

## ORIGINAL ARTICLE

# Appropriateness of Bronchodilator Therapy and Its Association with Exacerbation and Hospitalization among Asthma Outpatients: A GINA 2024-Based Assesment

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## ABSTRACT

Bronchodilator use and inadequate therapy escalation may increase the risk of asthma exacerbations and hospitalization. This study evaluated treatment-related factors and its association with exacerbation and hospitalization among asthma outpatients. A retrospective cross-sectional study was conducted using medical records of asthma outpatients at RSUD Kota Kendari over a 1-year observation period (January–December 2024). A total of 94 eligible patients were included. Treatment-related factors comprising ICS–LABA therapy, inhalation route appropriateness, dosing appropriateness, therapy escalation with add-on LAMA, and SABA overuse were analyzed using bivariate analysis. ICS–LABA was associated with the lower risk of exacerbation (OR = 0.276; 95% CI: 0.104–0.735) and hospitalization (OR = 0.201; 95% CI: 0.072–0.559). Correct dosing was associated with lower risks of exacerbation (OR = 0.142; 95% CI: 0.052–0.390) and hospitalization (OR = 0.116; 95% CI: 0.039–0.343). Inhalation therapy showed a strong protective effect against exacerbation (OR = 0.078; 95% CI: 0.022–0.282) and hospitalization (OR = 0.059; 95% CI: 0.016–0.218). Lack of therapy escalation with add-on LAMA markedly increased the risk of exacerbation (OR = 17.889; 95% CI: 3.898–82.091) and hospitalization (OR = 14.000; 95% CI: 3.040–64.473). SABA overuse was strongly associated with higher likelihood of exacerbation (OR 10.833; 95% CI: 2.987–39.288) and hospitalization (OR=14.167; 95% CI: 3.815–52.605). Asthma outcomes were mainly influenced by treatment-related factors. Optimizing inhaled controller therapy and applying stepwise treatment escalation according to GINA are essential to lower the risk of exacerbations and hospitalization.

**Keywords:** asthma; exacerbation; hospitalization; ICS–LABA; inhalation therapy; LAMA

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## Introduction

Asthma is a chronic inflammatory disease of the airways characterized by variable respiratory symptoms, airflow limitation, and recurrent exacerbations. Although effective pharmacological therapies are widely available, asthma remains inadequately controlled in a substantial proportion of patients, particularly in routine clinical practice. Poor asthma control is associated with an increased risk of exacerbations, emergency department visits, and hospitalizations, which contribute significantly to morbidity, reduced quality of life, and increased healthcare utilization (1–3).

Bronchodilators play a fundamental role in asthma management, both as reliever and controller therapy. Short-acting  $\beta_2$ -agonists (SABA) have traditionally been used for rapid symptom relief; however, excessive reliance on SABA has been consistently associated with poor asthma control and adverse clinical outcomes. Evidence from real-world studies and meta-analyses has demonstrated that overuse of SABA is strongly associated with increased risk of exacerbations, hospitalizations, and asthma-related mortality (4–6). As a result, contemporary asthma management strategies emphasize the

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importance of anti-inflammatory therapy rather than symptom-driven bronchodilation alone.

Inhaled corticosteroids (ICS), either as monotherapy or in combination with long-acting  $\beta_2$ -agonists (LABA), represent the cornerstone of controller therapy in asthma. ICS-containing regimens effectively suppress airway inflammation, improve symptom control, and reduce the frequency of exacerbations (7). The Global Initiative for Asthma (GINA) has updated its recommendations to discourage SABA monotherapy and to promote the use of ICS-based treatment tracks, including the use of ICS-formoterol as both maintenance and reliever therapy (8). Despite these recommendations, inappropriate use of bronchodilators, including inadequate controller therapy and continued overuse of SABA, remains common in clinical practice.

