A Cross-Sectional Multicentre Study of Prevalence of MDI Salbutamol Overuse and Associated Factors among Asthma Patients in Kedah

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Abstract

Introduction: Asthma affected over 1.4 million adults in Malaysia. The Global Initiative for Asthma (GINA) no longer recommended short-acting β2-agonist (SABA) monotherapy, as it did not reduce airway inflammation. SABA overuse, defined as the collection of more than two SABA inhalers per year, has been linked to an increased risk of exacerbations and hospitalisations.

Objective: This study aimed to investigate the prevalence of salbutamol metered dose inhaler (MDI) overuse, identify its associated factors, and assess its outcomes in asthma patients.

Methods: An observational, cross-sectional study was conducted at three health clinics and one hospital in Kedah. Adult asthma patients, diagnosed for at least one year and using both MDI salbutamol and inhaled corticosteroids (ICS) were included. Logistic regression analysis was applied to estimate the risk factors and poor outcomes associated with salbutamol overuse.

Results: A total of 252 patients were included. The prevalence of MDI salbutamol overuse was 42.1%. Statistically significant factors associated with overuse included family history of asthma (AOR = 2.26, 95% CI: 1.23–4.17, p = 0.009) and ACT score, with not well-controlled asthma (AOR = 2.53, 95% CI: 1.20–5.34, p = 0.003) and very poorly controlled asthma (AOR = 4.52, 95% CI: 1.58–12.92, p = 0.003). SABA overuse was associated with 2.19 times the odds of poor outcomes (95% CI = 1.26–3.80, p = 0.005).

Conclusion: The prevalence of MDI salbutamol overuse was nearly half of the patients at our institutions. Key factors associated with SABA overuse included poorly controlled asthma and family history of asthma. SABA overuse was associated with higher risk of exacerbations and/or hospitalisations, emphasising the need for prompt interventions.

Keywords: Short-Acting β2-agonist overuse, asthma, exacerbations, asthma control, Malaysia

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Introduction

The National Health and Morbidity Survey 2023 reported that over 1.4 million adults in Malaysia were living with asthma, with 8% experiencing more than three exacerbations in the past year (1). Asthma was characterised by chronic airway inflammation and hyperresponsiveness, leading to symptoms such as wheezing, dyspnoea, cough and chest tightness (2). Since 2019, the Global Initiative for Asthma (GINA) has advised against the use of short-acting β2-agonist (SABA) monotherapy for asthma management due to its inability to reduce airway inflammation or prevent exacerbations (2, 3). GINA guidelines for adult asthma management were structured into two treatment tracks (2). In Track 1, the

preferred therapy at Steps 1 and 2 was an as-needed combination of inhaled corticosteroids (ICS) and Formoterol (2). For Steps 3 to 5, the regular use of ICS and Formoterol was recommended, as maintenance therapy and for symptom relief, which was commonly referred to as maintenance-and-reliever therapy (MART) (2). In Track 2, patients at Step 1 could be prescribed an as-needed combination of SABA and low-dose ICS (2). For Steps 2 to 5, the management strategy involved regular ICS as maintenance therapy, with either SABA alone or an ICS-SABA combination as a reliever. (2)

SABA overuse, defined as the use of more than two canisters (200 doses) annually, which is equivalent to approximately one puff per day, has been associated with adverse clinical outcomes (2, 4). SABA overuse could lead to beta-receptor downregulation and reduced sensitivity, contributing to suboptimal asthma control (4). Additionally, patients who overused SABA often underused ICS, leaving underlying airway inflammation untreated (4). Consequently, SABA overuse has been linked to increased exacerbations, hospitalisations, higher healthcare costs, and mortality, regardless of asthma severity or GINA Steps classification (3–5). Frequent use of oral corticosteroids for exacerbations further increased the risk of systemic side effects, such as type two diabetes mellitus, hypertension, osteoporosis, and cataracts (3). Moreover, SABA overuse has environmental implications due to the carbon emissions associated with metered dose inhalers (MDIs) (6).

In Malaysia, medications at the government healthcare facilities were fully subsidised. However, due to the high costs of budesonide-formoterol combination therapy that is recommended by GINA, its usage remain limited. Instead, the primary reliever medication in public healthcare setting was MDI salbutamol, which was dispensed on an exchange basis or purchased over the counter at retail pharmacies. Observationally, some asthma patients frequently collected MDI salbutamol, with refill intervals as short as biweekly or monthly. Therefore, this study was conducted to investigate the prevalence of MDI salbutamol overuse among asthma patients, to identify factors associated with such overuse and to evaluate the clinical outcomes in patients with MDI salbutamol overuse within the study setting. By identifying the characteristics and risk factors associated with SABA overuse, early interventions can be implemented during patient encounters to prevent poor asthma outcomes in the future.

