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Volume 9 • Issue 1 • May 2026

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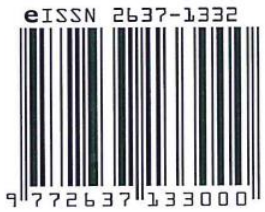
May 2026



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CONTENTS

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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Factors Affecting Adherence of Beta-Thalassaemia Patients towards Iron Chelation Therapy in Hospital Keningau

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Abstract

Introduction: Survival in patients with beta-thalassaemia major is strongly influenced by adherence to iron chelation therapy (ICT). Studies showed that half of these patients die before the age of 35 due to poor adherence.

Objective: To determine ICT adherence level and thalassaemia disease knowledge level, the association between thalassaemia disease knowledge and ICT adherence level, and to explore the factors affecting the ICT adherence.

Method: A cross-sectional study was conducted over three months from May to July 2018 involving thalassaemia patients in Hospital Keningau. A combination of self-administered questionnaire and data collection form was utilised. The questionnaire comprised four sections: baseline demographics, Thalassaemia Disease Knowledge Assessment and factors affecting adherence to deferiprone and desferrioxamine. Data collection form was used to collect clinical data and for ICT adherence level assessment. Spearman Rho correlation test was used to examine the relationship between thalassaemia disease knowledge and ICT adherence.

Results: A total of 52 patients, predominantly female (n=31, 59.6%) with a median age of 17 years old (IQR=7.5) were included in the study. The median ICT adherence level was 87.5% (IQR=33.3), while 61.5% (n=32) of patients had moderate to good level of thalassaemia disease knowledge. No association was found between thalassaemia disease knowledge level and adherence (ρ= -0.124, p=0.396). Laziness (n=10, 25.6%) and pain at injection site (n=10, 25.6%) were the main reasons for poor adherence reported by patients on desferrioxamine, compared to laziness (n=12, 29.3%) and drug side effects (n=10, 24.4%) for deferiprone.

Conclusion: ICT adherence among thalassaemia patients was suboptimal despite moderate disease knowledge, with no significant association between knowledge and adherence. Non-adherence was mainly influenced by patient and treatment-related factors. Targeted, patient-centred interventions addressing these barriers are needed to improve adherence and optimise patient outcomes.

Keywords: Thalassaemia, adherence, knowledge, factor

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Introduction

Thalassaemia is one of the common inherited blood disorders (1). It interferes with the body's ability to produce haemoglobin, leading to chronic anaemia, physical complications, and a significantly reduced quality of life (2). Treatment varies depending on the type and severity of the disease. In thalassaemia major, regular packed red blood cell transfusions are essential for survival (3, 4). However, repeated transfusions lead to iron overload, which necessitates consistent iron chelation therapy (ICT) for survival. Without adequate chelation, cardiac failure becomes the leading cause of death in thalassaemia patients, accounting for up to 71% of deaths (5). Hence, long-term prognosis depends not only on transfusion but also on adherence to ICT (6).

Adherence to ICT in Malaysia remains a persistent challenge. A 2023 study reported adherence rates of estimated 20% for oral-only treatment and 47.5% for combined subcutaneous and oral regimens (7). The consequences of poor adherence are detrimental. Over 50% of patients die before the age of 35, mainly due to avoidable organ damage, significant morbidity and mortality, and poor health-related quality of life (8, 9). These outcomes occur despite the availability of effective therapy, suggesting that the issue lies not only with the treatment itself, but is a complex phenomenon influenced by behavioural, cognitive, and psychological factors that influence adherence to ICT (10).

A profoundly good disease knowledge, a major component in health literacy, has been suggested to directly influence a patient's ability to cope with their medical condition, engage with treatment, and make informed decisions (11). However, the impact of thalassemia disease knowledge on adherence to ICT presents a complex picture. Among patients receiving combined subcutaneous and oral ICT, those with lower knowledge scores were significantly more likely to be non-adherent (7). Conversely, another study reported that while low monthly household income was associated with poor adherence, there was no correlation between thalassaemia knowledge and adherence levels (12). These inconsistent findings highlighted the need for further research to determine whether knowledge level is directly associated with adherence behaviour, or whether this relationship is mediated by other psychosocial factors. Without such evidence, healthcare professionals lack the focused and practical strategies needed to improve long-term ICT adherence. Addressing this gap will provide valuable insights for planning more effective and sustainable thalassaemia care (13).

In 2020, Sabah reported the highest number of thalassaemia patients in Malaysia at 22.72% (5). A substantial number of these patients reside in remote and rural areas, particularly in the Keningau district. The thalassaemia disease knowledge level in these patients remains underexplored. Prior research among thalassaemia patients in Sabah often focused on patients residing in urban areas. Differences in cultural beliefs and health literacy levels between urban and rural populations may also contribute to differences in ICT adherence (4, 14). Furthermore, searching through published literature yielded no previous studies that have specifically investigated the factors influencing ICT adherence among patients in rural areas. Therefore, this study aimed to determine the ICT adherence level, thalassaemia disease knowledge level, the association between disease knowledge and ICT adherence level, and to explore factors affecting ICT adherence. This study addressed the following research questions: How much do thalassaemia patients from rural communities understand about thalassaemia? Does knowledge affect ICT adherence among thalassaemia patients in rural areas? What factors affect ICT adherence among these patients? Our study hypothesises that a higher level of thalassaemia disease knowledge level is associated with better ICT adherence. Upon completion, this study will provide a clearer understanding of thalassaemia disease knowledge and ICT adherence level within rural communities, forming a basis for formulating effective, patient-oriented thalassaemia care strategies.