The effectiveness of asthma pharmacotherapy depends not only on appropriate drug selection but also on correct dosing, optimal route of administration, and suitability of therapy to individual patient characteristics. Inhalation is the preferred route of administration for asthma medications, as it delivers drugs directly to the airways with rapid onset and minimal systemic exposure (9). Inappropriate dosing, incorrect route of administration, or failure to escalate therapy according to disease severity may lead to persistent airway inflammation and increased risk of exacerbations and hospitalizations (10). Patients who remain uncontrolled despite medium- to high-dose ICS-LABA may require step-up therapy, including the addition of long-acting muscarinic antagonists (LAMA), as recommended in recent clinical guidelines (8,11).

Previous studies have shown that deviations from guideline-based asthma management, such as bronchodilator selection focus on ICS-LABA, underdosing of controller therapy, inhalation routes, and failure to individualize LAMA treatment on exacerbations status are strongly associated with poor clinical outcomes (5,6,12). However, data evaluating the appropriateness of bronchodilator use and its relationship with exacerbation and hospitalization outcomes in outpatient hospital settings remain limited, particularly in regional healthcare facilities in Indonesia.

Therefore, this study aimed to evaluate the appropriateness of bronchodilator therapy based on four

key indicators: drug selection, dosage, route of administration, and therapy escalation (add-on LAMA), according to the GINA 2024 guideline. In addition, this study analyzed the association between the appropriateness of bronchodilator use, SABA overuse, and clinical outcomes, including asthma exacerbations and hospitalizations, among outpatients at a regional public hospital. The findings of this study are expected to provide real-world evidence to support optimization of asthma management and improve clinical outcomes in routine practice.

## METHODS

### Study design

This analytical observational study employed a cross-sectional design using retrospective medical record data from the outpatient clinic of RSUD Kota Kendari, Southeast Sulawesi, Indonesia. The observation period covered asthma treatment from January to December 2024, with data collection conducted between October and December 2025. The primary objective was to evaluate the treatment-related factors based on the Global Initiative for Asthma (GINA) 2024 guideline among asthma outpatients. Secondary objectives included: (1) describing demographic and clinical characteristics; (2) identifying patterns of bronchodilator and adjunctive therapy use; (3) evaluating the treatment-related factors based on drug selection (ICS-LABA), dosing appropriateness, inhalation route appropriateness, and therapy escalation (add-on LAMA); and (4) analyzing the association between treatment-related factors, short-acting  $\beta_2$ -agonist (SABA) overuse, and clinical outcomes (asthma exacerbations and hospitalizations).

The final sample consisted of 94 patients, selected using a purposive sampling approach that included all eligible asthma outpatients meeting the inclusion criteria. No formal a priori sample size calculation was performed; the sample size was determined based on feasibility and representativeness of the outpatient asthma population during the study period. Consequently, some bivariate subgroups were relatively small, which may have affected the precision and stability of the odds ratio estimates, as reflected in the

wide confidence intervals for some associations (e.g., therapy escalation with add-on LAMA); this is acknowledged as a limitation of the study.

### Population and Sample

The study population comprised all asthma outpatients receiving bronchodilator therapy at RSUD Kota Kendari between January and December 2024. Inclusion criteria were: outpatients with a primary diagnosis of asthma, receipt of bronchodilator therapy, age  $\geq 25$  years, and complete medical record data (demographic information, clinical characteristics, medication history, and integrated patient progress notes).

Exclusion criteria included incomplete medical records, dominant pulmonary diseases other than asthma (e.g., COPD without asthma), referral patients whose therapy could not be fully evaluated, and patients receiving acute care for severe infections during the observation period.

### Variables and Operational Definitions

Independent variables included treatment-related factors, namely: bronchodilator drug selection of ICS-LABA, dosing appropriateness, inhalation route appropriateness, therapy escalation with add-on long-acting muscarinic antagonists (LAMA), and SABA overuse.

SABA overuse was defined as use more than twice per week or consumption of  $\geq 3$  canisters per year.

Dependent variables were asthma exacerbations and hospitalizations. Asthma exacerbation was defined as worsening symptoms requiring treatment intensification, additional outpatient visits, or systemic corticosteroid use. Hospitalization was defined as inpatient admission due to asthma attacks recorded in medical records.

