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The Relationship of Prescribed Inhaled Medications Adherence and Asthma Exacerbation: An Outpatient-Based Study in Aceh Province Hospital, Indonesia

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ABSTRACT

Background: Adherence to inhaler medication and appropriate pharmacotherapy is essential for optimal asthma control. Therefore, this study aimed to measure self-reported adherence and identify associations between inhaler adherence and asthma intensification.
Subjects and Method: This cross-sectional study was conducted in the outpatient pulmonary department of Zainoel Abidin Hospital, Aceh Province, Indonesia, in 2024. A total of 35 clinically confirmed asthma patients were interviewed. The main variables analyzed were asthma exacerbations and inhaler adherence. Inhaler adherence was measured using the Medication Adherence Report Scale Asthma (MARS-A) consisting of 10 items. Descriptive and multivariable tests were used to assess risk factors for poor inhaler adherence.
Results: Duration of inhaler use was significantly associated with adherence. Patients who had used inhalers for >7.5 years showed higher odds of adherence than those who had used inhalers for <7.5 years (100.0% vs. 62.5%; OR=14.11; 95% CI=0.74 to 267.61; p=0.033). This finding indicates that longer inhaler-use experience was associated with better adherence, although the wide confidence interval suggests limited precision of the estimate.
Conclusion: Patient education about inhalers plays a crucial role in asthma treatment. The duration of inhaler usage influenced adherence, making it essential to implement interventions that support long-term use. These interventions can enhance the quality of life of asthma patients and reduce the risk of exacerbations.

Keywords: asthma, adherence therapy, exacerbation

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BACKGROUND

Asthma is a chronic heterogeneous disease of the lower respiratory tract characterized by complaints of shortness of breath due to limited airflow and can be contracted by both children and adults (Papi et al., 2018; Cevhertas et al., 2020). According to the Global Burden of Disease Study, the disease caused 461,069 deaths in 2019 (Vos et al., 2020). Study data in Indonesia reported 1,017,290 asthma patients, with 2.3% from Aceh Province (Kemenkes RI, 2018). Corticosteroid inhalation, is the primary treatment choice for preventing asthma symptoms and exacerbations, as well as the need for hospitalization (Lycett et al., 2018). Despite the effectiveness of the medication, problems such as increasing rates of non-compliance exist (Miller et al., 2017). A study reported that compliance with asthma therapy ranged from 30% to 70%. To achieve optimal treatment outcomes, at a target of 80%, compliance with inhaler use should not be less than 30% (Lycett *et al.*, 2018). The low level of compliance with inhaler therapy presents a major health challenge. Asthma patients show lower compliance rates compared to other chronic disease (Usmani, 2019). It is important to acknowledge that non-compliance in using inhalation therapy can increase morbidity and mortality (Fadzila and Indriati, 2018), the risk of hospitalization by up to 50%, visits to the emergency unit, and the use of oral corticosteroids (Usmani, 2019).

Correct use of inhalation therapy and adherence to prescription are key aspects in achieving successful clinical control and improving the quality of life of asthma patients (Ilic et al., 2016; Price et al., 2017). Furthermore, the successful treatment also depends on factors related to the condition such as age, smoking, environmental and occupational factors, asthma-related comorbidities, choice of medication, and inhaler (Rafi et al., 2022). In this context, inhaler have become the preferred choice due to the significantly faster onset, high therapeutic efficacy, and lower risk of side effects (Fadzila and Indriati, 2018; Rafi et al., 2022). The therapy allows drugs to enter the respiratory tract and lungs efficiently, facilitating rapid relief from airway narrowing (Fadzila and Indriati, 2018). Asthma management includes the use of inhaler to control the condition and relieve the respiratory tract during an attack (reliever) which function as a broncho-dilator (Haryanti et al., 2016). Therefore, compliance with the use of the therapy is essential and needs to be considered.