Methodology

Study Design

This was a cross-sectional study conducted over a three-month period between May and July 2018 at the medical wards and Thalassaemia Day-Care Unit of Hospital Keningau. The Thalassaemia Day-Care Unit operates from Tuesday to Friday and is equipped with 11 beds for paediatric patients and 10 beds for adult patients. Patients typically attend for blood transfusion at the intervals of two to four weeks, depending on their haemoglobin levels. During each visit, their vital signs and weight are recorded, followed by pre-transfusion testing that include full blood count, blood grouping and cross-matching, as well as periodic liver and renal function tests and serum ferritin monitoring. In cases where thalassaemia patients develop significant anaemia or related complications, they are admitted to the medical ward for further management.

In our setting, desferrioxamine (DFO) is usually administered via subcutaneous continuous infusion using a portable pump over eight to 20 hours daily, for five to seven nights per week. Meanwhile, deferiprone (DFP) is administered orally in three divided doses daily (10). The average daily doses for DFO and DFP are 20–60mg/kg/day and 75–100mg/kg/day, respectively. As DFO and DFP were the most commonly prescribed ICT during the time of our study, they were selected as the therapies of interest for this study.

Study Population

All thalassaemia major patients who visited the Day-Care Unit for routine blood transfusions, and those who were admitted to the medical wards when complications arise were included in the study. During study commencement, there were only 72 registered thalassaemia patients in the hospital's registry. Therefore, no study sampling was carried out. Thalassaemia patients were recruited into the study if they were aged more than 12 years old, had regular follow-ups at the hospital, and were receiving ICT maintenance therapy (either DFO alone, DFP alone, or a combination of DFO and DFP). Patients were excluded if they were patients with neurological or psychological disorders or patients or caregivers who are unable to communicate in either Malay or English language.

Study Instrument

Data Collection Form

A data collection form was used to collect clinical data and for ICT adherence level assessment. The form consisted of three sections: Section A: Clinical Data, Section B: Adherence Assessment for Desferrioxamine, and Section C: Adherence Assessment for Deferiprone. For adherence assessment, study investigators asked patients to recall the actual dose and frequency of their medication taken at home. This information was then divided by the actual prescribed dose obtained from drug prescriptions (15). The calculated adherence level was between 0 (non-adherence) to 100% (adherence). The other clinical data in the data collection form was compiled by the pharmacist in charge of the medical wards or the Thalassaemia Day-Care Unit.

Self-administered Questionnaire

The self-administered questionnaire consisted of four sections: Section A: Patient baseline characteristics, Section B: Disease Knowledge Assessment, Section C: Factors affecting adherence to desferrioxamine, and Section D: Factors affecting adherence to deferiprone.

Section B: Disease Knowledge Assessment was adapted from the Disease Knowledge about Thalassaemia Major (DKTM) questionnaire (13). Permission to use the questionnaire was granted by the author. The original 20-item DKTM questionnaire was reviewed by an expert panel comprising two medical specialists and three senior pharmacists from the Thalassaemia Medication Therapy Adherence Clinic (TMTAC). The panel members independently reviewed all items for suitability, practicality, and relevance to the local context. Based on their evaluation, particularly considering the differences in perception and literacy between urban and rural populations, the final questionnaire adapted for our study consisted of ten items with either "Correct (*Betul*)" or "Wrong (*Salah*)" response options.

Subsequently, the questionnaire was translated into Malay language, and the accuracy of the translation was verified through back-translation by two language experts. To ensure face validity, a pilot study involving five patients was conducted to ensure that there were no conflicting and confusing terms and the sentences were simple and easy to understand.

Each item in the questionnaire was scored as 0 (for incorrect answers) or 1 (for correct answers). The total score ranged from 0 to 10 (maximum score), which was then converted to a percentage score from 0 to 100. Percentage scores below 50% were classified as poor disease knowledge, scores between 60% to 70% as moderate disease knowledge, and scores above 80% as good disease knowledge (16, 17).

For Section C and D, the factors affecting adherence to DFO and DFP were pre-identified based on literature reviews, clinical observations, and suggestions from the paediatricians (3, 4). Fifteen factors affecting adherence were identified for DFO, while twelve factors were identified for DFP. Patients were also asked to choose one most important factor affecting their own ICT adherence based on the type of ICT they received. If a patient received a combination of DFO and DFP, the patient had to answer both Section C and Section D.

Data Collection Procedure

Patients who met the inclusion criteria and exclusion criteria were approached, and written informed consent was obtained from the patients or their caregivers prior to data collection. All required data in this study were collected using a self-administered questionnaire and data collection form.

For adherence assessment, study investigators asked patients to recall the actual dose and frequency of their medication taken at home, and recorded the information in the data collection form. Then, the patients were asked to fill in the self-administered questionnaire. If any terms were unclear or confusion arose, patients may approach the study investigators for clarification. Study investigators would ensure that the questions were fully understood prior to patients' responses. To minimise bias in data collection, the study investigators were briefed on the data collection procedures and study terms definition to ensure standardisation, complete understanding, and consistency throughout the data collection process.