Potential confounding variables included age, outpatient visit frequency, and comorbidities. The distribution of comorbidities among study participants is reported descriptively in **Table 1**.

### Data Collection

Data were collected retrospectively from medical records of eligible asthma outpatients. Extracted data included demographic characteristics, clinical

information, and medication details related to bronchodilator therapy and adjunctive asthma treatments. Only medications prescribed for continuous outpatient use were included. Data were tabulated using Microsoft Excel prior to statistical analysis.

### Data Analysis

Statistical analysis was performed using IBM SPSS Statistics version 29.0. Descriptive statistics were presented as frequencies and percentages. Bivariate analyses using Chi-square or Fisher's Exact tests were conducted to assess associations between treatment-related factors, SABA overuse, and clinical outcomes. Associations were expressed as odds ratios (ORs) with 95% confidence intervals (CIs). A p-value  $< 0.05$  was considered statistically significant.

### Ethical Statement

This study was conducted in accordance with applicable ethical principles and national regulations. Prior to data collection, official permission to conduct the research was obtained from the Regional Research and Innovation Agency of Southeast Sulawesi Province, as documented in the Research Permit Letter No. 070/4124/X/2025, dated 17 October 2025, and approval from the management of RSUD Kota Kendari. The study utilized retrospective secondary data derived from medical records and was conducted solely for academic and scientific purposes. Ethical clearance for this study was obtained from the Research Ethics Committee of Universitas Padjadjaran, Bandung (Approval No. 208/UN6.KEP/EC/2026), issued prior to manuscript submission. The approximately one-year interval between the observation period (January–December 2024) and data collection (October–December 2025) reflects the time required to complete institutional research permit and ethical clearance procedures before medical record extraction could begin. As this study employed a retrospective design using anonymized medical record data, no direct patient contact or intervention was involved. Patient confidentiality was strictly maintained by removing all personal identifiers and ensuring that all data were analyzed anonymously.

## RESULT AND DISCUSSION

A total of 94 asthma outpatients were included in this study. The demographic and clinical characteristics of the study population are summarized in **Table 1**. Most patients were adults aged 25–59 years (87.2%), while elderly patients aged  $\geq 60$  years accounted for only 12.8%. This distribution indicates that asthma outpatient care at RSUD Kota Kendari predominantly involves individuals of productive age who remain actively engaged in daily activities and therefore require optimal asthma control to maintain functional capacity and quality of life. Treatment decisions should be guided by symptom control and exacerbation risk rather than age alone, supporting the relevance of focusing on disease control across all adult age groups (13).

Regarding healthcare utilization, most patients had 3–6 outpatient visits per year (75.5%), whereas approximately one-quarter had more than six visits annually, as shown in **Table 1**. Frequent outpatient visits may serve as an indirect marker of unstable asthma control, reflecting recurrent symptoms, suboptimal inhaler technique, or inadequate controller therapy. Repeated healthcare visits should prompt reassessment of symptom control, inhaler technique, adherence, and the need for treatment adjustment, including step-up therapy when indicated (13). Uncontrolled asthma is associated with increased healthcare utilization across outpatient, emergency, and inpatient settings (14,15)

Overuse of short-acting  $\beta_2$ -agonists (SABA) was identified in 14.9% of patients, while the majority did not exhibit SABA overuse (85.1%), as presented in **Table 1**. Although the proportion appears limited, this finding remains clinically significant. SABA overuse is a key marker of poor asthma control and increased risk of exacerbations and hospitalization, and therefore should trigger immediate evaluation and optimization of anti-inflammatory controller therapy (13). Excessive SABA use is strongly associated with adverse asthma outcomes, including exacerbations and hospitalization (4,16,17). These findings reinforce the importance of minimizing SABA reliance and prioritizing ICS-containing regimens (13).

