



Pharmacists' Ability in Recognising and Managing Angiotensin Converting Enzyme Inhibitor (ACEI)-Induced Cough in Self-Medicating Patients

Cecilia Brata^{1*}, Yosi Irawati Wibowo¹, Eko Setiawan¹, Steven Victoria Halim¹, Afina Razanah², Ima Mar'atus Sholikhah², Putri Rohmatu Lailla², Azilah Rahmadini², Ida Ayu Elsa Ratu Satwika Putri², Lyna Irawati³

1. Centre of Medicines and Pharmaceutical Care, Faculty of Pharmacy, University of Surabaya, Raya Kalirungkut Surabaya, 60293, Indonesia
2. Faculty of Pharmacy, University of Surabaya, Raya Kalirungkut Surabaya, 60293, Indonesia
3. School of Pharmacy, Management and Science University, University Drive, Off Persiaran Olahraga, Section 13, 40100 Shah Alam, Selangor, Malaysia

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Corresponding Author:
Cecilia Brata

Corresponding Author Email:
cecilia.brata@staff.ubaya.ac.id

ABSTRACT

Background: As ACEIs are widely used and patients with cough often self-medicate at community pharmacies, pharmacists must be able to recognise ACEI-induced cough and refer patients appropriately. However, literature on pharmacists' ability to manage ACEI-induced cough is limited.

Objectives: This study aims to describe pharmacists' ability to recognise and manage a vignette case of ACEI-induced cough in self-medicating patients.

Methods: This cross-sectional study was conducted in community pharmacies across a metropolitan city in Indonesia. All pharmacies were visited and pharmacists who were available and willing to participate were interviewed by five trained data collectors. An open-ended questionnaire featuring a vignette of ACEI-induced cough was used. Pharmacists were asked to provide their recommendations for the case and explain their reasoning. Responses were analysed using content analysis, involving systematic coding and categorisation of the textual data to identify underlying patterns and themes.

Results: Of 245 participating pharmacists, 189 (77%) could recognise that the cough was due to ACEI. However, only 101 of these 189 participants could provide an appropriate response (i.e., direct medical referral without recommending a product to treat the cough and/or changing or stopping the ACEI).

Conclusion: While many pharmacists may possess the necessary knowledge to recognise ACEI-induced cough in the case of a self-medicating patient, they may lack sufficient knowledge about the appropriate response of this problem. Educational intervention is needed to improve pharmacists' knowledge and ability to manage an ACEI-induced cough case.

Keywords: ACEI-induced cough; clinical reasoning; community pharmacists; pharmacists' recommendations.

INTRODUCTION

Cough is a respiratory reflex to clear the airway from bacteria, debris, and secretions. It is a defensive mechanism to protect the respiratory tract from inhaling foreign bodies and pathogens.¹ Cough is a common symptom that people often self-medicate and visit community pharmacies to seek advice or medicines.² The reported prevalence of cough is varied, ranging from 7% to 64% worldwide.³⁻⁵ Cough has many causes: viral infections, bacterial infections, tobacco use, pollutants, underlying medical conditions (such as asthma and/or

other respiratory diseases, gastro-oesophageal reflux disease, and heart disease), and medications' side effects such as the use of an ACEI (Angiotensin Converting Enzyme Inhibitors) or Angiotensin receptor blockers.^{6,7}

Cough as a side effect of ACEI has been well described in the literature. The cough is characterised as a persistent dry cough with a sore and itchy throat.^{8,9} It can be developed after hours of the first dose of ACEI or within weeks or months later.^{9,10} The prevalence of ACEI-induced cough varied across studied populations, ranging from 3,2% to 60%.¹¹ The incidence of ACEI-induced cough is reported to be higher in females and individuals of East Asian origins.^{11,12} The mechanism of ACEI-induced cough is not clear. However, it is commonly stated as related to the degradation and accumulation of bradykinin and substance P by ACE in the upper and lower respiratory tract. This then causes the airway smooth muscle to constrict leading to bronchoconstriction and cough.¹³ Other stated mechanisms in the literature include enhanced acetylcholine-induced contraction of the bronchial smooth muscle and gene polymorphisms.¹⁴