Ethics Approval

This study was registered with the National Medical Research Register (NMRR) and approved by the Ministry of Health Medical Research and Ethics Committee (MREC) with reference number NMRR-18-404-39581 (IIR).

Data Analysis

The data were analysed using Statistical Package for the Social Sciences (SPSS) version 20. Categorical data were presented in frequency and percentage, while continuous data were presented as mean and standard deviation (SD) for normally distributed data or median and interquartile range (IQR) for skewed data. Due to non-normally distributed characteristics, the Spearman Rho correlation test, a non-parametric analysis, was used to examine the relationship between thalassaemia disease knowledge and ICT adherence level. A *p* value of less than 0.05 was considered as statistically significant. Responses on factors affecting adherence were analysed descriptively.

Results

During the study period, a total of 72 patients were registered in the Thalassaemia Hospital Registry. Of these, 16 patients were no longer under follow-up and 4 patients had passed away. All the remaining 52 patients received ICT therapy, hence, 52 patients (72.2%) met all the inclusion criteria and were included in this study. Among these patients, 38 (73.1 %) received combined therapy, while remaining patients were treated with either DFO (n=5, 9.6%) or DFP (n=9, 17.3%) as monotherapy.

The baseline characteristics of the patients were summarised in Table 1. Patients were predominantly female (n=31, 59.6%), with median age of 17 years old (IQR= 7.5). Most patients (76.9%) were still attending school or pre-university, while the remaining 21% were not in school. The median monthly household income was RM500 (IQR=650). The median duration of journey from home to the hospital by any motorised vehicle was approximately 0.7 hours (IQR=0.7).

Table 2 summarised the median ICT adherence level assessment, with three missing data points reported for combined ICT. The overall median adherence level was 87.5% (IQR=33.3). Table 3 summarised the thalassaemia disease knowledge assessment scores among thalassaemia patients in Hospital Keningau. The detailed responses of the thalassaemia disease knowledge assessment were presented in Supplementary File 1. Overall, the median thalassaemia disease knowledge score was 60% (IQR=30). In our study, 61.5% of patients scored at least 60% and above in the disease knowledge assessment, while 20 patients (38.5%) scored ≤50%.

The relationship between thalassaemia disease knowledge and ICT adherence level was summarised in Table 4. There was no statistically significant relationship between thalassaemia disease knowledge and ICT adherence level with (ρ= -0.124, p=0.396).

Table 1: Baseline characteristics of patients (n=52)

Variables	Response received	Frequency, n (%)	Median (IQR)
Gender			
Male	52	21 (40.4)	
Female		31 (59.6)	
Age (years)	52		17 (7.5)
Household income (RM, monthly)	28		500 (650)
Highest education level			
No	51	11 (21.2)	
Primary School		12 (23.5)	
Secondary School		27 (52.9)	
Pre-University		1 (1.9)	
Duration from home to hospital (hours)	48		0.7 (0.7)
Iron chelation therapy			
(DFO+DFP)	52	38 (73.1)	
DFO		5 (9.6)	
DFP		9 (17.3)	
Splenectomy			
No	51	37 (72.6)	
Yes		14 (27.5)	
Long term antibiotics			
No	50	37 (74)	
Yes		13 (26)	
Family history of thalassaemia			
No	50	18 (36)	
Yes		32 (64)	
Eye examination			
No	51	29 (56.9)	
Yes		22 (43.1)	
Auditory examination			
No	51	32 (62.8)	
Yes		19 (37.3)	
Pneumococcal vaccination			
No	48	40 (83.3)	
Yes		8 (16.7)	
Serum ferritin (mcg/ml)	52		6102.5 (8885.1)

Abbreviation: SD = standard deviation, RM = Ringgit Malaysia, DFO = Desferrioxamine, DFP = Deferiprone, IQR = Interquartile Range

Table 2: ICT adherence level assessment (n=49)

Iron Chelation Therapy	Frequency, n	Adherence, %, median (IQR)
Iron Chelation Therapy		
Combination (DFO+DFP)	35	80 (33.5)
DFO	5	100 (0)
DFP	9	100 (33.3)
Overall	49	87.5 (33.3)

Abbreviation: DFO = Desferrioxamine, DFP = Deferiprone, IQR = Interquartile Range

Table 3: Thalassaemia disease knowledge assessment scores (n=52)

Category of Assessment Score	n (%)
≤ 5 (≤ 50%)	20 (38.5)
6 - 7 (60-70%)	18 (34.6)
8 - 10 (80-100%)	14 (26.9)

Abbreviation: IQR = Interquartile Range

Table 4: Spearman Rho correlation test between thalassaemia disease knowledge score and ICT adherence level

Variables	Frequency, n	ρ	p-value
Knowledge - Adherence	49	-0.124	0.396

Abbreviation: ρ= Spearman Rho

Figure 1 demonstrated the reported factors contributing to poor adherence to DFO, based on a total of 39 responses. The most frequently reported reasons were pain at injection sites such as phlebitis (n=10, 25.6%), laziness (n=10, 25.6%) and the unavailability of syringe pumps and fear of side effects (n=4, 10.3%, respectively). For DFP, a total of 41 responses were received. The most reported factors affecting adherence were laziness (n=12, 29.3%), the side effects experienced (n=10, 24.4%), and pill burden (n=7, 17.1%), as shown in Figure 2.