During the observation period, 26.6% of patients experienced asthma exacerbations, and 23.4% had a history of hospitalization due to asthma attacks (**Table 1**). These proportions indicate the presence of a subgroup with unstable disease control and increased risk of severe outcomes. History of exacerbations as one of the strongest predictors of future exacerbations and recommends intensified monitoring and therapy adjustment in such patients (13). Exacerbations remain a central indicator of asthma severity and treatment effectiveness, while hospitalization represents a substantial clinical and economic burden (1,18,19).

The profile of bronchodilator and adjunctive therapy use is presented in **Table 2**. Most patients received inhaled corticosteroid–long-acting  $\beta_2$ -agonist (ICS–LABA) combinations as controller therapy, with salmeterol–fluticasone and budesonide–formoterol being the most frequently prescribed regimens. The predominance of ICS–LABA therapy highlights its role in controlling airway inflammation and providing sustained bronchodilation, thereby reducing symptom recurrence and the risk of asthma exacerbations (13,20,21). The continued use of SABA and SAMA–SABA combinations in a subset of patients suggests the presence of persistent symptoms or recurrent exacerbations requiring additional bronchodilation, which may reflect suboptimal disease control despite controller therapy (11). The relatively high use of systemic corticosteroids further indicates that a considerable proportion of patients experienced moderate-to-severe exacerbations requiring escalation of

**Table 1.** Demographic and Clinical Characteristics of Asthma Outpatients (n = 94)

| Variable                   | Category                   | n  | %    |
|----------------------------|----------------------------|----|------|
| Age                        | Adult (25–59 years)        | 82 | 87.2 |
|                            | Elderly ( $\geq 60$ years) | 12 | 12.8 |
| Outpatient visit frequency | 3–6 visits per year        | 71 | 75.5 |
|                            | >6 visits per year         | 23 | 24.5 |
| SABA overuse               | No overuse                 | 80 | 85.1 |
|                            | Overuse                    | 14 | 14.9 |
| Exacerbation outcome       | No exacerbation            | 69 | 73.4 |
|                            | Exacerbation               | 25 | 26.6 |
| Hospitalization outcome    | No                         | 72 | 76.6 |
|                            | Yes                        | 22 | 23.4 |
| Comorbidity                | Present                    | 17 | 18.1 |
|                            | Absent                     | 77 | 81.9 |

**Table 2.** Profile of bronchodilator and adjunct therapy use among asthma outpatients (n = 94)

| Drug class                                    | Drug name                                       | Dosage form / strength         | Route of administration     | n  | %    |
|-----------------------------------------------|-------------------------------------------------|--------------------------------|-----------------------------|----|------|
| ICS–LABA (Controller)                         | Salmeterol + fluticasone (Respitide®)           | Fixed-dose inhaler             | Inhalation                  | 88 | 93.6 |
|                                               | Budesonide + formoterol (Symbicort® Turbuhaler) | Fixed-dose inhaler             | Inhalation                  | 15 | 16.0 |
| SABA (Reliever)                               | Salbutamol                                      | Tablet / inhalation (2.5–5 mg) | Oral / inhalation           | 22 | 23.4 |
|                                               | Fenoterol (Berotec®)                            | Metered-dose inhaler           | Inhalation                  | 4  | 4.3  |
| SAMA–SABA combination (Reliever)              | Ipratropium + salbutamol (Combivent®)           | Nebulization / inhalation      | Inhalation                  | 62 | 66.0 |
|                                               | Ipratropium + salbutamol (Farbivent®)           | Injection                      | Intravenous / intramuscular | 12 | 12.8 |
| ICS (Additional controller)                   | Budesonide (Budesma® suspension)                | Nebulized suspension           | Inhalation                  | 18 | 19.1 |
| Systemic corticosteroid (during exacerbation) | Methylprednisolone                              | Tablet (4–16 mg) / injection   | Oral / injection            | 49 | 52.1 |

therapy, which may be influenced by poor adherence, inadequate dosing of ICS, or delayed step-up treatment (22,23).