The most effective management of cough induced by ACEI is stopping ACEI therapy; the cough will usually resolve within 1 to 4 weeks after stopping the offending agent, but the resolution of the cough might be delayed up to three months in some patients.⁸ Some literature suggested switching ACEI to Angiotensin II Receptor Blockers (ARB) if possible, reducing the ACEI dose, or rechallenging with a different ACEI.¹⁵ Pinto et.al suggested that in cases of mild cough, patients might be able to continue ACEI treatment considering the probability of the cough naturally disappearing. If the cough worsens after observing for some time, the options could include: (1) switching to Angiotensin II Receptor Blockers (ARBs) or other drugs or (2) adding a calcium channel blocker with ACEI to reduce cough reflex. For moderate to severe cough, consider discontinuing current ACEI treatment and switching to an alternative option such as ARBs or other drugs depending on the patient's preference and comorbid conditions. Adding calcium channel blockers with ACEI to reduce cough reflex could also be an option.¹³ Rechallenge with ACEI and adding medications to suppress the cough (such as sodium cromoglycate, theophylline, sulindac, indomethacin, amlodipine, nifedipine, ferrous sulfate, and picotamide) can also be an option if cessation of ACEI is not an option and/or other drugs are contraindicated for the patient.^{8,13}

Although ACE inhibitors (ACEIs) are well-known for causing cough in patients, previous studies have highlighted challenges in recognizing this side effect in real-world clinical practice, as well as suboptimal management by medical doctors.¹⁶⁻¹⁸ In addition, limited knowledge about ACEI-associated adverse effects and the appropriate clinical response by medical doctors has been reported.¹⁹ Studies in community pharmacy settings related to recognising and managing ACEI induced cough is limited. A simulated patient study by Brata et al. in Eastern Indonesia found that pharmacy staff often failed to collect comprehensive information, leading to inadequate recommendations for managing ACEI-induced cough. Less than 5% of encounters that pharmacy staff asked about current medication used and medical history and only 5% of the 76 encounters that pharmacy staff advised direct medical referral for the case of ACEI-induced cough.^{20,21} However, the study population included all pharmacy staff—not necessarily qualified pharmacists, and therefore the ability of community pharmacists in recognising and managing ACEI induced cough is unknown. Given the widespread use of ACEIs and the tendency of individuals with cough to seek advice or self-medicate through community pharmacies, pharmacists are likely to encounter cases of ACEI-induced cough. It is therefore essential that pharmacists can recognise this adverse effect and respond appropriately, which involves referring patients for medical evaluation. This study aims to describe the ability of pharmacists to recognise and manage a vignette case of ACEI-induced cough for self-medicating patients.

METHODS

Study design

This study was a cross-sectional study, conducted across community pharmacies located in a metropolitan city of Indonesia. The city is a provincial capital situated in a well-developed part of Indonesia, where modern infrastructure and reliable internet access are widely accessible. The city is home to multiple pharmacy schools, both public and private, contributing to a strong and readily available pharmacist workforce.

Population and samples

The population of the study consisted of community pharmacists working in community pharmacies in a metropolitan city in Indonesia. The list of community pharmacies was obtained from the Indonesian Ministry of Health Directorate General of Pharmacy Affairs and Medical Instruments (Direktorat Jenderal Bina Kefarmasian dan Alat Kesehatan – Dirjen Binar (n=785)). Data collectors would then visit the addresses of all pharmacies in the list. Community pharmacists were eligible for inclusion if they (1) worked at pharmacies listed in the Dirjen

Binfar registry or (2) were employed at newly established pharmacies not yet included in the registry but identified by data collectors during fieldwork. Exclusion criteria were: (1) pharmacists working in pharmacies within beauty or specialist clinics that exclusively dispensed prescribed medications, and (2) those affiliated with pharmacies that had permanently closed or could not be located during data collection. Total sampling was used as the sampling method.