Methods

Study Design

A multicentre, observational, cross-sectional study was conducted from 1 June 2023 to 29 February 2024 at three health clinics and one hospital in Kedah, Malaysia (Bandar Sungai Petani Health Clinic, Taman Intan Health Clinic, Bandar Alor Setar Health Clinic and Sultan Abdul Halim Hospital). This study was registered with the National Medical Research Register (NMRR ID-23-01351-K7G) and received ethics approval from the Medical Research & Ethics Committee (MREC) of the Ministry of Health Malaysia.

Study Population

Patients aged 18 years and above who were using MDI salbutamol with regular ICS and had been diagnosed with asthma for at least one year were recruited. Exclusion criteria included patients diagnosed with chronic obstructive pulmonary disease (COPD), pregnant women, patients with unstable psychiatric disorders, those who did not understand Malay or English, and those who followed up at other institutions.

The sample size was calculated using the prevalence data from a study conducted in Taiwan, which included an exclusively Asian population. At the time of proposal development, the SABA Use IN Asthma (SABINA) III study in Malaysia had not yet been published (7,8). The prevalence of SABA overuse in Taiwan was reported as 15.9% (7). Using a precision of 5%, a 95% confidence interval, and accounting for an estimated 20% patient loss, a total of 248 subjects (62 participants per centre) were required for this study (9).

Data Collection

At the outpatient pharmacy registration counters of participating centres, all new prescriptions containing MDI salbutamol and ICS issued between 1 June 2023 and 29 February 2024 were referred to trained investigators for screening based on inclusion and exclusion criteria. Eligible patients or their

caregivers were then invited to the counselling room, where the study was briefly explained and further eligibility assessment was conducted. A patient information sheet was provided and explained to the patients or their representatives, allowing them to review it at home. Patients could participate immediately or schedule a meeting on another day if additional time was needed for consideration. After confirming the eligibility, patients who agreed to participate were asked to sign an informed consent form. Participation was entirely voluntary, and withdrawal was permitted at any time during the study period.

Data were collected through face-to-face interviews with recruited participants and/or caregivers by trained data collectors. Information obtained during the interview included smoking status, asthma triggers, duration of asthma diagnosis, family history of asthma, number of asthma-related exacerbations and/or hospitalisations within the past year, comorbidities, concurrent medications, Asthma Control Test (ACT) score, Reliever Reliance Test (RRT) score, inhaler technique score, compliance to ICS, number of MDI salbutamol used in the past year (including those obtained via prescription and over-the-counter from other healthcare facilities), and the numbers of MDI salbutamol doses used within the past one week (2, 10, 11). Medical records, retrieved from the electronic medical record system or hard-copy patient files, were reviewed to obtain data on patients' demographic characteristics, GINA classification, duration of asthma diagnosis, allergy status, number of asthma-related exacerbations and/or hospitalisations in the past year, concurrent medications, comorbidities, and the type of ICS prescribed. Data collected were documented in an access-restricted electronic data collection form.

There was no follow-up for participants. In cases of missing data or discrepancies between interview data and medical records, patients or their caretakers were contacted via telephone for clarification.

Definitions

The prevalence of MDI salbutamol overuse, defined as the percentage of patients who obtained more than two canisters of MDI salbutamol per year, was calculated (2, 4). Additionally, the percentage of patients with high RRT scores (18–25) and the proportion of patients using more than two doses of MDI salbutamol per week for any reason were assessed to evaluate their alignment with the prevalence of MDI salbutamol overuse (11, 12).

The ACT score was measured using a validated questionnaire from the Malaysian Respiratory Medication Therapy Adherence Clinic (RMTAC) Protocol: Asthma / COPD (Adult & Paediatric) and the GINA Strategy Report during investigator-patient encounter (2, 10). The ACT score was categorised as follows: 20–25 (well-controlled asthma), 16–19 (not well-controlled asthma) and 5–15 (very poorly controlled asthma) (2, 10). Inhaler technique was evaluated using assessment forms in RMTAC Protocol during patient interview, where a score of 6 indicated good technique, 4–5 was considered satisfactory and 0–3 was classified as poor technique (10). The RRT score was assessed using a validated questionnaire (11) with scores of 18–25 indicating high risk of reliever over-reliance, 11–17 classified as medium risk, and ≤10 represented low risk (11). Compliance to ICS was determined based on self-reported regular use of ICS therapy.

Poor outcomes were defined as any asthma exacerbation and/or hospitalisation due to asthma in past one year. An exacerbation was characterised as an asthma-related event that required outpatient management by general practitioners, emergency departments, or other outpatient units, such as health clinics, necessitating treatment with nebulisation and/or systemic corticosteroids without hospitalisation. This information was obtained from patient-reported histories. Additionally, medical records and the Pharmacy Information Systems were reviewed to verify the history of treatments for exacerbations, including nebulisation, systemic corticosteroid use and hospital referrals.