The bivariate analysis demonstrated that several components of bronchodilator appropriateness were significantly associated with asthma exacerbations, as shown in **Table 3**. Patients who received inappropriate drug selection had a substantially higher proportion of exacerbations (46.2%) compared with those who received guideline-concordant therapy (19.1%). This association was statistically significant ( $p = 0.008$ ), with an odds ratio (OR) of 0.276 (95% CI: 0.104–0.735), indicating that appropriate drug selection is associated with the lower risk of exacerbation by approximately 72%. ICS–LABA–based controller therapy reduces the risk of asthma exacerbations and remains a cornerstone of asthma management (13). More importantly, this finding is directly supported by a retrospective cohort study conducted at a tertiary hospital in Saudi Arabia, in which only 24.4% of asthma patients were prescribed GINA Track 1 regimens (ICS-formoterol) while the majority (75.6%) received Track 2 (SABA-based) regimens; patients on guideline-concordant Track 1 therapy had significantly fewer exacerbations, with an

adjusted OR of 3.8 (95% CI: 1.12–13.2,  $p = 0.032$ ) favoring Track 1 over Track 2. Although the specific comparators differ (appropriateness of drug selection broadly versus a specific GINA-track comparison), both studies converge on the same conclusion that a substantial proportion of real-world asthma prescribing remains discordant with current guideline recommendations, and this discordance is consistently associated with a higher risk of exacerbation (24).

Patients who received inappropriate doses experienced exacerbations more frequently (51.5%) than those receiving appropriate doses (13.1%). This association was highly significant ( $p < 0.001$ ), with an OR of 0.142 (95% CI: 0.052–0.390), suggesting that patients treated with appropriate dosing had an approximately 86% lower risk of exacerbation. Adequate dosing of inhaled corticosteroids is essential to suppress chronic airway inflammation, whereas underdosing may lead to persistent inflammation and recurrent exacerbations (7,10,13). A comparable direction of association was reported in a real-world retrospective, observational, multicenter study conducted in Malaysia, which found that suboptimal reliever-to-controller balance was associated with significantly lower odds of achieving at

**Table 3.** Bivariate analysis of factors associated with asthma exacerbation among outpatients (n = 94)

| Variable                                                  | Category               | Exacerbation<br>n (%) | No exacerbation<br>n (%) | p-value | OR    | 95% CI           |
|-----------------------------------------------------------|------------------------|-----------------------|--------------------------|---------|-------|------------------|
| Drug selection<br>(Track 1 GINA<br>stepwise ICS-LABA)     | Inappropriate          | 12 (46.2)             | 14 (53.8)                | 0.008   | 0.27  | 0.104–<br>0.735  |
|                                                           | Appropriate            | 13 (19.1)             | 55 (80.9)                |         |       |                  |
| Dosage                                                    | Inappropriate          | 17 (51.5)             | 16 (48.5)                | <0.001  | 0.14  | 0.052–<br>0.390  |
|                                                           | Appropriate            | 8 (13.1)              | 53 (86.9)                |         |       |                  |
| Inhalation route                                          | Inappropriate          | 11 (73.3)             | 4 (26.7)                 | <0.001  | 0.07  | 0.022–<br>0.282  |
|                                                           | Appropriate            | 14 (17.7)             | 65 (82.3)                |         |       |                  |
| Appropriateness of<br>therapy escalation<br>(add-on LAMA) | Inappropriate          | 23 (46.0)             | 27 (54.0)                | <0.001  | 17.89 | 3.898–<br>82.091 |
|                                                           | Appropriate            | 2 (4.5)               | 42 (95.5)                |         |       |                  |
| SABA use                                                  | Overuse                | 10 (71.4)             | 4 (28.6)                 | <0.001  | 10.83 | 2.987–<br>39.288 |
|                                                           | No overuse             | 15 (18.8)             | 65 (81.3)                |         |       |                  |
| Age                                                       | Elderly (≥60<br>years) | 5 (41.7)              | 7 (58.3)                 | 0.206   | 2.21  | 0.632–<br>7.755  |
|                                                           | Adult (25–59<br>years) | 20 (24.4)             | 62 (75.6)                |         |       |                  |
| Outpatient visit<br>frequency                             | >6 visits/year         | 4 (17.4)              | 19 (82.6)                | 0.250   | 0.50  | 0.152–<br>1.652  |
|                                                           | 3–6 visits/year        | 21 (29.6)             | 50 (70.4)                |         |       |                  |
| Comorbidity                                               | Present                | 6 (35.3)              | 11 (64.7)                | 0.370   | 1.66  | 0.542–<br>5.111  |
|                                                           | Absent                 | 19 (24.7)             | 58 (75.3)                |         |       |                  |