Study instruments

A questionnaire consisting of two sections: (1) pharmacy and participant demographic characteristics and (2) a vignette case of ACEI-induced cough (Table 1). The case was adopted from Brata et.al. The case has been validated in previous research and has been tested on a population of pharmacy staff in Eastern Indonesia.²¹ Before using the questionnaire in this research setting, the questionnaire was re-assessed for its content and wording by four Indonesian pharmacy academics (CB, ES, YIW, and SV). Unlike studies involving medical doctors—which typically assess their ability to recognize and manage ACEI-induced cough using real clinical cases, such as pharmacovigilance reports or medical and prescription records—we employed a vignette case involving a self-medicating patient experiencing ACEI-induced cough.¹⁶⁻¹⁸ This approach was necessary because records of self-medicating patients are generally not available in community pharmacies in the research setting. No significant changes were made in the questionnaire and data from the pilot were included in the analysis.

Data collection

Five data collectors (final year BPharm students - AfR, IMS, PRL, AzR, and IAERSP) determined the location of the pharmacies and visited each pharmacy in person. Upon arrival at the pharmacy, the data collectors asked for the pharmacist. They explained the study and provided informed consent to pharmacists who agreed to participate. If the pharmacist was not present in the pharmacy at the first visitation, the data collectors would ask for the pharmacist's contact number to arrange a subsequent meeting. Each pharmacy was represented by a pharmacist. If two or more pharmacists were working in a pharmacy, the first available pharmacist would be chosen as the participant. The first section of the questionnaire (pharmacy and participant demographic characteristics) was self-administered. The second section of the questionnaire (a vignette case of ACEI-induced cough) was administered using a face-to-face interview.

A structured interview format was used. Open-ended questions were employed, yielding narrative data. To ensure consistency and reliability across interviews, all interviewers underwent standardized training prior to data collection. This training covered procedures for approaching participants, conducting interviews with pharmacists, and accurately completing the questionnaire. During the interview, data collectors read a predefined case scenario, then asked pharmacists for their recommendations regarding the case. They subsequently asked about the reasons behind those recommendations, without additional probing, in order to maintain uniformity in data elicitation (Table I). At the interview, the data collector recorded participants' answers in writing and the interviews were also audio recorded.

Table I. The cough scenarios and the appropriate recommendation according to the literature

Topic	Case	Appropriate recommendation
<i>ACEIs-induced cough</i>	A woman, aged about 60 years old, comes into this pharmacy and asks you for a recommendation for her cough. The woman says that she has experienced a non-productive cough constantly over the last 4 weeks. She has tried Bisolvon elixir for her cough but it did not help. The woman tells you that she was diagnosed with hypertension 2 months ago. Her daily medication is captopril 25mg, three times a day, which she has taken for 2 months. What would you advise this woman? Why do you recommend the advice?	Direct medical referral.

Data Analysis

Data related to pharmacy and participant's demographic characteristics were analysed descriptively. Open-ended data related to pharmacists' advice and the reasons for the advice for the case of ACEI-induced cough was transcribed verbatim and entered into an Excel database. Inductive content analysis as described by Elo and Kyngas was used to analyse the open-ended data.²² First, this involved familiarisation with the data by reading participants' responses several times and noting ideas. Then, the coding process was done by generating initial codes from participants' statements. The initial codes were then clustered into categories. The process of generating categories was reviewed and refined by going back and forth between the categories, the codes, and the original participant statements. Lastly, the number of participants corresponding to the categories was then counted. The data analysis process was conducted by CB. When there was doubt in interpreting participants' responses, YIW was consulted. The final code was obtained through consensus. Next, participants who identified the case as an ACEI-induced cough were considered to have recognised the case and their responses were counted. Participants who were able to provide appropriate management were also counted. Appropriate management was defined as participants who recommended direct medical referral without recommending a product to treat the cough and/or changing or stopping the ACEI, as stated in the literature.^{18,23-25} This type of analysis has been employed in previous clinical decision-making research within pharmacy settings similar to this study.²⁶

RESULTS AND DISCUSSION

From the Dirjen BINFAR list, there were 785 community pharmacies in the area. Of these, 264 pharmacies were excluded (83 pharmacies were inside the specialist clinics that only serve doctor's prescriptions, and 181 pharmacies were closed down or could not be located by the data collectors). Therefore, the number of pharmacies visited from the list was 521. During fieldwork, there were 30 new pharmacies found by the data collectors, making the total number of pharmacies visited equal to 551. Of these 551 pharmacies, only 245 participated (the response rate was 44%) (Figure 1).

