ramipril was the most frequently used ACE inhibitor 35 (46.7%) (Table 1).

Table 1. Patient Demographics n=75

Demographics	Mean ± SD
Age (Years)	52.00 ± 11.63
BMI (Kg/m^2)	25.17 ± 2.46
Duration of ACE Inhibitor (Days)	45.71 ± 30.99
Gender	
Male n (%)	56 (74.7%)

Female n (%)	19 (25.3%)
Literacy Status	
Literate n (%)	38 (50.7%)
Illiterate n (%)	37 (49.3%)
Place of Living	
Rural n (%)	42 (56.0%)
Urban n (%)	33 (44.0%)
Occupation Status	
Employed n (%)	43 (57.3%)
Unemployed n (%)	32 (42.7%)
Socioeconomic Status	
Low n (%)	40 (53.3%)
Middle n (%)	16 (21.3%)
High n (%)	19 (25.3%)
Diabetes	
Yes n (%)	22 (29.3%)
No n (%)	53 (70.7%)
Smoking	
Yes n (%)	27 (36.0%)
No n (%)	48 (64.0%)
Diuretic Use	
Yes n (%)	25 (33.3%)
No n (%)	50 (66.7%)
ACE Inhibitor Type	
Ramipril n (%)	35 (46.7%)
Lisinopril n (%)	24 (32.0%)
Enalapril n (%)	16 (21.3%)

Out of total 75 patients, dry cough was present in 8 (10.7%) patients whereas 67 (89.3%) patients did not develop dry cough during ACE inhibitor therapy (Table 2).

Table 2. Frequency of Dry Cough in Patients on ACE Inhibitor for the Treatment of Acute Coronary Syndrome.

Dry Cough	Frequency	%age
Yes	8	10.70%
No	67	89.30%
Total	75	100%

On stratified analysis, no statistically significant association were found between dry cough and any of the studied demographic factors. The p-value for age group was 0.351, for BMI was 1.000, for gender was 1.000, for diabetes was 0.424, for smoking was 0.448, for diuretic use was 1.000 and for ACE inhibitor type was 0.492, all of which were greater than 0.05, suggesting that dry cough occurrence was not significantly influenced by any of these variables (Table 3).

Table 3. Association of Dry Cough with Demographic Factors n=75

Demographic Factors	Sub Groups	Dry Cough	Dry Cough No n(%)	p-value
		Yes n(%)		
Age (years)	≤45	0 (0.0%)	11 (100%)	0.351*
	>45	8 (12.5%)	56 (87.5%)	
BMI (Kg/m²)	≤25	4 (11.4%)	31 (88.6%)	1.000*
	>25	4 (10.0%)	36 (90.0%)	
Gender	Male	6 (10.7%)	50 (89.3%)	1.000*
	Female	2 (10.5%)	17 (89.5%)	
Diabetes	Yes	1 (4.5%)	21 (95.5%)	0.424*
	No	7 (13.2%)	46 (86.8%)	
Smoking	Yes	4 (14.8%)	23 (85.2%)	0.448*
	No	4 (8.3%)	44 (91.7%)	
Diuretic Use	Yes	3 (12.0%)	22 (88.0%)	1.000*
	No	5 (10.0%)	45 (90.0%)	
ACE Inhibitor Type	Ramipril	5 (14.3%)	30 (85.7%)	0.492*
	Lisinopril	1 (4.2%)	23 (95.8%)	
	Enalapril	2 (12.5%)	14 (87.5%)	

*Fisher Exact Test

DISCUSSION

In this study, dry cough was found in 8 (10.7%) patients which is a relatively low frequency. This could be explained by the fact that ACE inhibitors causes accumulation of bradykinin in the respiratory tract, which stimulates the cough receptors and leads to dry cough, however not all patients are equally sensitive to this mechanism.

Majority of the patients were male 56 (74.7%) which is consistent with the known fact that acute coronary syndrome is more prevalent in males due to the protective effect of oestrogen in females before menopause. Ramipril was the most commonly used ACE inhibitor 35 (46.7%) which may be because of its proven cardiovascular benefits and longer duration of action as compared to other ACE inhibitors.