least partly controlled asthma (OR 0.42; 95% CI: 0.27–0.67) and higher odds of severe exacerbation among patients with inadequate controller dosing regimens (25). Although the magnitude of association differs likely reflecting differences in sample size, population characteristics, and the specific definition of dosing appropriateness used both studies support the same underlying conclusion that suboptimal matching of ICS dose to disease severity or reliever use pattern is consistently associated with a greater risk of exacerbation in real-world asthma populations, particularly in the Asian regional context relevant to the present study population.

The inhalation route was significantly associated with the risk of asthma exacerbation. Patients who did not receive bronchodilator therapy via inhalation experienced exacerbations in 73.3% of cases, whereas only 17.7% of patients treated using the inhalation route developed exacerbations. This association was statistically significant ( $p < 0.001$ ), with an odds ratio of

0.078 (95% CI: 0.022–0.282), demonstrating a strong protective effect of inhalation therapy. Inhaled drug delivery ensures optimal deposition in the airways and enhances both anti-inflammatory and bronchodilatory effects, while non-inhalation use may lead to inadequate asthma control (9,13,26).

Therapy escalation with add-on long-acting muscarinic antagonists (LAMA) showed a very strong association with exacerbation risk. Nearly all patients who experienced exacerbations but did not receive add-on LAMA therapy had exacerbation events (95.5%), compared with 54.0% among patients who received appropriate therapy escalation. This association was highly significant ( $p < 0.001$ ), with an odds ratio of 17.889 (95% CI: 3.898–82.091), indicating that patients who did not undergo therapy escalation with LAMA had an almost 18-fold higher risk of exacerbation. The observed association can be explained by the pharmacological action of LAMA on airway smooth muscle. LAMA agents such as tiotropium act as competitive antagonists

at muscarinic acetylcholine receptors on airway smooth muscle, predominantly blocking the M3 subtype, which mediates acetylcholine-induced bronchoconstriction and mucus gland secretion. Unlike short-acting muscarinic antagonists, LAMAs exhibit kinetic selectivity, dissociating slowly from M3 receptors while dissociating more rapidly from the presynaptic M2 autoreceptors that normally inhibit further acetylcholine release; this differential dissociation allows sustained M3 blockade with a once-daily dosing profile and confers a bronchodilator effect that persists over 24 hours. Beyond acute bronchodilation, sustained M3 blockade is also thought to reduce airway mucus hypersecretion and may attenuate cholinergically-mediated airway smooth muscle remodeling with chronic use, both of which are relevant to reducing exacerbation frequency in patients with persistent airway hyperresponsiveness despite ICS-LABA therapy. Through this mechanism, LAMA addresses a pathway of bronchoconstriction and mucus hypersecretion that ICS-LABA therapy alone does not fully target, consistent with the higher exacerbation rates observed among patients who did not receive escalation in the present study.

This finding should nevertheless be interpreted with caution given the wide confidence interval, which likely reflects small cell counts within this retrospective sample. A national real-world registry study of add-on LAMA prescribing patterns found that physicians preferentially escalate therapy with LAMA in older patients with uncontrolled asthma, lower FEV<sub>1</sub>, and more frequent severe exacerbations (27), a pattern that suggests confounding by indication may partly explain the strength of the bivariate association observed in the present study, since patients who did not receive LAMA escalation despite clinical need for it may represent a subgroup with unrecognized or undertreated severe disease. LAMA is recommended for patients who remain symptomatic or experience recurrent exacerbations despite receiving ICS-LABA therapy (13). Failure to implement appropriate therapy escalation may therefore contribute substantially to persistent disease instability and recurrent exacerbations (11,28,29).