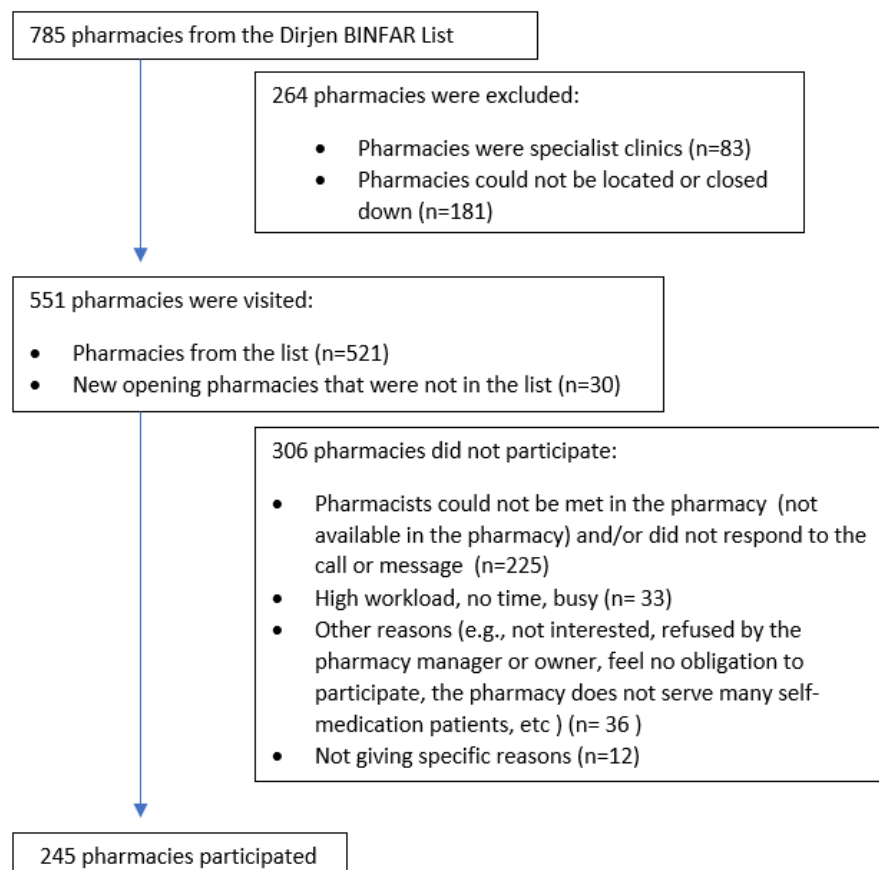


Figure 1: Participants' recruitment

Pharmacist and pharmacy characteristics

A large number of participating pharmacists (88%) were female. The median age was 31 and the median working experience was 5 years. 80% of them were pharmacist managers, 79% of them did not have any side jobs other than being a pharmacist in the pharmacy, and more than half (57%) attended training related to self-medication after graduating from formal education. In terms of pharmacy characteristics, the median number of patients asking for self-medication services was higher than patients asking for prescription services (20 vs 10 per day respectively). Details of participants and pharmacy characteristics are presented in Table II.

The demographic characteristics of pharmacists in this study were similar to previous Indonesian studies, with most pharmacists being female, having a mean/median age of around 30 years old, and possessing approximately five years or less of work experience.^{21,27,28} The findings related to pharmacy characteristics also align with previous Indonesian studies, which reported that pharmacies most commonly serve patients seeking self-medication rather than those requiring prescription medicines.^{21,27,28} This indicates the importance of ensuring pharmacists' competence in providing quality self-medication services to benefit of public's health.