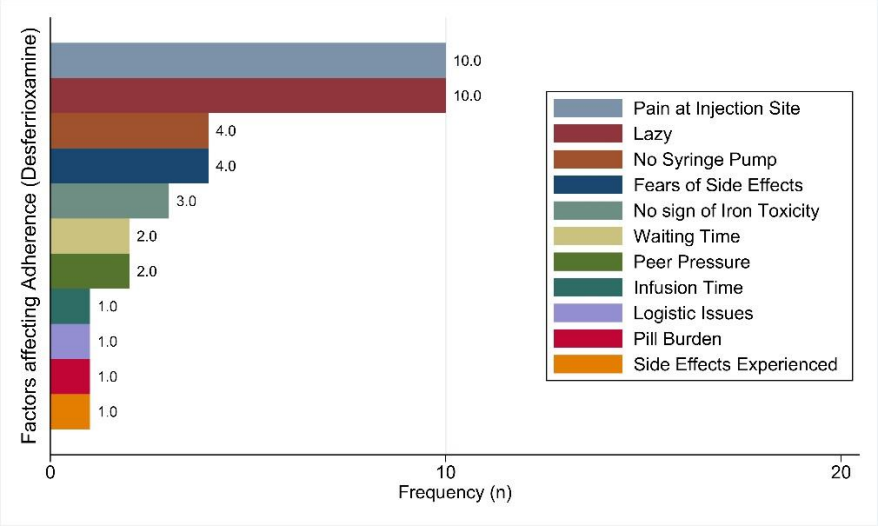

Figure 1: Factors affecting adherence to Desferrioxamine (n=39)

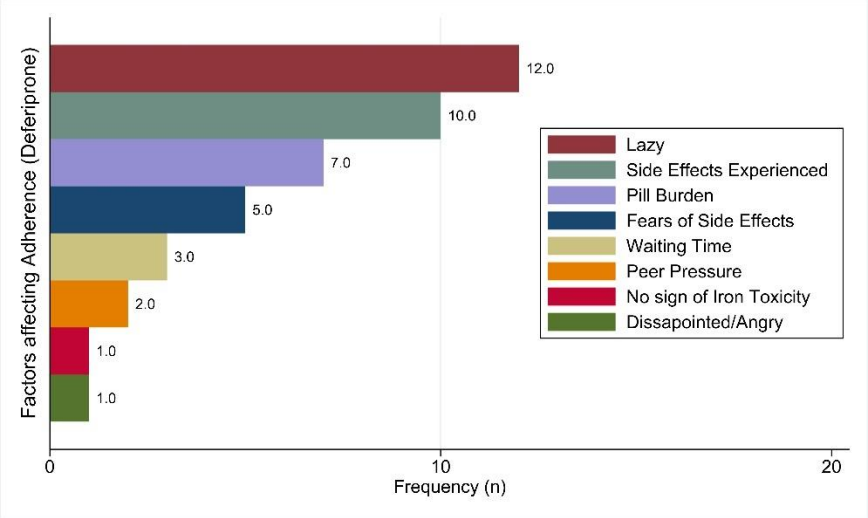

Figure 2: Factors Affecting Adherence to Deferiprone (n=41)

Discussion

Adherence to ICT remains a critical determinant of optimal clinical outcomes in transfusion-dependent thalassaemia patients. In our study, ICT was predominantly administered as combination therapy among the 52 included patients, with only a minority receiving desferrioxamine or deferiprone as monotherapy. Combination therapy is often introduced in patients who remain inadequately chelated on monotherapy; however, our findings demonstrate notable differences in adherence between regimens (18). Adherence was high among patients receiving monotherapy, whereas those on combination therapy exhibited comparatively lower adherence. This trend aligned with previous reports suggesting that more complex regimens, particularly those requiring multiple daily doses or simultaneous administration of different chelators, are more difficult for patients to adhere to (8, 19). The lower adherence observed in combination therapy underscored the practical challenges faced by patients in managing intricate treatment schedules. It further highlighted the need for interventions that simplify therapy and provide additional support to ensure consistent administration (20).

Disease knowledge is widely recognised as a key component in promoting self-management and adherence among patients with chronic conditions, including thalassaemia (13). In this study, while a substantial proportion of patients possess adequate knowledge about thalassaemia and its management, a significant subset demonstrated limited understanding. This knowledge gap may impair patients' ability to fully engage in effective self-care, recognise the importance of consistent ICT, and make informed treatment decisions. This highlighted the need for targeted educational interventions, particularly for younger patients or those from lower socioeconomic backgrounds, to strengthen disease literacy and support long-term treatment success (20).

Despite its importance, our analysis revealed no significant correlation between disease knowledge and adherence to iron chelation therapy, suggesting that higher knowledge scores may not necessarily translate into better adherence. This finding is consistent with studies by Al-Kloub et al. and Mohamed et al., both of which similarly reported no association between thalassaemia knowledge and treatment adherence among adolescent patients, a population comparable to ours (12, 16). Conversely, other studies have reported a weak but significant positive relationship between disease knowledge and adherence. Alnaami et al. found that patients with a greater understanding of their disease were more likely to follow their treatment plans, a perspective supported by Moustafa et al., who emphasised the need for educational strategies for patients and caregivers to improve adherence (17, 21). Together, these findings suggested that while understanding the disease is important, knowledge alone is often insufficient to overcome practical and behavioural barriers to consistent therapy. Prior research confirmed that adherence is more strongly influenced by factors such as regimen complexity, treatment-related side effects, and patient motivation rather than disease knowledge alone (8, 12). This underscored the need for multifaceted interventions that not only educate patients but also address real-world challenges, provide psychosocial support, and simplify therapy regimens to improve adherence and clinical outcomes.