According to the Indonesian Society of Respirology (IRS), asthma severity is divided into intermittent, mild, moderate, and severe persistent. It is important to acknowledge that each level has different therapeutic options (Yunus et al., 2021). In asthma management, the primary goal is to achieve good symptom control, prevent air-way remodeling, and avert asthma attacks (Shayo, Omary and Mugusi, 2022). Therefore, regular treatment is crucial, as it improves quality of life, reduces recurrence rate, and decreases the incidence of exacerbations. These improvements can lead to better health outcomes and lower hospitalization rates (Stanford *et al.*, 2012; Ichinose *et al.*, 2017). Previous studies have explored the relationship between inhaler adherence and asthma exacerbations. For example, Williams et al. showed that patients with high adherence to inhaler experienced a lower risk of severe exacerbations (Williams et al., 2011). The level of compliance was directly proportional to better asthma symptom control and decreased asthma-related hospitalizations (Williams et al., 2011). Various studies have assessed the compliance rates concerning the daily use of asthma controller medication. The results

showed low levels which are associated with increased visits to the emergency unit and higher hospitalization rates, contributing to mortality among patients (Ferliani et al., 2017). Aceh, a province in Indonesia with a fairly high prevalence of asthma still faces challenges in managing the condition, specifically within outpatient units. Data on the relationship between compliance with inhaler use and the incidence of severe exacerbations among outpatients in this province remains limited. Therefore, this study aims to determine the relationship between compliance with inhaler use and the incidence of asthma exacerbations in outpatients at Aceh Provincial Hospital. The results are expected to serve as a basis for treating severe cases and provide guidelines to help improve compliance with medication, thereby enhancing quality of life.

SUBJECTS AND METHOD

1. Study design

This study was conducted from April 2024 to July 2024, at the Pulmonary Outpatient Polyclinic of Zainoel Abidin Hospital, a referral hospital in Aceh Province. The method used was a facility-based cross-sectional design.

2. Population and sample

The population comprised all adult asthmatic patients (aged ≥18 years) who visited the Pulmonary Polyclinic. The inclusion criteria were patients aged ≥18, diagnosed with asthma by a pulmonary specialist, and using at least one inhaler such as a Metered Dose Inhaler (MDI) or Dry Powder Inhaler (DPI). Meanwhile, the exclusion criteria were asthma-COPD overlap disease, other obstructive pulmonary disease, chronic debilitating conditions (eg, carcinoma), and pregnant females. The sample comprised eligible patients from the beginning to the end of the study period.

3. Study variables

The study variables include inhaler adherence and asthma exacerbation. For subsequent analysis, inhaler adherence will be treated as the independent variable, while asthma exacerbation will serve as the dependent variable. Variables included in the analysis consisted of gender, education level, employment status, smoking status, comorbidity status, allergy history, age group, duration of inhaler therapy, inhaler adherence, and asthma exacerbation. In the analysis of factors associated with adherence, gender, education level, employment status, smoking status, comorbidity status, allergy history, age group, and duration of inhaler therapy were treated as explanatory variables, while inhaler adherence was treated as the outcome variable.

4. Operational definition of variables

Inhaler adherence means the extent to which the patient acts by the intervals and dosage regimen prescribed by the doctor and measured using the Medication Adherence Report Scale Asthma (MARS-A), which consisted of 10 items based on a validated five-point Likert scale designed to assess the level of medication adherence (Albassam, Alharbi and Awaisu, 2020). Asthma exacerbation was defined as the occurrence of worsening asthma symptoms or shortness of breath requiring clinical assessment or treatment, based on interview information and medical record review. Gender was categorized as male or female. Education level was categorized as bachelor, master, or senior high school. Employment status was categorized as working or not working. Smoking status was categorized as smoker or non-smoker. Comorbidity status was categorized as no comorbidity, one comorbidity, or more than two comorbidities. Allergy history was categorized as present or absent. Age was grouped according to the study categories of 18–25, 25–35,

35–45, and >45 years, and was further classified as <35 or >35 years for factor analysis. Duration of inhaler therapy was categorized as <7.5 years or >7.5 years. Type of inhaler therapy was classified as Dry Powder Inhaler, Metered Dose Inhaler, combined Dry Powder Inhaler and Metered Dose Inhaler, nebulizer, oral therapy, or nebulizer combined with oral therapy (Albassam, Alharbi and Awaisu, 2020).