Table II. Pharmacist and pharmacy characteristics (n=245)

Pharmacist and pharmacy characteristics	N	
Age (years; median, IQR)*:	31	IQR= 25-39
Gender: Female	216	(88%)
Year of graduation as a pharmacist (median, IQR)**:	2012	IQR= 2004-2017
Working experience (years; median, IQR#)***:	5	IQR= 2-10
Position in the pharmacy:		
Pharmacist managers	195	(80%)
Pharmacists	50	(20%)
Ever attended training on self-medication after graduation from the highest education qualification:		
Yes	139	(57%)
No	106	(43%)
Pharmacists have jobs other than being a pharmacist in the pharmacy:		
Yes	52	(21%)
No	193	(79%)
Pharmacists as preceptors:		
Yes	30	(12%)
No	215	(88%)
Estimated number of patients served for self-medication per day in the pharmacy (median, IQR)***:	20	IQR= 10-39
Estimated number of patients served for prescription per day in the pharmacy (median, IQR)**:	10	IQR = 5-20

IQR = Interquartile range

*calculated from 229 data; **calculated from 243 data; ***calculated from 244 data

The recognition and management of an ACEI-induced cough case by pharmacists

Of the total 245 participating pharmacists, 189 (77%) could recognise or suspect that the cough was due to ACEI (lisinopril use) (Table III), but only 101 of these 189 participants provided appropriate management (i.e., referring the patient to a doctor without recommending products for cough or without stopping/changing the lisinopril by themselves) (Table III). Recommending products for cough was not considered appropriate because the evidence did not show any effectiveness of adding cough medicines for an ACEI-induced cough.^{8,18} Stopping or changing the ACEI into another antihypertensive by a pharmacist was also considered inappropriate because, by Indonesian law, all antihypertensives are classified into prescription medicines and pharmacists do not have the authority to change prescription medicines or initiate new prescriptions.^{24,25}

Table III. Pharmacists' advice in an ACEI-induced cough vignette case and the reasons for the advice (n=245)

Pharmacists' reasons for providing the advice	n	Pharmacists' management/advice	n
Recognising/suspecting ACEI-induced cough with or without identifying warning symptoms*	189	Direct medical referral with or without other advice^	101
		Direct medical referral and recommending products for the cough	51
		Direct medical referral and stopping/changing the ACEI to another antihypertensive	11
		Direct medical referral and stopping/changing the ACEI to another antihypertensive and recommending products for the cough	1
		Stopping or changing the ACEI to other antihypertensives with or without other advice^^	9
		Recommending products for the cough with or without other advice^^	10
		Recommending products for the cough and stopping/changing the ACEI to another antihypertensive with or without other advice^^	5
		Other advice (non-pharmacology)	1
Identifying warning symptoms but did not state that the cough was due to ACEI	10	Direct medical referral with or without other advice^	6
		Direct medical referral and recommending products for the cough	3
		Recommending products for the cough with or without other advice^^	1
The patient has hypertension, therefore the doctor can choose proper cough medicines for a hypertensive patient.	2	Direct medical referral	2
Suspecting Tuberculosis	1	Direct medical referral	1
The doctor knows better about the condition of the patient	1	Direct medical referral and recommending products for the cough	1
The recommended product is for the symptoms	12	Recommending products for the cough with or without other advice^^	12
Bisolvon is not suitable for the patient's cough	22	Recommending products for the cough other than Bisolvon (Bromhexine)	21
		Other advice (i.e., stopping bisolvon)	1
The recommended product is safe for the patient's condition (i.e. not contraindicated with hypertensive patients, herbal medicines are safer for the patient)	2	Recommending products for the cough (i.e., herbal medicines)	2
The cough is due to improper diet	1	Non-pharmacological advice (i.e., modifying to a healthy diet and lifestyle)	1
No specific reason is provided, participants only stated the advice for the patients	5	Recommending products for the cough, providing non-pharmacological advice, educating about how to take the ACEI, or recommending other advice (i.e., checking the blood pressure and stopping Bisolvon)	5

*warning symptoms were defined as participants stating the long duration of cough. ^with or without other advice in here was defined as participants stating either non-pharmacological advice, stopping the Bisolvon, or checking the blood pressure. ^^with or without other advice was defined as participants stating either non-pharmacological advice, stopping the Bisolvon, follow-up (i.e., going to the doctor if symptoms persist or worsen), or checking the blood pressure.