In both treatment groups, laziness was reported as a factor affecting adherence in more than 50% of patients. Laziness, a patient-related factor, was also identified by Chong et al. as a result of emotional distress or negativity associated with thalassaemia, as well as difficulties in integrating the time-consuming medication regimen into daily routines (4). Participants in their study reported using avoidance coping strategies to manage these challenges and stressful situations, particularly during periods of low haemoglobin (4). The difficulty in integrating the medication regimen into daily routines may be attributed to the restrictions on physical activities imposed by both the severe disease condition and the treatment regimen involving desferrioxamine. As reported by Chat Chai et al., desferrioxamine therapy is particularly challenging due to its long infusion duration, which can significantly disrupt daily routines (10). Furthermore, activity restriction is a key component of quality-of-life assessments. The study by Trachtenberg et al. found that impaired quality of life, resulting from such restrictions, was associated with poor adherence with ICT (22).

Fear and concerns regarding the side effects associated with ICT are more prevalent among Asian patients compared to White patients (22). Patient-related factors such as laziness and fear of side effects can be addressed through several strategies, including the Three-Factor Interventional Model and Attachment Theory (20). Both approaches emphasise the importance of a strong, collaborative relationship between patients and clinicians. By integrating the patient's individual

concerns, beliefs, and motivations into the decision-making process, these strategies promote mutual understanding and facilitate the development of practical disease management goals and expectations. At our hospital, the Thalassaemia Medication Therapy Adherence Clinic (TMTAC), provided by pharmacists, offers counselling services designed to enhance patient adherence through personalised support, education, and guidance on effective medication management.

Other noteworthy factors affecting adherence in our patients include pain during desferrioxamine infusion and side effects experienced by patients on deferiprone, such as nausea, vomiting, and diarrhoea. Pain or irritation at the injection site was also reported by 51% of participants in another study, making it the second most common reason for non-adherence to ICT (23). Additionally, a study found that 91.7% of patients made errors during desferrioxamine administration, with most errors occurring during the dilution process (24). Using a more concentrated solution may cause irritation during injection, but this risk can be mitigated through proper preparation. Patients should be educated about the common side effects and practical management strategies, especially at the beginning of treatment. This approach helps to manage patients' expectations, address concerns, and foster trust and active participation in disease management. Patients are encouraged to report side effects so that they can be addressed by clinicians during visits, which helps to minimise intentional non-adherence.

If therapy-related factors remain intolerable despite the strategies outlined above, a change in therapy may be considered. In Sabah, desferrioxamine was the most commonly prescribed iron chelator, followed by deferasirox, which is predominantly used in paediatric patients, while combination therapy with desferrioxamine and deferiprone was introduced in 2018. Deferasirox, a newer once-daily iron chelator, may mitigate several barriers to adherence, including infusion-site pain, pill burden, and complex dosing regimens. Some formulations are available as dispersible tablets, facilitating administration in children. Its simplified dosing schedule has been associated with improved adherence compared to deferiprone (22). A meta-analysis by Qadah reported that deferasirox was comparable in efficacy to desferrioxamine, supporting its use as an alternative in patients who experience difficulty in adhering to other iron-chelating regimens (25).

There were a few limitations in our study. Firstly, there was a possibility of recall bias, especially with questions about adherence. Patients were asked to recall the number of times they have taken or injected their medications over the past week, and inaccuracies in their recollection or omission of details could lead to inaccurate data and adherence percentages. Secondly, the potential for misinterpretation of certain questions may have affected the reliability of the responses. Lastly, our study population was limited to patients who are 12 years old and older. Consequently, the findings may not be generalisable to younger paediatric patients, who often depend more heavily on parental oversight for disease management.

Conclusion

This study found that adherence to ICT among patients with thalassaemia remains suboptimal, despite a moderate level of disease knowledge. The absence of a significant association between thalassaemia knowledge and ICT adherence suggested that knowledge alone is insufficient to drive optimal treatment behaviour. Instead, practical and patient-related factors may play a more critical role in influencing adherence. These findings highlighted the need for a more comprehensive and patient-centred approach to improve ICT adherence, focusing not only on education but also on addressing behavioural, psychological, and treatment-related barriers. Interventions such as enhanced patient support, side effect management, improved access to administration devices, and regimen simplification should be considered. Ultimately, the insights from this study can guide healthcare professionals in developing targeted, effective, and sustainable care strategies to optimise adherence and improve clinical outcomes among patients with thalassaemia.

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Conflict of Interest Statement
No external funding was received and the authors declared no conflict of interest.

