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### **Research Article**

## Knowledge and Practice of Yemeni Physicians Regarding Management of Angiotensin-Converting Enzyme Inhibitor (ACEI)-Induced Cough: A Cross-Se ctional Study among Public and Private Hospitals - Aden, Yemen.

Aisha Al-yumaini<sup>1</sup>, Mazen Mohammed<sup>1</sup>, Azzam Khaled<sup>1</sup>, Ahmed Al-ozybi<sup>1</sup>, Ali

Mohammed<sup>1</sup>, Qusai Fouad<sup>1</sup>, Shareefa Abdullah<sup>1</sup>, Fares M.S Muthanna<sup>1</sup>\*

<sup>1</sup>Basic Science Department, Faculty of Medicine & Health Sciences, University of Science &

Technology, Aden, Yemen

<sup>\*</sup>Corresponding author: <u>fares.mu.wu@gmail.com</u>

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#### Abstract:

**Background** : ACEIs are a cornerstone treatment for cardiovascular conditions, but resulting into cough as a frequent and disruptive side effect, potentially leading to medication non-adherence. Optimal management strategies require physician knowledge and adherence to evidence-based guidelines. This study aimed to evaluate the physician's understating of ACEIs induced cough.

**Methods** : A cross-sectional survey was conducted among 65 physicians in public and private hospitals across Aden Governorate, Yemen. The survey assessed the knowledge regarding ACEI-induced cough, and current management practices. Descriptive statistics was used for analysis by SPSS version 26.

**Results** : The majority of participants were young (under 30) and female (55.4%). While nearly 70% monitored hemoglobin for anemia (a potential ACEI side effect), only 18% routinely used iron supplements for cough. Interestingly, 76% of doctors reported encountering patients with cough as a side effect. Overall satisfaction with current medication options for hypertension and cough was high (83%). This study provides a preliminary look at Yemeni physician practices regarding ACEI-induced cough.

**Conclusion** : The findings suggest a potential gap between physician awareness of ACEI-induced cough and its management practices. Monitoring for anemia is positive after using ACEIs, but the low use of iron supplements for cough warrants further investigation. Physician rationale, alternative cough treatments used, and established guidelines in Yemen need exploration. Further research with a broader scope can inform the development of culturally-sensitive and evidence-based guidelines to improve patient care and medication adherence in Yemen. **Keywords**: ACEI, cough, physician knowledge, practice, Yemen

#### **INTRODUCTION**

Angiotensin-converting enzyme inhibitors (ACEIs) are essential treatments for hypertension and heart failure, significantly reducing morbidity and mortality [1]. However, a notable drawback is the frequent occurrence of cough, affecting up to 30% of patients [2]. This side effect can disrupt quality of life and lead to medication non-adherence, compromising therapeutic benefits [3]. Despite the prevalence of ACEI-induced cough, optimal management strategies remain a subject of ongoing

discussion. Ideally, physicians would switch patients to alternative medications with similar efficacy but lacking the cough-inducing effect. However, this decision-making process is influenced by various factors, including physician knowledge, attitudes, and current practices [4,5].

While the prevalence of cough associated with ACEIs varies considerably, reported ranges between 3.9% and 35% [6], the precise mechanism underlying this side effect remains unclear. Several potential pathways are thought to be involved. One study suggests that ACEIs may heighten the cough reflex's sensitivity [7]. A prevailing theory posits that ACE inhibitors lead to the breakdown of bradykinin and other inflammatory peptides within the lungs [7]. Alternatively, ACEI-induced cough might be attributed to the failure of bradykinin breakdown, resulting in elevated bradykinin levels [8]. When patients experience cough as a side effect of ACEI therapy, angiotensin receptor blockers (ARBs) are often prescribed as a substitute.