Adherence-related behavior was assessed on a scale, where 5, 4, 3, 2, and 1 represent never, rarely, sometimes, often, and always, respectively. The scores for each item were summed to generate a total, which ranged from 10-50. Higher scores signified greater levels of reported adherence. Specifically, a score of 40 to 50 showed very good compliance, signifying the ability to follow treatment instructions effectively. A score of 30 to 39 is considered fairly good compliance, suggesting consistent adherence with some instances of non-compliance. For statistical analysis, adherence was dichotomized into compliant and non-compliant categories according to the MARS-A classification used in this study.

5. Study instruments

Face-to-face interviews were conducted using questionnaires, supplemented by the collection of essential patient data from medical records. The interview questions were divided into (i) socio-demographic characteristics of patients, (ii) information about the types and duration of inhaler used, (iii) history of allergies and hospitalizations for shortness of breath, and (iv) assessment of compliance. The reliability, sensitivity, and specificity of the questionnaire were 0.65, 0.82, and 0.69, respectively (Albassam, Alharbi and Awaisu, 2020).

6. Data analysis

Descriptive statistics were used to summarize patient characteristics, inhaler therapy, adherence level, and asthma exacerbation. Bivariate analysis using Fisher's exact test was performed to assess the relationship between inhaler adherence and asthma exacerbation. Factors associated with inhaler adherence were analyzed by comparing adherence status across gender, education level, employment status, smoking status, comorbidity status, allergy history, age group, and duration of inhaler therapy. The results were reported using odds ratios (OR), 95% confidence intervals (95% CI), and p-values, with statistical significance set at $p<0.05$. Finally, all statistical analyses were performed using Statistical Package for Social Sciences (SPSS) version 21.0.

7. Research ethics

Ethical approval was received from the Ethics Review Committee of Zainoel Abidin Hospital, No: 025/ETIK-RSUDZA/2024. Each respondent was demanded to provide Informed Consent before participating in this study.

RESULTS

1. Sample Characteristics

A total of 35 asthma patients were successfully recruited for this study, with the majority being 35-45 years old (37.1%), female (68.6%), and had allergies (82.9%). Approximately two-thirds of the participants had a senior high school education history (60.0%) and were primarily housewives (33.4%). The Dry Powder Inhaler (DPI) was used by 68.57% of the patients, followed by oral medication (14.29%). In terms of the duration of inhaler usage, 68.6% of the sample used inhaler for <7.5 years. Most participants reported no history of smoking (97.1%) and did not have comorbidities (80.0%). Among the 35 participants, 74.29% were classified as compliant with inhaler usage as recommended by clinicians. The demographic characteristics of asthma patients are shown in Table 1.

Table 1. Demographic Characteristics of Asthma Patients

Variables	Frequency (n)	Percentage (%)
Gender		
Male	11	31.4
Female	24	68.6
Last education		
Bachelor	11	31.4
Master	3	8.6
Senior High School	21	60.0
Work		
Not Working	19	54.3
Working	16	45.7
Smoke		
Yes	1	97.1
No	34	2.9
Comorbid		
Yes	5	80.0
No	28	14.3
More Than 2 Comorbidities	2	5.7
Allergy History		
Yes	29	17.1
No	6	82.9
Adherence Level		
Very good	9	25.7
Quite good	12	34.3
Average	5	14.3
Not compliant	9	25.7
Exacerbation		
Yes	13	62.9
No	22	37.1
Age		
18 – 25	8	22.9
25 – 35	10	28.6
35 - 45	13	37.1
>45	4	11.4
Inhaler Therapy Duration		
<7.5	24	68.6
>7.5	11	31.4
Adherence		
Compliant	26	74.3
Not Compliant	9	25.7
Inhaler Therapy		
Powder Dry Inhaler (PDI)	24	68.57
Metered Dose Inhaler (MDI)	0	0

Variables	Frequency (n)	Percentage (%)
PDI and MDI	2	5.71
Nebulizer	3	8.57
Oral	5	14.29
Nebulizer and Oral	1	2.86

2. Bivariate analysis

An analysis was conducted to evaluate the relationship between adherence and exacerbation. The level of adherence was grouped into compliant and non-compliant. The results showed a significant relationship between adherence with inhaler use and asthma exacerbation (OR=2.476; 95% CI=1.131 to 5.423; p=0.033). Specifically, non-compliant patients had a 2.476 times greater tendency to experience asthma exacerbation, with the OR, 95% CI, and p-value presented consistently in Table 2.