A large number of pharmacists in this research setting, 189 of 245 pharmacists – 77% were able to identify that the vignette case was an ACEI-induced cough. This is similar to what was reported by Humbert et.al in the general practitioners (GPs) population; 92% of 690 GPs in France, Canada-Quebec, Belgium, and Switzerland were able to diagnose the vignette case as an ACEI-induced cough.²⁹ However, our study found that appropriate management related to this side effect needs further attention; of the 245 participating pharmacists, 189 (77%) were able to identify the cough was due to ACEI, but only 101 (41%) provided correct management. Poor knowledge of the correct management of ACEI-induced cough was reported in a 2005 study by Lombardi et.al; where only 15% of 52 GPs, 0% of 48 cardiologists, and 6% of allergists provided correct answers related to the management of ACEI-induced cough.¹⁹ Since ACEI-induced cough could be considered a common side effect,³⁰ our findings indicate the need for educational interventions to improve Indonesian community pharmacists' knowledge in the management of ACEI-induced cough.

However, studies in real clinical settings often reported sub-optimal results for identifying cough caused by ACEI. Olsen reported that physicians often made a significant delay in making the final diagnosis of ACEI-induced cough.¹⁷ Similarly, Vegter et.al and Humbert et.al also suggested that cough due to ACEI was often not recognised as being ACEI-related.^{16,18} Vegter et.al added that the cough was often symptomatically treated with ineffective antitussive treatment; the estimated frequency of antitussive treatment of ACEI-induced cough reported in this study was 15% of all cases.¹⁸ Different results in identifying ACEI-induced cough between clinical vignettes and real clinical settings may be due to the variations in the method used. It might also be interpreted that the knowledge of health care professionals regarding ACEI-induced cough was quite good, but their skills in identifying ACEI-induced cough still needed improvement. Humbert et.al proposed that the difficulty in identifying the link between ACEI and cough onset in real clinical settings might be due to the delayed onset of cough following the initiation of ACEI.¹⁶

In community pharmacy settings, sub-optimal management provided by pharmacy staff in the case of ACEI-induced cough might be due to inadequate patient assessment.^{21,31} A patient simulation study using a case of ACEI-induced cough, designed to mimic real practice in community pharmacy settings, showed suboptimal management of this case. Only 5 of 76 encounters (7%) that pharmacy staff recommended appropriate advice (i.e., direct medical referral) and the authors postulated that this was due to insufficient information gathered by pharmacy staff.²¹ Another patient simulation study involving the case of cough, where the patient also used an ACEI concurrently, similarly showed that pharmacy staff gathered inadequate information.³¹ While this article did not specifically measure the appropriateness of advice, the authors reported sub-optimal provision of pharmaceutical care in terms of information-gathering and patient counselling.³¹

Theoretically, to accurately identify and manage the vignette case, our participants must demonstrate proficiency in clinical decision-making skills. A general model of clinical decision making process in pharmacy includes four key steps: (1) Information gathering – assessing the patient, identifying the need for intervention, reviewing lab data, setting treatment goals, and considering individual risk factors; (2) Clinical reasoning – integrating evidence, scientific knowledge, and critical thinking; (3) Clinical judgment – evaluating and prioritizing options; and (4) Decision-making – choosing and implementing a patient-centred solution.³² Clinical decision making can be divided into 3 approaches: Rationalist – decisions guided by clinical evidence, Phenomenological – decisions informed by intuition and experience, and Hypothetico-Deductive – a balanced approach combining the first two.³³ For community pharmacy setting, Rutter PM suggested to use a hypothetico-deductive reasoning for making a decision. Particular steps proposed by Rutter for serving self-medicating patients included: using epidemiological data, assessing patient characteristics, applying hypothetico-deductive reasoning, and incorporating safety-netting strategies like symptom warnings or conditional referrals.³⁴ Therefore, pharmacists in this setting needed to strengthen their clinical decision-making skills to enhance the recognition and management of self-medication cases.