Notably, while both ACE inhibitors and ARBs demonstrate comparable efficacy in preventing cardiovascular events such as myocardial infarction, stroke, and heart failure hospitalization, ACE inhibitors have shown superiority in reducing overall and cardiovascular mortality compared to ARBs [9]. A recent meta-analysis and systematic review found that ACEIs are more likely to cause cough than ARBs or calcium channel blockers (CCBs). Among ACEIs, moexipril carries the highest risk of cough, while spirapril has the lowest [10]. This study aimed to investigate physicians' knowledge, attitudes, and practices regarding appropriate drug selection for managing ACEI-induced cough in Aden Governorate, Yemen. By focusing on this specific region, we aimed to gain deeper insights into the challenges and practices faced by healthcare professionals in that context. Understanding these aspects is crucial for identifying potential gaps and areas for improvement, ultimately leading to better patient care and medication adherence.

#### **METHODS**

#### Study design and setting

A cross-sectional survey was conducted among physicians working in primary care and cardiology departments of public and private hospitals and clinics in Aden, Yemen. The target population included nearly all physicians with prescribing privileges who manage patients with hypertension, heart failure, or other conditions requiring ACEI therapy.

#### Sample Size

A convenience sampling approach was employed to recruit a representative sample of physicians practicing in diverse healthcare settings within the district. The minimum required sample size was determined using standard methodology for cross-sectional studies, expressed by the formula:  $n=Z^2 \times P \times (1-P) / d^2$ . A 95% confidence level was applied (Z = 1.96), and an estimated prevalence of 50% (P = 0.5) was assumed for the characteristic under investigation, such as physician knowledge regarding ACEI-induced cough. A precision level of 10% (d = 0.1) was chosen as the acceptable margin of error. According to this calculation, a minimum sample size of 96 participants was necessary. However, due to practical constraints like feasibility based on pilot studies, the final sample size recruited for this study was 65 participants.

#### Data collection procedure

A self-administered questionnaire was specifically developed for this study to assess the knowledge and practices of Yemeni physicians regarding the management of ACEI-induced cough. The questionnaire content underwent a multi-step validation process to ensure its accuracy and relevance to the target population. Initially, three medical professionals with expertise reviewed the questionnaire items for content validity, ensuring the questions accurately reflected the intended areas of inquiry and addressed the research objectives. Following this review, a pilot study involving 15 Yemeni physicians was conducted; these pilot participants were excluded from the final analysis.

Data from the pilot test were used to assess the questionnaire's internal consistency through Cronbach's alpha analysis, yielding a coefficient of 0.86, indicating strong reliability of the instrument. This rigorous approach ensured the questionnaire captured the desired information accurately and consistently, providing a reliable foundation for data collection on Yemeni physician practices related to ACEI-induced cough. The questionnaire consisted of three sections:

- *Demographics*: This section collected basic information about the participants, including age, gender, years of experience, specialty, and practice setting.
- *Knowledge*: This section assessed participants' knowledge about ACEI-induced cough, including its mechanisms, prevalence, risk factors, and potential management strategies, using multiple-choice questions and true/false statements.
- *Attitude and Practice*: This section explored participants' attitudes towards different treatment options for ACEI-induced cough, including angiotensin receptor blockers (ARBs), alternative antihypertensives, and cough suppressants. Additionally, it investigated their current practices in managing this side effect, including preferred medications, diagnostic approaches, and referral patterns.

#### Data Analysis

Data were entered into a statistical software program version 26 for analysis. Descriptive statistics were used to summarize demographic characteristics, knowledge scores, and responses to attitude and practice questions.

#### Ethical Considerations

This study adhered to ethical principles outlined in the Declaration of Helsinki [Human Experimentation 1964] [11]. Participation was voluntary and informed consent was obtained from all participants before data collection. The anonymity of participants was ensured throughout the study. The study protocol was reviewed and approved by the relevant institutional review board of the university of science and technology – Aden – Yemen, approval number (MEC No/AD019).