Table 2. Relationship between compliance with inhaler use and the incidence of asthma exacerbations

Adherence	Exacerbation		Total	OR	95% CI		p
	Yes n (%)	No n (%)			Lower limit	Upper Limit	
Compliant	7 (26.9)	19 (73.1)	26	Ref.			
Non-compliant	6 (60.0)	3 (30.0)	9	2.48	1.13	5.42	0.033

3. Multivariate analysis

An analysis was conducted on factors affecting inhaler adherence in asthma patients. The results showed that there was no significant difference in compliance based on gender (OR=1.00; 95% CI=0.21 to 4.83; p=1.000), education level (p=0.928), employment status (OR=1.07; 95% CI=0.26 to 4.45; p=1.000), smoking habits (OR=not estimable due to a zero-cell count; p= 1.000), comorbidities (p=0.701), history of allergies (OR=0.52; 95% CI=0.05 to 5.89; p= 1.000), and age (OR=0.43; 95% CI=0.09 to 2.03; p=0.443). However, the duration of inhaler use showed a significant relationship with adherence (OR=14.11; 95% CI=0.74 to 267.61; p=0.033). Asthma patients who had used inhaler for more than 7.5 years had compliance of 100%, while those in the less than 7.5 years category had 62.5% compliance, as shown in Table 3.

DISCUSSION

The results of this study show that 37.1% and 68.6% of asthmatic patients are aged 35–45 and female, respectively. The prevalence of asthma among adult, specifically in females, is related to the influence of the hormone estrogen and genetic factors that affect the immune system, thereby worsening the symptoms (Dharmage, Perret and Custovic, 2019). According to Kuruvilla et al., there is a change in the prevalence of asthma from male to female after puberty (Kuruvilla *et al.*, 2019). Despite the exact role of sex hormones not being fully understood, it is known that testosterone reduces inflammation of the respiratory tract, allowing the prevalence of adult females to be higher than males (Kuruvilla *et al.*, 2019). Furthermore, most participants also had a history of allergies (82.9%). This is in accordance with a study where allergies are among the main risk factors in the development of asthma (Akar-Ghibril *et al.*, 2020).

Table 3. Factors associated with the level of adherence with inhaler use

Variables	Categories	Adherence:		Total	OR	95% CI		p
		Compliant n (%)	Not Compliant n (%)			Lower Limit	Upper Limit	
Gender	Male	8 (72.70)	3 (27.30)	11	1.00	0.21	4.83	1.000
	Female	18 (75.00)	6 (25.00)	24	Ref.	Ref.	Ref.	
Last education	Bachelor	8 (72.70)	3 (27.30)	11	Ref.	Ref.	Ref.	0.928
	Master	2 (66.70)	1 (33.30)	3	0.75	0.05	11.62	
	Senior High School	16 (80.00)	5 (25.00)	20	1.20	0.24	5.96	
Work status	Not working	14 (73.70)	5 (26.30)	19	1.07	0.26	4.45	1.000
	Working	12 (75.00)	4 (25.00)	16	Ref	Ref.	Ref.	
Smoking status	Non-smoker	25 (73.50)	9 (26.50)	34	Ref	Ref.	Ref.	1.000
	Smoker	1 (100.00)	0 (0.00)	1	Not estimable	Not estimable	Not estimable	
Comorbidity status	No comorbidity	21 (75.00)	7 (25.00)	28	Ref.	Ref.	Ref.	0.701
	One comorbidity	4 (80.00)	1 (20.00)	5	1.33	0.13	14.08	
	>=2 comorbidities	1 (50.00)	1 (50.00)	2	0.33	0.01	9.39	
Allergy history	No	5 (83.30)	1 (16.70)	6	Ref.	Ref.	Ref.	1.000
	Yes	21 (72.40)	8 (27.60)	29	0.52	0.05	5.89	
Age group	<35 years	14 (82.40)	3 (17.60)	17	Ref.	Ref.	Ref.	0.443
	>=35 years	12 (66.70)	6 (33.30)	18	0.43	0.09	2.03	
Duration of inhaler therapy	<7.5 years	15 (62.50)	9 (37.50)	24	Ref.	Ref.	Ref.	0.033*
	>=7.5 years	11 (100.00)	0 (0.00)	11	14.11	0.74	267.61	
Total		26 (74.29)	9 (25.71)	35				

In this study, 60.0% of participants had a high school education history. No significant relationship was observed between education level and inhaler compliance. This is supported by other studies showing that education level is not always a determining factor in compliance with asthma treatment. Additionally, understanding and effective communication with health workers plays a more critical role (Zhang *et al.*, 2023).