Of the 245 participating pharmacists, 10 (4%) pharmacists did not state that the cough was ACEI induced but they were able to identify the warning symptoms in the case (i.e. long duration of cough) (Table III). Of these 10 pharmacists, 6 pharmacists provided appropriate management (i.e. direct medical referral without recommending products or stopping/changing lisinopril by themselves). According to the standard for Indonesian Pharmacists Professional, the competence of Indonesian pharmacists concerning self-medication services is related to the competence of performing appropriate information-gathering, identifying whether a condition is minor or alarm symptoms are present, and providing recommendations for the patient. The recommendations could involve referring the patient to a doctor if alarm symptoms are present or recommending medicines if the condition is minor and determining the treatment time scale.³⁵ Therefore, it could be stated that the 6 pharmacists who could identify alarm symptoms and provided proper management

have fulfilled the competence of the Indonesian Pharmacists Professional standard in self-medication services, although they could not identify the use of ACEI as the cause of the cough.

Cross-tabulation between the ability to identify ACEI-induced cough and appropriate management (i.e., direct medical referral without recommending products for cough or without stopping/changing the lisinopril) showed that participants who knew that the cough was ACEI-induced were more likely to state appropriate management than those who did not; 101 of 189 participants (53%) compared to 9 of 56 participants (16%), respectively; $p < 0.05$ (Table IV). This may indicate that when pharmacists understand the underlying cause of the symptoms, they can provide more appropriate recommendations to manage the condition or alleviate patients' symptoms; hence better outcomes for patients. Therefore, educational interventions need to be focused on improving pharmacists' skills in understanding the cause of the symptoms in self-medicating patients and how to manage the conditions.

Table IV: Cross-tabulation of pharmacists' ability to identify the case as an ACEI-induced cough and the appropriateness of the management provided

	The appropriateness of the management provided (n=245)			Chi-square p-value
	Appropriate*	Not appropriate	Total	
Ability to identify/suspect that the case was an ACEI-induced cough				
Stated that the cough was related to ACEI	101	88	189	0.000
Did not state that the cough was related to ACEI	9	47	56	

*Appropriate management was defined as i.e., direct medical referral without recommending products for cough or without stopping/changing the lisinopril

Strength and Limitation

Previous studies related to this topic have been conducted only in the population of medical doctors. This is the first study that describes the ability of pharmacists to identify and manage a vignette case of ACEI-induced cough for self-medicating patients; thus contributing to the body of knowledge.

The response rate was only 44% and therefore the results might be prone to non-response bias. However, a low pharmacists' response rate in responding to surveys is quite common and has been reported in other community pharmacy studies.^{36,37} While the findings of this study provide insights into pharmacists' knowledge specifically regarding ACEI-induced cough, it cannot be assumed that their competence in managing other medication-related issues would be similar. Further research may be needed to explore pharmacists' competence in managing various medication-related issues comprehensively. Furthermore, we interviewed only one available pharmacist per pharmacy. In pharmacies with multiple pharmacists, the results may not reflect the abilities of those not interviewed, even though they also work at the same location. However, we limited interviews to the available pharmacist because, in most cases, the schedules of other pharmacists were unclear, and many did not work at the pharmacy on a daily basis. In addition, open-ended questions were used, and five different interviewers conducted the interviews; this may have introduced variability in interview style and influenced participant responses. To minimize this, all interviewers received standardized training on participant approach, interview procedures, and questionnaire completion. During interviews, they presented a predefined case, asked for pharmacists' recommendations, and then asked for reasoning without further probing to ensure consistency.