#### RESULTS

#### **Demographics**

This study examined the characteristics and prescribing habits of 65 Yemeni physicians. The group skewed young, with over half (53.8%) under 30 years old, and female (55.4%).

Notably, most doctors (60%) worked in public healthcare settings and had less than five years of experience (53.8%). These findings are presented in Table 1.

Variables		N (%)		
	$\leq$ 30 years	35 (53.8%)		
Age Group	>30 years	30 (46.1%)		
~	Male	29 (44.6%)		
Gender	Female	36 (55.4%)		

*Table 1. demographic of participating physicians* (*n*=65). [12]

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Veen of Europeienee	$\leq$ 5 years	35 (53.8%)		
Year of Experience	> 5 years	30 (46.1%)		
	Public	26 (40%)		
Working Area	Private	39 (60%)		

#### Knowledge and Attitude and Practice

Table 2 delves deeper into physician prescribing practices for cough and ACE inhibitors. Interestingly, asthma medication doesn't seem to be a dominant factor. Only 73% of doctors prescribe daily medication, and just to a quarter (0-25%) of their patients. This suggests that asthma may not be as prevalent a condition as others they manage.

For coughs, dextromethorphan reigns supreme (46%) as the most frequently prescribed medication, followed closely by guaifenesin (41%). Pseudoephedrine appears to be a less common choice (12%).

The survey also explored practices related to ACE Inhibitors. Nearly 70% of doctors monitor hemoglobin levels sometimes, likely to ensure the medication isn't causing anemia as a side effect. Interestingly, 76% of doctors have encountered patients experiencing cough as a side effect of ACE Inhibitors, but only 18% typically address this cough with iron supplements.

Finally, on the topic of medication satisfaction, the majority of doctors (83%) expressed satisfaction with the current selection of medications for asthma, cough, and allergies. Only a small minority (9%) were dissatisfied. These findings are summarized in Table 2.

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	Items	MCQ1	MCQ2	MCQ3	MCQ4
1.	What percentage of your patients do you prescribe asthma medications to on a dailybasis?	0-25% 48 (73%)	26-50% 15 (23%)	51-75% 2 (3%)	76-100% 0 (0%)
2.	What are the most common cough medications you prescribe?	Dextromethorphan 30 (46%)	Guaifenesin 27 (41%)	Pseudoephedrine 8 (12%)	Codeine 0 (0%)
3.	When you prescribe any ACEIs do you monitor hemoglobin level before or after?	Yes sometimes 40 (69%)	Never 15 (23%)	It is not a serious matter 10 (15.3%)	
4.	ACEIs can induce cough. Do you experience such a side effect?	Yes sometimes 50 (76%)	Never 15 (23%)	It is not a serious matter 0 (0%)	
5.	Do you prescribe any iron supplements with ACEIs induce cough?	Yes sometimes 12 (18%)	Never 4 (6%)	It is not a serious matter 49 (75.3%)	
6.	How satisfied are you with the current selection of asthma, cough, and histaminemedications available?	Very satisfied 22 (33%)	Somewhat 33 (50%)	Neither satisfied nor dissatisfied 4 (6.1%)	Somewhat dissatisfied & Very dissatisfied 6 (9%)
7.	Are there any specific asthma, cough, or histamine medications that you would like to develop?	Yes 14 (21%)		No 51 (78.4%)	
8.	How often do you prescribe dextromethorphan for cough?	Never 31 (47%)	Rarely 31 (47%)	Sometimes 2 (3%)	Often and always 1 (1%)

**Table 2**: *Knowledge and Practice regarding ACEIs induced cough* (n = 65).

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#### DISCUSSION

This study provides valuable insights into the knowledge, and practice of physicians in Aden-Yemen regarding ACEI-induced cough management. While some participants demonstrated adequate knowledge about the mechanisms and prevalence of this side effect, there were concerning gaps in their confidence and adherence to evidence-based guidelines.