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Supplementary Data

Results of Thalassaemia Disease Knowledge Assessment (n=52)

	Correct answer	Responses			
		Correct *(Betul)*		Wrong *(Salah)*	
Thalassaemia adalah sejenis penyakit genetic *(Thalassaemia is a genetic disease)*	Correct	29	55.7%	23	44.2%
Setiap pesakit thalassaemia memerlukan rawatan transfusi darah *(Each patient with thalassaemia needs blood transfusion treatment)*	Wrong	51	98.1%	1	1.9%
Suntikan *Desferal*© adalah untuk menyingkirkan serum ferritin berlebihan dan untuk mengelakkan pengumpulan ferritin serum *(The reason for Desferal© injection is to get rid of excess serum ferritin and to avoid serum ferritin sedimentation)*	Correct	50	96.2%	2	3.8%
Punca bengkak hati dan limpa adalah disebabkan oleh kemusnahan sel darah merah yang berlebihan *(The cause of swelling of the liver and spleen is attributed to rapid destruction of red blood cell)*	Correct	30	57.7%	22	42.3%
Apabila pankreas bengkak / radang, ia akan menyebabkan kencing manis *(Once the pancreas is swollen/ inflamed, it will cause diabetes)*	Correct	12	23.1%	40	76.9%
Kadang-kala doktor mencadangkan untuk mengeluarkan limpa pesakit supaya dapat mengelakkan kemusnahan sel darah merah dengan cepat *(Sometimes doctor suggest removing the patient's spleen to avoid rapid cell destruction)*	Correct	45	86.5%	7	13.5%
Tahap hemoglobin harus dikekalkan melebihi 10g/dL untuk pesakit thalassaemia *(The level of haemoglobin should be maintained above 10g/dL in patients with thalassaemia)*	Correct	32	61.5%	20	38.5%
Jika kedua-dua ibu bapa adalah pembawa thalassaemia, maka kesemua anak yang dilahirkan akan menghidapi thalassaemia *(If both parents are the carriers of thalassaemia, all their children will be born with thalassaemia)*	Wrong	31	59.6%	21	40.4%
Tahap normal bagi serum ferritin adalah di bawah 1000mcg/L *(The normal range of serum ferritin levels is less than 1000mcg/L)*	Correct	31	59.6%	21	40.4%
Diet untuk pesakit thalassaemia adalah makanan yang mengandungi zat besi yang rendah *(The diet for thalassaemia patient should be low in iron)*	Correct	3	5.8%	49	94.2%

Herbal Healing: COVID-19 Survivors' Use and Beliefs of Herbal/Oral Dietary Supplements in Suburban Malaysia

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Abstract

Introduction: The global surge in COVID-19 cases and limited treatment options resulted in widespread concern and a search for alternative preventive measures. In Malaysia, many individuals have turned to Herbal and Oral Dietary Supplements (HODS) to support their health.

Objective: This study aimed to examine the prevalence of HODS use among surveyed COVID-19 survivors, evaluate their usage and beliefs regarding HODS consumption, and to find the association between sociodemographic variables and HODS use.

Methods: This cross-sectional study was conducted among COVID-19 survivors from May to August 2022. Data were collected through Google Forms distributed via WhatsApp®, utilising patient information obtained from the Hospital Hulu Terengganu COVID Operation Centre. Multiple logistic regression was employed to identify the factors associated with HODS usage.

Results: A total of 341 patients participated in the study. The mean age of respondents was 32.7± standard deviation (SD) of 10.2 years. The majority were female (71.3%), Malay (96.2%), and had higher education (85.0%). Overall, 44.9% (n=153) of respondents reported using HODS to manage or prevent COVID-19 symptoms. The patients used HODS to strengthen immunity (95.4%) and maintain overall health and wellness (94.0%). Despite sourcing HODS from pharmacies (59.5%), many users relied on suggestions from friends or relatives (68.6%). Age (adjusted odds ratio (AOR): 0.97; 95% CI: 0.94-0.99; p=0.013), male (AOR: 2.87; 95% CI: 1.66-4.97; p<0.001), and not employed (AOR: 0.40; 95% CI: 0.23-0.69; p=0.001) were significantly associated with HODS usage.

Conclusion: HODS use was prevalent among COVID-19 survivors, with the usage significantly higher among younger, male, and employed individuals. These findings highlighted a critical need for pharmacists and public health authorities to provide proactive, evidence-based guidance to ensure safe and rational HODS consumption.

Keywords: Herbal/Oral Dietary Supplements, COVID-19, Survivors

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Introduction

Coronavirus Disease 2019 (COVID-19) is an infectious illness caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) virus. It spreads through respiratory droplets or when contaminated hands come into contact with the mucous membranes of the mouth, nose, or eyes (1). The first reported case in Malaysia occurred in January 2020, and this disease began to spread rapidly throughout the country, reaching 5.3 million confirmed cases by March 2025 (2, 3). The rapid rise in positive cases and high infection rate gained extra attention from the nation in combating the disease (4). It challenged human resource management, facility utilisation, and medical supply management among healthcare providers, leading to emotional distress and burnout (5). The disease's symptoms are highly variable, taking up to 14 days for symptoms to appear after virus exposure, with one-third of infected people remain asymptomatic (6).