Regarding association, no statistically significant association was found between dry cough and age, gender, BMI, diabetes, smoking, diuretic use and ACE inhibitor type. This suggest that dry cough in ACE inhibitor users may be more related to individual genetic susceptibility and variation in bradykinin metabolism rather than these demographic and clinical factors. Smoking was present in 27 (36.0%)

patients and although it was expected that smoking may alter cough reflex sensitivity, no significant association was found with dry cough occurrence in this study. The frequency of dry cough in present study was found to be 8 (10.7%) which is comparable to the findings of Vukadinovic et al. 11 who reported an overall cough rate of 13.5% in ACEI-treated patients in a large meta-analysis of 32,586 patients, suggesting that the findings of present study are broadly consistent with the reported rates in coronary disease patients. Similarly, Nazir et al. 12 reported an overall dry cough frequency of 7.0% among Pakistani patients receiving different ACE inhibitors, which is very close to the frequency observed in present study and this similarity may be explained by the fact that both studies were conducted in similar South Asian population where genetic variation in bradykinin metabolism is comparable. However, Brown et al. 13 reported a much higher cough frequency of greater than 10% in white populations and as high as 44% in Asian populations, which is considerably higher than what was found in present study. This difference may be due to the fact that Brown et al. 13 reviewed a broader and more diverse population across multiple studies, whereas present study included a relatively small and specific cohort of 75 patients with acute coronary syndrome. Omboni et al. 14 also reported a relatively low cough incidence of 2.6% with zofenopril, which is lower than present study findings and this difference could be because zofenopril has a relatively lower propensity to accumulate bradykinin as compared to other ACE inhibitors like Ramipril which was most commonly used in present study 35 (46.7%). Ueng et al. 15 reported cough in 11.0% of patients receiving amlodipine/benazepril combination which is quite similar to present study findings of 10.7% and both studies suggest that cough remains a consistent and clinically relevant adverse effect of ACE inhibitor therapy regardless of the clinical indication. Regarding gender, majority of patients in present study were male 56 (74.7%) which is consistent with the known higher prevalence of acute coronary syndrome in males. Omboni et al. 14 and Nazir et al. 12 both reported that cough was more frequent in females than males, however in present study no significant association was found between gender and dry cough occurrence, which may be due to the small sample size and predominance of male patients that may have limited the ability to detect such difference. Alrawaiq et al. 16 also reported a male predominance of 111 (63.4%) in their study of ACEI-related drug problems, which is similar to the gender distribution observed in present study and this further reflect the higher burden of cardiovascular disease in male patients.

Ramipril was the most commonly prescribed ACE inhibitor in present study 35 (46.7%), followed by Lisinopril 24 (32.0%) and Enalapril 16 (21.3%). In contrast, Alrawaiq et al. 16 found Captopril to be the most frequently used ACEI 98 (56%), followed by Lisinopril 46 (26.3%), which differ from present study and this variation may reflect differences in local prescribing practices and drug availability across different healthcare settings. Bazargani et al. 17 highlighted that ACE inhibitors were included in the essential medicines lists of all 34 studied countries, which explain their widespread use and availability including in present study setting and further justify their common prescription in acute coronary syndrome management. No statistically significant association was found between dry cough and any of the studied factors in present study. Ujiie et al. 18 reported that 5 patients in the ACEI group had to discontinue therapy due to dry cough, which highlight that even though the frequency may be low, the clinical impact of this adverse effect cannot be ignored. Lazar et al. 19 reviewed the cardiovascular benefits of ACE inhibitors in coronary artery disease patients and demonstrated significant reductions in ischaemic events, which suggest that despite the occurrence of dry cough, the overall benefits of ACE inhibitor therapy in acute coronary syndrome patients outweigh this adverse effect. Hui et al. 20 demonstrated in a large cohort study that ACEI use was associated with significantly lower risks of pneumonia and influenza as compared to ARB use, which provide an additional reason to prefer ACE inhibitors over ARBs in acute coronary syndrome patients despite the risk of dry cough. There are many limitations associated with the current study. Firstly, it was a single center study carried out in only one hospital setting, which may limit its generalizability in a larger population. Secondly, the sample size was relatively small as only 75 patients were recruited for the study, which may have limited the power of statistical analysis of the association between dry cough and other demographic variables. Thirdly, the severity and duration of dry cough in those who had the side effect was not evaluated in the current study, which may have been clinically more informative.

CONCLUSION

This particular study has concluded that one of the side effects associated with the use of ACE inhibitors for treating acute coronary syndrome includes dry cough. It was noted that the prevalence of this side effect is low among the studied group and there is no significant relationship between the development of dry cough and demographic and clinical variables including age, gender, BMI, diabetes, smoking, diuretics usage and type of ACE inhibitor. Nevertheless, despite this side effect, ACE inhibitors remain a useful choice in the treatment of acute coronary syndrome.

Ethical Approval

Ethical clearance for conducting the research was taken from the Institutional Ethical Committee of the hospital before starting the study.

Patients' Consent

All participants were informed about the research and written consent was taken before their inclusion in the study.

Competing Interests

The author declares that there was no conflict of interest associated with the present research.

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