A list of risk factors associated with MDI salbutamol overuse and poor outcomes of asthma was ascertained through literature review, which included age, gender, race, allergy status, working status, GINA Step, smoking status, education level, years since asthma diagnosis, family history, comorbidities, compliance with ICS, asthma control, and inhaler technique score.

Data Analysis

Descriptive data were presented as frequencies and percentages, means with standard deviations (SD) or medians with interquartile ranges (IQR), unless otherwise specified. Simple logistic regression was conducted to estimate the odds ratio (OR) for potential risk factors associated with MDI salbutamol overuse and poor outcomes of asthma. Variables with p-values < 0.25 in the simple logistic regression analysis were selected as candidate predictors. These variables were subsequently entered into a multiple logistic regression model using a stepwise approach (forward and backward likelihood ratio). Non-significant variables were automatically excluded during the stepwise selection process. Only variables with p-values < 0.05 were retained in the final model. All statistical analyses were performed using Statistical Package for Social Sciences (SPSS) version 25.0. The adjusted OR (AOR) with 95% confidence interval (CI) was presented. A p value less than 0.05 was considered statistically significant.

Results

A total of 280 patients met the eligibility criteria for the study, but 27 patients declined participation. One participant withdrew consent during the study, resulting in the data exclusion. A total of 252 subjects were successfully recruited. Most patients (83.0%) were classified under GINA Steps 1 and 2 based on a review of patients' medical records and the prescribed treatments. The mean age of patients was 52.9 years (SD 15.0), with female comprising the majority (70.2%) (Table 1).

Table 1: Demographics and characteristics of patients (n=252)

Characteristics	n (%)
Age, mean (SD)	52.9 (15.0)
Gender	
Female	177 (70.2)
Male	75 (29.8)
Race	
Malay	193 (76.6)
Chinese	20 (7.9)
Indian	37 (14.7)
Other	2 (0.8)
Allergy status	
No	204 (81.0)
Yes	48 (19.0)
Working status	
No	140 (55.6)
Yes	112 (44.4)
GINA Step	
1	39 (15.5)
2	170 (67.5)
3	38 (15.1)
4	5 (2.0)
5	0 (0.0)
Smoking status	
Non-smoker	173 (68.7)
Current smoker	8 (3.2)
Second hand smoker	55 (21.8)
Ex-smoker	16 (6.3)
Education level	
None	7 (2.8)
Primary	52 (20.6)
Secondary	128 (50.8)
Tertiary	65 (25.8)
Years of diagnosis of asthma, mean (SD)	21.4 (17.6)
Family history	
No	108 (42.9)
Yes	144 (57.1)

Comorbidities	
No	49 (19.4)
1 comorbid	76 (30.2)
≥2 comorbidities	127 (50.4)
Compliance to ICS	
Yes	209 (82.9)
No	43 (17.1)
Asthma Control Test	
Well controlled	178 (70.6)
Not well controlled	48 (19.0)
Very poorly controlled	26 (10.3)
Inhaler technique score	
Good	124 (49.2)
Satisfactory	92 (36.5)
Poor	36 (14.3)
Reliever Reliance Test	
Low risk	79 (31.3)
Medium risk	61 (24.2)
High risk	112 (44.4)
MDI salbutamol Use ⩾3 times a week for any reason	
No	178 (70.6)
Yes	74 (29.4)
Types of ICS	
MDI budesonide	196 (77.8)
MDI beclomethasone	1 (0.4)
MDI fluticasone	24 (9.5)
Fluticasone 250mcg + salmeterol 50mcg Accuhaler	31 (12.3)
Number of MDI salbutamol canisters / year, median (IQR)	2 (1-4)
Number of MDI salbutamol canisters / year	
0	4 (1.6)
1-2	142 (56.3)
3-5	61 (24.2)
6-9	25 (9.9)
≥10	20 (7.9)
MDI salbutamol overuse (⩾3 canisters / year)	
No	146 (57.9)
Yes	106 (42.1)
Poor outcomes (Asthma exacerbation and/or hospitalisations in the past one year)	
No	146 (57.9)
Yes	106 (42.1)

Abbreviation: GINA = The Global Initiative for Asthma; ICS = inhaled corticosteroid; MDI = metered dose inhaler; SD = standard deviation; IQR = interquartile range.

Prevalence of MDI Salbutamol Overuse

The prevalence of MDI salbutamol overuse was 42.1%. Additionally, 44.4% of patients had high RRT scores (18–25), and 29.4% reported using more than two doses per week for any reason. The median number of MDI salbutamol canisters collected annually was two (IQR: 1–4).

Associated Factors for MDI Salbutamol Overuse

Variables entered into the multiple logistic regression model included GINA Step, smoking status, education level, years of diagnosis of asthma, family history of asthma, ICS compliance, ACT score, and inhaler technique score. Significant factors associated with MDI salbutamol overuse were family history of asthma (AOR = 2.27, 95% CI: 1.23–4.17, p = 0.009) and ACT score, with not well-controlled asthma (AOR = 2.53, 95% CI: 1.20–5.34, p = 0.003) and very poorly controlled asthma (AOR = 4.52, 95% CI: 1.58–12.92, p = 0.003). These results were summarised in Tables 2 and 3.