In Malaysia, the use of HODS was already common before the pandemic. Studies from 2014 to 2019 showed that many people, including those with chronic diseases such as hypertension, diabetes, and dyslipidaemia, used HODS (7). A local study revealed that 41.9% of respondents had

utilised HODS during the COVID-19 pandemic, and the author highlighted several concerns, such as the concurrent use of HODS with conventional medications, dependence on unreliable information sources, and insufficient consultation with healthcare providers (HCPs) (7). Along with a sense of uncertainty and widespread misinformation, this disease has prompted the population to seek and adopt remedies that promise to prevent the COVID-19 outbreak (8). Online misinformation regarding COVID-19 has undermined the government's efforts to control this novel coronavirus outbreak (9).

Herbal medicines are considered as a category of dietary supplements that encompass herbs, herbal materials, preparations, and products derived from plant parts or plant-based compounds. These contain natural chemicals such as tannins, terpenoids, alkaloids, coumarins, flavonoids, and polyphenols, which have demonstrated effectiveness against harmful microorganisms (10, 11). These compounds are known to inhibit viral enzymes and proteins, aiding in the prevention of viruses from entering and spreading within host cells (12). Historically, natural products and herbal medicines have been used to treat acute respiratory infections and typically exhibit acceptable toxicity levels (13). Their low toxicity further positions them as promising candidates for developing new treatments and alleviating COVID-19 symptoms (13, 14). Furthermore, physicians worldwide expressed considerable interest in using vitamins and mineral supplements to help prevent or treat COVID-19 (11).

During the COVID-19 pandemic, many Malaysians have turned to HODS to strengthen their immunity alongside the national vaccination program that was launched by the Ministry of Health Malaysia in February 2021 (7). In addition to practicing good personal hygiene, people have taken extra preventive measures, such as using HODS, and the usage has even shown an increasing pattern among HCPs (15). It was estimated that 80% of the world's total population in developing countries depends on HODS as their primary health care (16). Compared to the early years of the pandemic, Malaysians were initially sceptical about HODS due to their strong belief in vaccination or modern treatments. However, despite receiving their vaccines, many still contracted COVID-19, which prompted them to place more considerations in HODS products to enhance their immune systems (17).

Understanding the use of HODS during the pandemic is essential for ensuring patient safety and enhancing healthcare delivery. Unregulated or uninformed use of HODS can lead to adverse drug reactions, toxicities, or dangerous interactions with prescribed COVID-19 treatments (18). A systematic review encompassing 62 studies showed that the prevalence of self-medication during COVID-19 ranged from 7.14% to 88.3%. The Singapore's Traditional Chinese Medicine clinics conducted a study and found that 62.65% of patients reported using Chinese Herbal Medicine (CHM) and conventional medications concurrently. Patients using both were 3.65 times more likely to experience adverse events compared to those using only CHM (19).

This widespread self-medication highlighted the need for HCPs to provide guidance and regulate such practices (20). Dependence on unproven remedies may lead to delayed access to appropriate medical care, worsening patient outcomes. Investigating HODS usage can help to identify common misconceptions and misinformation, enabling HCPs to develop targeted educational interventions and promote evidence-based practices to ensure patient safety (21). Therefore, this study aimed to identify the prevalence of HODS use among surveyed COVID-19 survivors at Hospital Hulu Terengganu. It also aimed to evaluate their usage and beliefs regarding HODS consumption and to find the association between demographic variables and HODS use. The findings may help in developing strategies to promote the safe use of HODS among the public.

Methods

Study design

A cross-sectional study was carried out from May to August 2022, involving patients who received COVID-19 treatment at Hospital Hulu Terengganu, which was designated as a fully COVID-19 hospital during the COVID-19 pandemic. Ethical approval was obtained from the MOH Medical Research and Ethics Committee (MREC), and the study was registered in the National Medical Research Register (NMRR-22-01620-JON).

Study population

The inclusion criteria included COVID-19 survivors aged 18 and older who received treatment for COVID-19 at Hospital Hulu Terengganu. The exclusion criteria were patients who were illiterate. Using the single proportion formula for objective 1 (prevalence of HODS use) with an 80% factor of interest and estimating the expected proportion with 5% absolute precision and 95% confidence interval (CI), the minimum required sample size was n=230. However, for objective 3 (association between demographic variables and HODS use), by employing G Power with a significance criterion of alpha=0.05, power=0.80, and effect size=0.668, the minimum sample size needed was n=210. Therefore, final minimum sample size required to complete this study was 230 patients.

Patients' data, including contact numbers, were retrieved from the COVID Operation Centre at Hospital Hulu Terengganu. Approximately 3,000 patients were recorded in the patient registry, and through systematic sampling, every fifth patient was selected. Patients were assured that participation was voluntary and that they could withdraw from the study anytime.

Data collection

During the data collection period, an online survey form was distributed to the selected patients by sending the Google Forms link via the WhatsApp® application. All participants were provided with a written explanation of the research's purpose and methodology at the start of the survey, along with an assurance of confidentiality. Written informed consent was obtained before data collection. Patients' information was displayed, and clicking "next" indicated that the patient had voluntarily consented.

The research tool was a self-administered online questionnaire that was adapted from a validated questionnaire, used with permission from Alyami et al. (22). The questionnaire was translated to Malay to ensure the response rate among the predominantly Malay-speaking targeted population. Following back-to-back translations by two bilingual experts, a pilot study was conducted with 30 patients, yielding a Cronbach's alpha of 0.81. The pilot study indicated that the questionnaire items were clear and that using Google Forms as the survey administration tool was feasible. Patients from the pilot study were excluded from the final data analysis. The survey instrument consisted of a set of questions that took approximately five to ten minutes to complete.