In terms of occupation, one-third of the participants were housewives (33.4%). Several studies have shown that occupation or role in the household does not directly affect medication adherence. However, time organization and daily routines can affect the consistency of medication usage. Nieuwlaat et al (2014) stated that patients who successfully integrated medication into their daily routines tended to be more consistent in long-term compliance (Nieuwlaat *et al.*, 2014). This study suggests that compliance is more influenced by the ability to adjust medication schedules to personal routines, rather than by specific occupations or social roles (Nieuwlaat *et al.*, 2014). In the literature, it is mentioned that gender differences in job distribution affect different risk factors (Agrawal *et al.*, 2014). However, the influence of work among females has not been observed.26 The duration of inhaler use is also an important predictor. The duration of inhaler use showed a statistically significant association with compliance, where respondents who had used inhalers for more than 7.5 years demonstrated a higher compliance rate (100%) compared to those who had used inhalers for less than 7.5 years (62.5%). Prolonged experience in using inhaler enhances understanding of the importance of consistent compliance with asthma treatment Nieuwlaat *et al.*, 2014).

Almost all respondents had no smoking history (97.1%) and comorbidities (80.0%). Other studies have also shown that not having a smoking history can improve asthma prognosis. Recent evidence from the Global Burden of Disease places smoking second among the major risk factors for Disability-adjusted life years (DALYs) associated with asthma (Safiri et al., 2022). It is important to acknowledge that comorbidities such as cardiovascular disease or obesity can worsen asthma control and reduce medication adherence. Obesity will increase airway oxidative stress, making it more difficult for patients to breathe.21.

Inhaler adherence is an important factor in asthma control. Table 2 shows that patients who are compliant with inhaler have a lower risk of experiencing asthma (Zhang et al., 2023). The results are consistent with the reports of several other studies that non-compliance to inhaler treatment is correlated with increased asthma exacerbations, hospitalizations, and use of emergency health services (Usmani, 2019; Zhang et al., 2023). This is also in line with a study by Engelkes et al. (2015) where good compliance tends to be associated with a lower risk of severe exacerbations. The results showed that a 25% increase in compliance was associated with a 10% decrease in the risk of severe exacerbations (Engelkes et al., 2015).

Further analysis showed that factors such as gender, education level, smoking habits, comorbidities, history of allergies, and age did not have a significant effect on the level of inhaler compliance. This is in line with other studies where the demographic factors had a significant effect on medication compliance. However, psychosocial factors such as patient perception of disease, relationship with healthcare providers, and belief in the effectiveness of

treatment play a greater role in influencing compliance (Zhang et al., 2023).

In conclusion, the study emphasized the importance of patient education and routine monitoring in promoting effective inhaler use, particularly among new asthma patients. The duration of inhaler use was identified as a significant factor influencing adherence. This emphasized the need for interventions that support long-term use to improve the quality of life of asthma patients and reduce the risk of exacerbations.

This study has several limitations. First, the sample size was relatively small, with only 35 asthma patients, which may have limited the statistical power and precision of the estimated associations. Second, this study was conducted in a single outpatient pulmonary department at Zainoel Abidin Hospital, Aceh Province, and the findings may not be generalizable to asthma patients in other hospitals, primary care settings, or different geographic regions. Third, the cross-sectional design prevents causal interpretation between inhaler adherence and asthma exacerbation. Fourth, several subgroup analyses involved small cell counts, particularly for smoking status and longer duration of inhaler therapy, resulting in unstable OR estimates and wide confidence intervals. Future studies should include larger multicenter samples, prospective designs, and objective adherence measurements such as pharmacy refill records or electronic inhaler monitoring to strengthen the evidence regarding inhaler adherence and asthma outcomes.

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CONFLICT OF INTEREST

This research has no conflicts of interest.

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