Table 2: Baseline characteristics of study groups based on MDI salbutamol overuse (total n=252)

Characteristics	Overuse	
	Yes, n (%) / mean ± SD (n=106)	No, n (%) / mean ± SD (n=146)
Age, mean (SD)	53.1 ± 15.6	52.8 ± 14.6
Gender		
Female	71 (40.1)	106 (59.9)
Male	35 (46.7)	40 (53.3)
Race		
Malay	82 (42.5)	111 (57.5)
Non-Malay	24 (40.7)	35 (59.3)
Allergy status		
No	83 (40.7)	121 (59.3)
Yes	23 (47.9)	25 (52.1)
Working status		
No	59 (42.1)	81 (57.9)
Yes	47 (42.0)	65 (58.0)
GINA Step		
1	15 (38.5)	24 (61.5)
2	64 (37.6)	106 (62.4)
3	24 (63.2)	14 (36.8)
4	3 (60.0)	2 (40.0)
Smoking status		
Non-smoker	64 (37.0)	109 (63.0)
Current smoker	6 (75.0)	2 (25.0)
Second hand smoker	27 (50.9)	26 (49.1)
Ex-smoker	9 (50.0)	9 (50.0)
Education level		
None	3 (42.9)	4 (57.1)
Primary	22 (42.3)	30 (57.7)
Secondary	59 (46.1)	69 (53.9)
Tertiary	22 (33.8)	43 (66.2)
Years of diagnosis of asthma, mean (SD)	25.0 ± 19.2	18.8 ± 15.9
Family history		
No	33 (30.6)	75 (69.4)
Yes	73 (50.7)	71 (49.3)
Comorbidities		
No	21 (42.9)	28 (57.1)
1 comorbid	30 (39.5)	46 (60.5)
≥2 comorbidities	55 (43.3)	72 (56.7)
Compliance to ICS		
Yes	79 (37.8)	130 (62.2)
No	27 (62.8)	16 (37.2)
Asthma Control Test		
Well controlled	54 (30.3)	124 (67.7)
Not well controlled	32 (66.7)	16 (33.3)
Very poorly controlled	20 (76.9)	6 (23.1)
Inhaler technique score		
Good	46 (37.1)	78 (62.9)
Satisfactory	37 (40.2)	55 (59.8)
Poor	23 (63.9)	13 (36.1)

Abbreviation: SD = standard deviation; GINA = The Global Initiative for Asthma; ICS = inhaled corticosteroid; MDI = metered dose inhaler

Table 3: Factors associated with MDI salbutamol overuse using multiple logistic regression (n=252)

Characteristics	Simple Logistic Regression			Multiple Logistic Regression[a]		
	(b)	Crude OR (95% CIs)	p-value	(b)	Adjusted OR (95% CIs)	p-value
Age	0.001	1.00 (0.98-1.01)	0.909			
Gender						
Female	0	1.00				
Male	0.27	1.31 (0.76-2.25)	0.336			
Race						
Malay	0	1.00				
Non-Malay	-0.07	0.93 (0.51-1.68)	0.805			
Allergy status						
No	0	1.00				
Yes	0.29	1.34 (0.71-2.52)	0.362			
Working status						
No	0	1.00				
Yes	-0.01	0.99 (0.60-1.64)	0.977			
GINA Step						
1	0	1.00				
2	-0.04	0.97 (0.47-1.98)	0.033			
3	1.01	2.74 (1.09-6.90)				
4	0.86	2.40 (0.36-16.08)				
Smoking status						
Non-smoker	0	1.00				
Current smoker	1.63	5.11 (1.00-26.07)	0.072			
Second hand smoker	0.57	1.77 (0.95-3.29)				
Ex-smoker	0.53	1.70 (0.64-4.51)				
Education level						
None	0	1.00				
Primary	-0.02	0.98 (0.20-4.82)	0.142			
Secondary	0.13	1.14 (0.25-5.30)				
Tertiary	-0.38	0.68 (0.14-3.32)				
Years of diagnosis of asthma	0.02	1.02 (1.01-1.04)	0.006			
Family history						
No	0	1.00		0	1.00	
Yes	0.85	2.34 (1.38-3.95)	**0.001**	0.82	2.27 (1.23-4.17)	**0.009**
Comorbidities						
No	0	1.00				
1 comorbid	-0.14	0.87 (0.42-1.80)	0.860			
≥2 comorbidities	0.02	1.02 (0.52-1.98)				