The dominance of young, female physicians in public settings aligns with reports of a youthful healthcare workforce in Yemen due to ongoing shortages [13]. However, the high proportion of females is noteworthy. Further research could explore if this trend holds across the country or is specific to this region. Additionally, investigating factors influencing this trend, such as educational opportunities or cultural shifts, would be valuable.

The limited use of daily asthma medication could indicate lower asthma prevalence compared to other regions like Saudi Arabia [14]. However, alternative explanations exist. Perhaps these doctors manage asthma primarily through quick-relief inhalers or focus on non-medicinal interventions like allergen avoidance. Studies exploring asthma management strategies employed by Yemeni physicians would provide a clearer picture.

The high satisfaction rate with current medication options is encouraging. However, satisfaction can be subjective and may not reflect the effectiveness of all available medications. Studies comparing treatment outcomes with different medications in the Yemeni context would provide a more nuanced understanding.

Yemeni physicians' knowledge and practices regarding ACE inhibitor-induced cough present a mixed picture. While nearly 70% of doctors monitor hemoglobin levels for anemia, a potential side effect of ACEIs, only 18% prescribe iron supplements for the frequently reported cough. This suggests a potential gap between awareness and practice. However, a definitive assessment is hindered by unknowns. We don't know if doctors use alternative cough treatments or if established guidelines exist for iron supplements in Yemen. Further research is needed to explore physician rationale and patient preferences to understand this gap more clearly.

The prevalence of Dextromethorphan and Guaifenesin as cough suppressants aligns with global trends [15], suggesting these medications are effective and widely trusted. However, investigating the availability and cost of alternative cough treatments in Yemen could shed light on whether these choices reflect global trends or a lack of other options.

The emphasis on monitoring hemoglobin levels to detect potential ACE inhibitor-induced anemia is noteworthy. This finding is similar to previous outcome [16]. Nevertheless, the observed disparity between the high incidence of reported cough as a side effect and the infrequent utilization of iron supplements to manage it raises intriguing questions. Several potential explanations can be considered: first, whether healthcare providers in Yemen prefer alternative treatments for ACE inhibitor-induced cough; second, whether there are established guidelines in Yemen specifically recommending the use of iron supplements for this type of cough; and third, whether cultural preferences among Yemeni patients influence their choice of remedies for cough over iron supplements. Further investigation into these factors is essential to elucidate this discrepancy and inform effective management strategies.

#### Limitations

It's important to acknowledge the limitations of this study. The sample size (65) and geographic focus (Aden Governorate) limit generalizability. Additionally, self-reported data can be biased. Future research with larger, geographically diverse samples alongside qualitative studies exploring physician decision-making processes would offer a richer understanding of Yemeni prescribing habits

#### CONCLUSION

This study provides valuable insights into the prescribing practices of Yemeni physicians. Understanding these practices and the factors influencing them is crucial for optimizing patient care. Further research with a broader scope and a focus on context can pave the way for the development of evidence-based, culturally sensitive guidelines for Yemeni physicians. This, in turn, can contribute to the advancement of personalized medicine in Yemen.

#### Future Research Directions

Despite these limitations, the study highlights a potential knowledge gap regarding the use of iron supplements for ACEI-induced cough. This gap could lead to missed opportunities to offer patients alternative treatment options or could result in unnecessary medication changes if cough persists due to a lack of knowledge about iron supplementation.

Future research directions could involve conducting a larger, multi-center study to enhance the generalizability of the findings. Additionally, exploring the reasons behind the knowledge gap through interviews or focus groups with physicians could provide valuable insights. Furthermore, investigating the potential effectiveness of iron supplementation for ACEI-induced cough through controlled clinical trials would be crucial to determine its validity as a treatment option.

#### Disclaimer

The article has not been previously presented or published, and is not part of a thesis project.

#### **Conflict of Interest**

There are no financial, personal, or professional conflicts of interest to declare.

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