Overuse of short-acting  $\beta_2$ -agonists (SABA) was one of the strongest predictors of exacerbation. Patients

with SABA overuse experienced exacerbations in 71.4% of cases, compared with only 18.8% among those without overuse. This association was highly significant ( $p < 0.001$ ), with an OR of 10.833 (95% CI: 2.987–39.288), indicating that patients with SABA overuse were more than ten times more likely to experience exacerbations. This direction of association is consistent with a recent systematic review and meta-analysis of 27 studies, which reported that SABA overuse was associated with a significantly increased risk of acute exacerbations, with pooled risk ratios of 1.88 (95% CI: 1.43–2.47) in retrospective cohort studies and 2.23 (95% CI: 1.04–4.77) in cross-sectional studies (4). Similarly, a large observational cohort study involving more than 115,000 asthma patients reported adjusted incidence rate ratios of 1.36 (95% CI: 1.18–1.56) and 1.32 (95% CI: 1.27–1.38) across two provincial cohorts (6). Although the direction of effect in the present study is concordant with these larger studies, the magnitude of association observed here is considerably higher, which may be attributable to the smaller sample size, the retrospective single-center design, and the lack of adjustment for confounding variables inherent to bivariate analysis. Predictors of excessive SABA use identified in a retrospective analysis of a Polish prescription database further support the clinical relevance of controller therapy coverage in mitigating SABA overuse risk (12). Excessive SABA use reflects inadequate anti-inflammatory control and is strongly associated with poor asthma outcomes (4,16,17).

In contrast, age category, visit frequency, and comorbidity status were not significantly associated with exacerbation outcomes ( $p > 0.05$ ), suggesting that exacerbation risk was primarily driven by pharmacotherapy-related factors rather than demographic characteristics alone.

Comparable trends were also observed for hospitalization outcomes (Table 4). Inappropriate controller selection was associated with a substantially higher hospitalization rate (46.2%) compared with appropriate therapy (14.7%) ( $p = 0.001$ ), with an odds ratio of 0.201 (95% CI: 0.072–0.559), indicating an approximately 80% reduction in hospitalization risk with appropriate drug selection. Inappropriate dosing showed a similarly strong association, as nearly half of

**Table 4.** Bivariate analysis of factors associated with asthma-related hospitalization among outpatients (n = 94)

| Variable                                                  | Category               | Hospitalization<br>n (%) | No<br>hospitalization n<br>(%) | p-<br>value | OR    | 95%<br>CI        |
|-----------------------------------------------------------|------------------------|--------------------------|--------------------------------|-------------|-------|------------------|
| Drug selection<br>(Track 1 GINA stepwise<br>ICS-LABA)     | Inappropriate          | 12 (46.2)                | 14 (53.8)                      | 0.001       | 0.20  | 0.072–<br>0.559  |
|                                                           | Appropriate            | 10 (14.7)                | 58 (85.3)                      |             |       |                  |
| Dosage                                                    | Inappropriate          | 16 (48.5)                | 17 (51.5)                      | <0.001      | 0.12  | 0.039–<br>0.343  |
|                                                           | Appropriate            | 6 (9.8)                  | 55 (90.2)                      |             |       |                  |
| Inhalation route                                          | Inappropriate          | 11 (73.3)                | 4 (26.7)                       | <0.001      | 0.06  | 0.016–<br>0.218  |
|                                                           | Appropriate            | 11 (13.9)                | 68 (86.1)                      |             |       |                  |
| Appropriateness of<br>therapy escalation (add-on<br>LAMA) | Inappropriate          | 20 (40.0)                | 30 (60.0)                      | <0.001      | 14.00 | 3.040–<br>64.473 |
|                                                           | Appropriate            | 2 (4.5)                  | 42 (95.5)                      |             |       |                  |
| SABA use                                                  | Overuse                | 10 (71.4)                | 4 (28.6)                       | <0.001      | 14.17 | 3.815–<br>52.605 |
|                                                           | No overuse             | 12 (15.0)                | 68 (85.0)                      |             |       |                  |
| Age group                                                 | Elderly (≥60<br>years) | 4 (33.3)                 | 8 (66.7)                       | 0.384       | 1.78  | 0.480–<br>6.583  |
|                                                           | Adult (25–59<br>years) | 18 (22.0)                | 64 (78.0)                      |             |       |                  |
| Outpatient visit frequency                                | >6 visits/year         | 4 (17.4)                 | 19 (82.6)                      | 0.433       | 0.62  | 0.186–<br>2.065  |
|                                                           | 3–6 visits/year        | 18 (25.4)                | 53 (74.6)                      |             |       |                  |
| Comorbidity                                               | Present                | 6 (35.3)                 | 11 (64.7)                      | 0.201       | 2.08  | 0.667–<br>6.482  |
|                                                           | Absent                 | 16 (20.8)                | 61 (79.2)                      |             |       |                  |