Compliance to ICS						
Yes	0	1.00				
No	1.02	2.78 (1.41-5.47)	0.003			
Asthma Control Test						
Well controlled	0	1.00		0	1.00	
Not well controlled	1.52	4.59 (2.33-9.06)	**<0.001**	0.93	2.53 (1.20-5.34)	**0.003**
Very poorly controlled	2.03	7.65 (2.91-20.12)		1.51	4.52 (1.58-12.92)	
Inhaler technique score						
Good	0	1.00	0.019			
Satisfactory	0.13	1.14 0.66-1.98)				
Poor	1.10	3.00 (1.39-6.49)				

[a] Enter Multiple Logistic Regression model was applied.
Constant -2.740
Multicollinearity and interaction term were checked and not found.
Hosmer and Lemeshow Test, p=0.973; Classification table 75%; Area under ROC curve 0.813 (95%CI:0.76-0.87)
Abbreviation: b = estimated coefficients; OR = odd ratio; 95%CI = 95% confidence interval; SD = standard deviation; GINA = The Global Initiative for Asthma; ICS = inhaled corticosteroid; MDI = metered dose inhaler

Associated Factors of Poor Outcomes of Asthma

In the past year, 106 patients (42.1%) experienced exacerbations and/or hospitalisations due to asthma. Variables entered into the multiple logistic regression model included age, working status, GINA Step, comorbidities, ICS compliance, ACT, and MDI salbutamol overuse. Factors significantly associated with poor asthma outcomes were age (AOR = 0.98, 95% CI: 0.96–0.99, p = 0.039), GINA Step (AOR = 4.76, 95% CI: 1.79–12.63, p = 0.004), presence of comorbidity (AOR = 0.35, 95% CI: 0.16–0.76, p = 0.016), and MDI salbutamol overuse (AOR = 2.19, 95% CI: 1.26–3.80, p = 0.005). The results were presented in Tables 4 and 5.

Table 4: Baseline characteristics of study groups based on reported poor outcomes of asthma (hospitalisations and/or exacerbations) within a year (n=252)

Characteristics	Asthma's Poor Outcomes	
	Yes, n (%) / mean ± SD (n=106)	No, n (%) / mean ± SD (n=146)
Age, mean (SD)	51.5 ± 15.5	54.1 ± 14.5
Gender		
Female	34 (45.3)	105 (59.3)
Male	72 (40.7)	41 (54.7)
Race		
Malay	84 (43.5)	109 (56.5)
Non-Malay	22 (37.3)	37 (62.7)
Allergy status		
No	84 (41.2)	120 (58.8)
Yes	22 (45.8)	26 (54.2)
Working status		
No	50 (35.7)	90 (64.3)
Yes	56 (50.0)	56 (50.0)
GINA Step		
1	12 (30.8)	27 (69.2)
2	66 (38.8)	104 (61.2)
3 & 4	28 (65.1)	15 (34.9)
Smoking status		
Non-smoker	68 (39.3)	105 (60.7)
Current smoker	6 (75.0)	2 (25.0)
Second hand smoker	23 (43.4)	30 (56.6)
Ex-smoker	9 (50.0)	9 (50.0)
Education level		
None	3 (45.9)	4 (57.1)
Primary	23 (44.2)	29 (55.8)
Secondary	56 (43.8)	72 (56.3)
Tertiary	24 (36.9)	41 (63.1)
Years of diagnosis of asthma, mean (SD)	21.3 ± 17.6	21.5 ± 17.7
Family history		
No	43 (39.8)	65 (60.2)
Yes	63 (43.8)	81 (56.3)
Comorbidities		
No	27 (55.1)	22 (44.9)
1 comorbid	22 (28.9)	54 (71.1)
≥2 comorbidities	57 (44.9)	70 (55.1)
Compliance to ICS		
Yes	82 (39.2)	127 (60.8)
No	24 (55.8)	19 (44.2)
Asthma Control Test		
Well controlled	63 (35.4)	115 (64.6)
Not well controlled	25 (52.1)	23 (47.9)
Very poorly controlled	18 (69.2)	8 (30.8)
Inhaler technique score		
Good	48 (38.7)	76 (61.3)
Satisfactory	44 (47.8)	48 (52.2)
Poor	14 (38.9)	22 (61.1)
SABA Overuse		
No	50 (34.2)	96 (65.8)
Yes	56 (52.8)	50 (47.2)

Abbreviation: SD = standard deviation; GINA = The Global Initiative for Asthma; ICS = inhaled corticosteroid; MDI = metered dose inhaler

Table 5: Factors associated with reported poor outcomes of asthma (hospitalisations and/or exacerbations) within a year using a multiple logistic regression (n=252)