CONCLUSION

While many pharmacists may possess the necessary knowledge to recognise ACEI-induced cough in the case of a self-medicating patient, they may lack sufficient knowledge about the appropriate management of this problem. Continuing education is needed to improve pharmacists' knowledge and ability to manage ACEI-induced cough cases. Further research to explore pharmacists' competence in managing various medication-related issues comprehensively is warranted.

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STATEMENT OF ETHICS

Ethics approval was obtained from the Ethical Committee University of Surabaya, Indonesia, number: 074/KE/V/2019. To protect the identity of the participants, any identifying information was not published.

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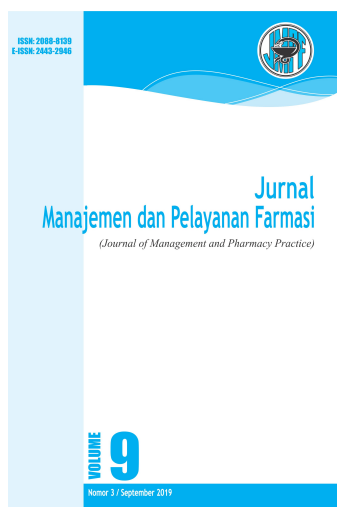
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This new APC rate will apply to all manuscripts accepted for publication starting from Vol. 15 No. 4 (December 2025) onward.

We appreciate your continued support and understanding as this adjustment is necessary to maintain and improve the quality of our publication services.

If you have any questions or concerns, please do not hesitate to contact us.

Warm regards,

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*Posted: 2019-03-18*[More...](#)[More Announcements...](#)

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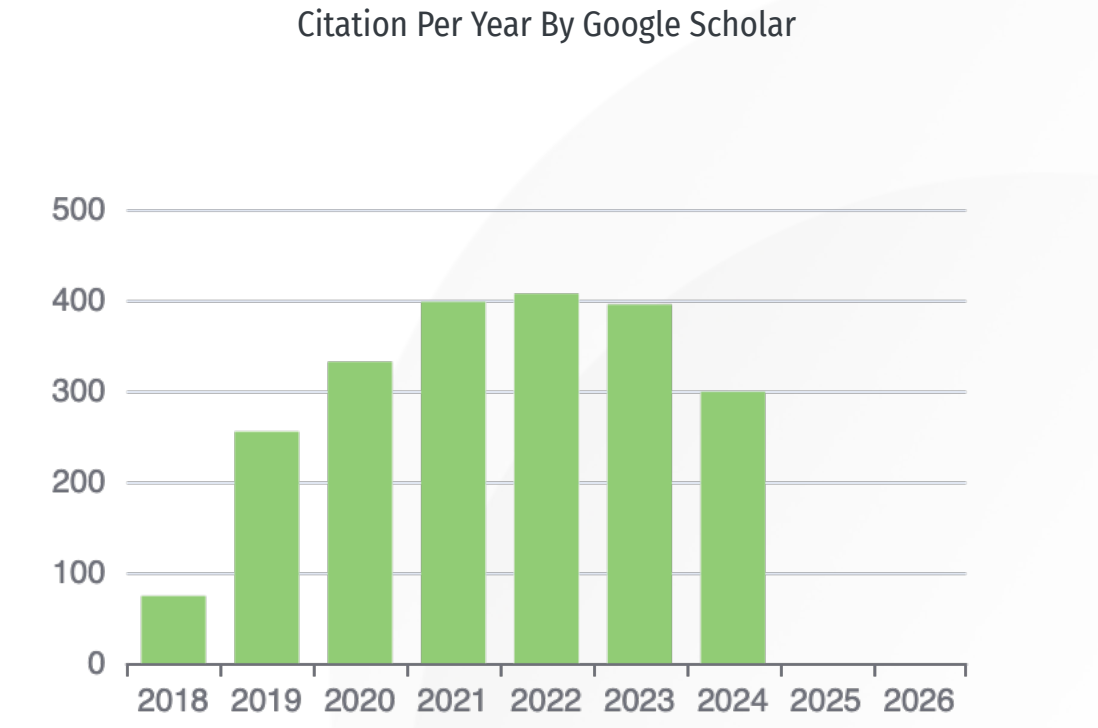
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