patients receiving non-recommended doses required hospitalization (48.5%), compared with only 9.8% among those receiving appropriate doses ( $p < 0.001$ ; OR = 0.116; 95% CI: 0.039–0.343).

Use of inhalation therapy showed a particularly strong protective association against hospitalization. Patients who did not receive bronchodilators via inhalation experienced hospitalization in 73.3% of cases, whereas hospitalization occurred in only 13.9% of patients treated with inhaled therapy. This association was highly significant ( $p < 0.001$ ), with an odds ratio of 0.059 (95% CI: 0.016–0.218), indicating that inhaled therapy reduced hospitalization risk by more than 90%. These findings underscore the essential role of inhaled treatment in preventing severe asthma outcomes (10,13).

Therapy escalation with add-on LAMA was also strongly associated with hospitalization risk. Patients who did not undergo appropriate therapy escalation based on their clinical profile had a markedly higher likelihood of hospitalization (OR = 14.000; 95% CI: 3.040–64.473;  $p < 0.001$ ). This finding reflects the clinical impact

of failing to intensify treatment, particularly the omission of LAMA in patients with recurrent exacerbations despite ongoing controller therapy, as recommended in stepwise asthma management strategies (8,27). Overuse of SABA remained a strong predictor of hospitalization. Patients with SABA overuse had a hospitalization rate of 71.4%, compared with 15.0% among patients without overuse ( $p < 0.001$ ), with an OR of 14.167 (95% CI: 3.815–52.605). Excessive reliance on SABA masks ongoing airway inflammation and substantially increases the risk of severe exacerbations requiring inpatient care (5,6,30).

Conversely, age, visit frequency, and comorbidity status were not significantly associated with hospitalization outcomes, reinforcing that severe asthma outcomes are more strongly influenced by the appropriateness of pharmacological management rather than demographic factors. These findings collectively emphasize that strict adherence to guideline-based, patient-tailored asthma therapy—particularly avoidance of SABA overuse, appropriate dosing, correct

inhalation route, and timely therapy escalation is essential to reduce exacerbations and hospitalization in outpatient asthma care.

## CONCLUSION

This study demonstrates that asthma outcomes among outpatients at RSUD Kota Kendari are primarily influenced by treatment-related factors rather than demographic characteristics. Appropriate use of inhaled controller therapy, avoidance of excessive SABA use, correct inhalation delivery, and timely therapy escalation with add-on LAMA were strongly associated with lower risks of exacerbation and hospitalization, underscoring the importance of stepwise asthma management in accordance with the GINA 2024 recommendations.

Despite these findings, the retrospective design and single-center setting limit the generalizability of the results, and the use of bivariate analysis precludes adjustment for potential confounding factors. Future prospective and multicenter studies with multivariable approaches are needed to better elucidate independent predictors of poor asthma outcomes. From a practical perspective, these findings highlight the need for

continuous evaluation of asthma control, optimization of inhaled therapy, and appropriate therapy escalation to improve long-term clinical outcomes and reduce the burden of asthma-related complications.

## CONFLICT OF INTEREST

The authors have no conflicts of interest regarding this investigation.

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