Characteristics	Simple Logistic Regression			Multiple Logistic Regression[a]		
	(b)	Crude OR (95% CIs)	p-value	(b)	Adjusted OR (95% CIs)	p-value
Age	-0.02	0.98 (0.96-0.99)	**0.008**	-0.02	0.98 (0.96-0.99)	**0.039**
Gender						
Female	0	1.00				
Male	0.19	1.21 (0.70-2.09)	0.494			
Race						
Malay	0	1.00				
Non-Malay	-0.26	0.77 (0.42-1.41)	0.397			
Allergy status						
No	0	1.00				
Yes	0.19	1.21 (0.64-2.28)	0.557			
Working status						
No	0	1.00				
Yes	0.59	1.80 (1.09-2.99)	0.023			
GINA Step						
1	0	1.00		0	1.00	
2	0.36	1.43 (0.68-3.01)	**0.003**	0.56	1.74 (0.78-3.90)	**0.004**
3 & 4	1.44	4.20 (1.67-10.59)		1.56	4.76 (1.79-12.63)	
Smoking status						
Non-smoker	0	1.00				
Current smoker	1.53	4.63 (0.91-23.62)	0.256			
Second hand smoker	0.17	1.18 (0.64-2.21)				
Ex-smoker	0.43	1.54 (0.58-4.09)				
Education level						
None	0	1.00				
Primary	0.06	1.06 (0.22-5.21)	0.813			
Secondary	0.04	1.04 (0.22-4.82)				
Tertiary	-0.25	0.78 (0.16-3.79)				
Years of diagnosis of asthma	0.001	1.00 (0.99-1.02)	0.932			
Family history						
No	0	1.00				
Yes	0.16	1.18 (0.71-1.95)	0.531			
Comorbidities						
No	0	1.00		0	1.00	
1 comorbid	-1.10	0.33 (0.16-0.70)	**0.011**	-1.07	0.35 (0.16-0.76)	**0.016**
≥2 comorbidities	-0.41	0.66 (0.34-1.29)		-0.29	0.75 (0.36-1.57)	

Compliance to ICS						
Yes	0	1.00				
No	0.67	1.96 (1.01-3.80)	0.047			
Asthma Control Test						
Well controlled	0	1.00				
Not well controlled	0.69	1.98 (1.04-3.78)	0.002			
Very poorly controlled	1.41	4.11 (1.69-9.98)				
Inhaler technique score						
Good	0	1.00				
Satisfactory	0.37	1.45 (0.84-2.51)	0.374			
Poor	0.01	1.01 (0.47-2.16)				
MDI salbutamol Overuse						
No	0	1.00	**0.002**	0	1.00	**0.005**
Yes	0.79	2.20 (1.32-3.67)		0.78	2.19 (1.26-3.80)	

[a] Enter Multiple Logistic Regression model was applied.
Constant 0.187
Multicollinearity and interaction term were checked and not found.
Hosmer and Lemeshow Test, p= 0.715; Classification table 63.5%; Area under ROC curve 0.714 (95%CI: 0.652-0.777)
Abbreviation: b = estimated coefficients; OR = odd ratio; 95%CI = 95% confidence interval; SD = standard deviation; GINA = The Global Initiative for Asthma; ICS = inhaled corticosteroid; MDI = metered dose inhaler

Discussion

Our study demonstrated a comparable prevalence of MDI salbutamol overuse (42.1%) to that reported in the Malaysian cohort of the SABINA III study (47.4%) (8). The characteristics of the subjects in both studies were similar, including mean age, gender distribution, duration of asthma diagnosis, education level and smoking status (8). However, most of the subjects in our study were classified under GINA Steps 1 and 2, whereas most patients in the SABINA trials suffered from moderate to severe asthma (GINA Steps 3 to 5) (8).

SABINA trials conducted across various countries reported a wide range of prevalence rates of SABA overuse, including 74.9% in South Africa, 71.4% in Brazil, 38% in the United Kingdom, 37% in Indonesia, 30% in Sweden, 29% in Spain, 23.9% in Turkey, 16% in Germany, 15.9% in Taiwan, 10.6% in the Philippines, 9% in Italy, and 4% in China (7, 13–19). South Africa and Brazil recorded alarmingly high prevalence rates of SABA overuse, with the majority of subjects in these countries being overweight or obese and experiencing poorly or inadequately controlled asthma (13, 14). While body mass index (BMI) was not analysed in our study due to missing data, the European cohorts of SABINA III did not report BMI data for their subjects (15). The relatively low prevalence observed in the China cohort was probably attributed to the exclusion of patients treated in primary care settings (19).

Most SABINA studies relied on prescription databases (13–19). In contrast, our study included data on SABA collection from both prescriptions and over-the-counter purchases at retail pharmacies over the past year, providing a more comprehensive assessment of SABA usage patterns. A previous study suggested assessing SABA overuse by asking patients how frequent they used SABA in the past week (12). However, our findings indicated that this approach would only identify half of the actual cases of SABA overuse compared to assessing the number of canisters used over the past year, as recommended by GINA. Therefore, we advocate for healthcare providers to routinely inquire about patients' annual SABA canister usage or to utilise the reliever reliance test for a more accurate assessment of SABA overuse. While evaluating SABA use in the past week was useful for assessing asthma control, it was insufficient for detecting SABA overuse.

The SABINA trials examined the prevalence and outcomes of SABA overuse and overprescribing across various countries, however, they did not investigate the factors associated with SABA overuse. Conversely, our study investigated the associated factors of MDI salbutamol overuse. Our findings demonstrated that patients with a family history of asthma and those with ACT scores below 20 had significantly higher odds of MDI salbutamol overuse.

De Simoni A et al. identified several predictors of SABA over prescription over the past year. These included age over 60 years, female gender, Asian or Asian British ethnicity, current or former smoking status, repeat prescription systems, asthma classified as GINA Steps 2 to 5, oral corticosteroid use, and the presence of physical or mental comorbidities (20). In contrast, our study did not identify any significant association between age, gender, smoking status, GINA Step, or the presence of comorbidities and MDI salbutamol overuse. The association with oral corticosteroid use was not examined, as information regarding prescriptions from other healthcare facilities, particularly those in the private sector, could not be retrieved. While our study focused solely on Asian participants, no significant differences in SABA overuse were observed between racial subgroups. De Simoni et al. did not assess the association between ACT scores and MDI salbutamol overuse, however, they suggested that improving asthma control might reduce SABA overuse (20). Their study also reported that only approximately half of the patients who overused SABA had reasonable refills of ICS prescriptions (20).

Dijkman et al. reported that a higher Asthma Control Questionnaire (ACQ-5) score, current or former smoking status, elevated BMI, and longer asthma duration were associated with increased SABA use (21). Our study revealed similar finding that patients with poorly controlled asthma were more likely to overuse SABA, although ACT, instead of ACQ-5, was used to assess asthma control. Inadequate asthma control might lead to increased reliance on SABA for rapid symptom relief during exacerbations, thereby elevating the risk of SABA overexposure and subsequent airway remodelling. Excessive long-term SABA use could lead to beta receptor down-regulation, diminishing SABA sensitivity over time (4, 21). As a result, these patients might require progressively higher doses of SABA to manage their symptoms. However, unlike Dijkman et al., we found no association between SABA overuse and gender, smoking status, GINA treatment Step, asthma duration, or comorbidities. Most patients in our study were classified under GINA Steps 1 or 2 and none were categorised under Step 5, which probably explained the lack of association with GINA classification. Furthermore, oral corticosteroid uses and mental comorbidities were not analysed due to challenges in extracting retrospective data and the low prevalence of mental health conditions within our study population.

Our findings indicated that patients with a family history of asthma had higher odds of MDI salbutamol overuse. This might be attributed to the misconception, potentially influenced by parental beliefs and previous clinical practices, that MDI salbutamol was the primary and life-saving treatment for asthma. Conversely, patients without a family history of asthma might have greater exposure to recent evidence, technological advancements, and online educational resources. As a result, they might have a better understanding of the inflammatory nature of asthma.

De Simoni A et al. investigated SABA prescribing rather than actual usage and defined over prescription as the issuance of six or more SABA canisters within the past 12 months (20). In contrast, our study defined overuse as the use of three or more canisters within the same period (2, 20). These methodological differences likely contribute to the discrepancies observed between the studies.

A systematic review by Loh ZC et al. highlighted that 1.4%-39.6% of patients purchased SABA over the counter, with 14–66.4% of these individuals overusing it (22). Factors associated with overuse included nonadherence to ICS therapy, concerns about ICS adverse effects, lack of awareness regarding the SABA overuse, and moderate to severe asthma (22). In contrast, our study did not find these factors as significant contributors to SABA overuse. However, our study did not investigate the association between concerns about ICS adverse effects and the lack of knowledge contributing to SABA overuse. It also remained unclear whether genetic factors play a role in SABA overuse. The observed association between family history of asthma and SABA overuse in our study could be attributed to parental influence regarding misconception of ICS adverse effects and the belief that SABA was the primary treatment for asthma exacerbations.

A study by Blakeston S and colleagues emphasised that many patients overusing SABA were emotionally dependent on it for rapid symptom relief, unaware that frequent SABA use signifies poor asthma control, or hold misconceptions about ICS therapy (23). These findings highlighted the urgent need for patient education on the risks of SABA overuse and the critical importance of ICS adherence.

Our study demonstrated that MDI salbutamol overuse was associated with 2.19 times increase in the odds of poor asthma outcomes. This finding was consistent with the Malaysia cohort of SABINA III study which showed that patients with SABA overprescribing were twice more likely to suffer from severe exacerbations in the past year (AOR = 2.04, 95% CI = 1.44-2.87) (8). Similar results have been observed across all other SABINA cohort studies (13-19). Furthermore, FitzGerald JM and colleagues discovered that excessive SABA use was associated with an increased risk of asthma-related emergency department visits and hospital admissions (24).

Therefore, healthcare providers were recommended to routinely assess the number of MDI salbutamol canisters utilised by patients over the past year or conduct RRT during each clinical encounter (2, 12). All individuals with asthma should be encouraged to maintain an asthma diary, and a personalised asthma action plan should be developed for all patients whenever feasible. The use of SABA monotherapy should be discouraged, and the misconception that SABA serves as the sole or primary treatment for exacerbations must be addressed (2, 8). This goal could be achieved through comprehensive education targeting patients and caregivers, initiated at the time of diagnosis, and reinforced during subsequent consultations. To enhance patient self-management, we proposed the development of a mobile application to facilitate patient self-reporting of asthma symptoms, SABA, and ICS usage (25). Additionally, an electronic pharmacy system capable of detecting and alerting pharmacists to excessive SABA collection by patients should be implemented to support optimal asthma management (26).

Prescribers should be vigilant for patients at high risk of SABA overuse, including those with low ACT scores and with family history of asthma. These patients should receive targeted education on the risks of SABA overuse. MDI salbutamol use should be monitored at each visit, with its supply regulated, ideally on an exchange basis (8). Additionally, we suggested considering the ICS+LABA combination (e.g., budesonide 160 mcg + formoterol 4.5 mcg/dose Turbuhaler, 30 doses) as first-line therapy for Step one patients using fewer than 30 puffs of reliever annually. This approach was cost-effective and might improve asthma control and outcomes (2, 27). Finally, we recommended that regulatory authorities consider restricting over-the-counter sales of MDI salbutamol by reclassifying it as a prescription-only medication, as SABA overuse may lead to significant poor asthma outcomes.

In our study, increasing age was associated with lower odds of poor asthma outcomes. This contrasted with previous studies, which reported that the risk of asthma exacerbations and hospitalisations increased with age (28, 29). Younger adults might be more frequently exposed to occupational triggers or had limited awareness regarding the importance of regular asthma follow-up and control. Consistent with this, the US CHRONICLE study reported that adults younger than 40 years had a higher risk of exacerbations compared to those aged 40 years and above, potentially due to a higher prevalence of nasal polyps and allergic diseases in the younger population (30). Simms-Williams et al. had also identified younger age as the risk factors for admission to intensive care unit due to asthma (31).

Our study also demonstrated that having one comorbidity was associated with lower odds of poor asthma outcomes. This might be due to more frequent clinical follow-ups, patient education, and closer monitoring among patients with at least one comorbidity, compared to those without any other disease. Patients with multiple concomitant diseases might also be managed under specialised multidisciplinary teams, providing more structured care. The CARN study reported that increasing age, COPD, and coronary heart disease were associated with a higher incidence of asthma-related hospitalisations, whereas allergic rhinitis was associated with lower hospitalisation rates (32). However, our study excluded patients with COPD and did not assess the association of specific types of diseases on asthma exacerbations or hospitalisations. Moreover, the CARN study included patients aged 14 years and above with a minimum asthma diagnosis of three months, while our study did not include adolescents and required a minimum asthma duration of one year (32). The CARN study further observed that patients with five comorbidities had similar hospitalisation rates to those with none or only

one comorbidity, while patients with two to four and more than five comorbidities demonstrated progressively increasing hospitalisation rates as the number of comorbidities increased (32).

One of the strengths of our study was the incorporation of both MDI salbutamol use obtained through prescriptions and over-the-counter purchases at retail pharmacies. The associated factors were investigated in the study, which enabled us to identify and monitor patients at higher risk of SABA overuse more closely. However, several limitations must be acknowledged. Recall bias was a potential issue, as patients were required to retrospectively report the number of MDI salbutamol inhalers they had used over the past one year. Moreover, the sample size was not calculated based on the prevalence reported in the SABINA III Malaysian study because we were already in the data collection phase when that study was published (8).

Most of our patients used MDI budesonide as a preventer, which restricted our ability to analyse whether different ICS or ICS plus long-acting β2-agonist (LABA) combinations contributed to MDI salbutamol overuse. Mental health conditions, such as depression and anxiety, were reported in only three subjects, making it challenging to evaluate their potential impact on SABA overuse. Furthermore, analysis of BMI was not feasible due to missing height and/or weight data for the majority of patients, as well as time constraints that limited the collection of these measurements during patient interviews. Finally, we did not examine the use of oral steroids and antibiotics in relation to MDI salbutamol overuse. This limitation arose from challenges in retrospectively retrieving these records over the past year.

Conclusion

The prevalence of MDI salbutamol overuse was found to be nearly half of asthma patients at our institutions. Key factors associated with SABA overuse included poorly controlled asthma and family history of asthma. MDI salbutamol overuse was associated with higher risk of asthma exacerbations and/or hospitalisations. Therefore, timely and targeted interventions were crucial to mitigate poor asthma outcomes in these patients.

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Conflict of Interest Statement

No conflict of interest was declared by the authors.

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