The questionnaire was divided into three parts comprising 28 questions. Part 1 focused on demographic data, covering socio-demographic characteristics, medical history, COVID-19 status, and vaccination details. Part 2 was split into three subsections: the first subsection asked about HODS usage for COVID-19 treatment and was completed by all patients, while the second and third subsections concentrated on reasons for using or not using HODS and were answered only by HODS users and non-HODS users, respectively. These subsections contained closed-ended questions with yes or no responses. Additionally, three specific questions were included for HODS users, and all questions were a mix of closed-ended and open-ended formats. The open-ended question prompted patients to provide details about the types or examples of HODS they had taken during the COVID-19 pandemic. Patients were permitted to submit more than one HODS, allowing them the opportunity to list multiple treatments or remedies used during that time. The final part, entitled 'Belief towards HODS,' included five questions with multiple-choice answers of ‘Yes,’ ‘No,’ ‘Maybe,’ and ‘Not sure’ that should be answered by all respondents.

Statistical analysis

Data were analysed using Statistical Package for Social Sciences (SPSS) version 27 for Windows. Categorical data were presented descriptively, utilising frequencies (n) and percentages, while continuous data were summarised as the mean and standard deviation (SD). Following the completion of data exploration and cleaning, simple logistic regression was performed to examine the relationships between the variables associated with HODS usage. Variables with a p-value below 0.25 in the simple logistic regression were subsequently included in the multiple logistic regression model. Adjusted odds ratios (AOR) and 95% confidence interval (CI) were reported, with a p-value less than 0.05 considered statistically significant.

Results

From the 3,000 patients in the data registry, approximately 500 Google Form links were distributed. By the end of the study period, 341 completed questionnaires were received, resulting in a response rate of 68.2%. Although the target number of distributed questionnaires was 600 (every fifth patient in the data registry), the distribution was halted at 500 because the selected patients had already yielded a response rate exceeding expectation.

Table 1 presents the characteristics of the respondents. The mean age was 32.7 years old ± SD 10.2 years. The majority of the respondents were female (71.3%), Malay (96.2%), and with higher education status (85.0%). Most of them had their first COVID-19 infection (89.7%) and had received at least one dose of vaccination (92.4%). The distribution of HODS and non-HODS users was nearly equal, with 44.9% (n=153) of the patients had used at least one HODS to prevent or manage COVID-19 symptoms.

Table 1: Sociodemographic characteristics between the HODS user and non-HODS user groups

Variable	Total (n=341)	HODS User (n=153)	Non-HODS User (n=188)
Age (years old), mean ± SD	32.7 ± 10.21	33.7 ± 11.47	31.0 ± 9.01
Gender, n (%)			
Male	98 ((28.7)	31(20.3)	67 (35.6)
Female	243 (71.3)	122 (79.7)	121 (64.4)
Marital Status, n (%)			
Unmarried	157 (46.0)	73 (47.7)	84 (44.7)
Married	184 (54.0)	80 (52.3)	104 (55.3)
Race, n (%)			
Malay	328 (96.2)	144 (94.1)	184 (97.9)
Non-Malay	13 (3.8)	9 (5.9)	4 (2.1)
Higher Education, n (%)			
Yes	290 (85.0)	129 (84.3)	161 (85.6)
No	51 (15.0)	24 (15.7)	27 (14.4)
Employment Status, n (%)			
Yes	258 (75.7)	105 (68.6)	153 (81.4)
No	83 (24.3)	48 (31.4)	35 (18.6)
Chronic Illness, n (%)			
Yes	55 (16.1)	32 (20.9)	23 (12.2)
No	286 (83.9)	121 (79.1)	165 (87.8)
Number of COVID-19 Infection, n (%)			
1	306 (89.7)	137 (89.5)	169 (89.9)
More than 1	35 (10.3)	16 (10.5)	19 (10.1)
Vaccination Status, n (%)			
No	26 (7.6)	10 (6.5)	16 (8.5)
At least one dose	315 (92.4)	143 (93.5)	172 (91.5)

Abbreviation: SD = Standard Deviation; HODS = Herbal/Oral Dietary Supplements

Table 2: Reported reasons of HODS usage (n=341)

Reasons for Using and Not Using HODS [a]	n (%)
HODS users (n=153)	
To strengthen the immune system	146 (95.4)
To maintain overall health & wellness	144 (94.0)
To reduce COVID-19 symptoms	138 (89.5)
Inadequate dietary intake and nutritional deficiency	78 (51.0)
Non-HODS users (n=188)	
Satisfied with conventional / modern treatment	152 (80.9)
Concern about its efficacy and adverse effects	139 (74.0)
Less knowledge regarding dietary supplements	105 (55.8)
Dietary supplements are expensive	90 (48.0)

[a] Respondents were allowed to provide more than one response.
Abbreviation: HODS = Herbal/Oral Dietary Supplements

Table 2 presents the reported reasons for HODS usage. For HODS users, the belief that HODS could strengthen their immune system (95.4%, n=146) was the primary reason, followed by the desire to maintain overall health and wellness (94.0%, n=144). Among non-HODS users, the majority reported being satisfied with modern treatment (80.9%, n=152). They also expressed concerns about its efficacy and side effects (74.0%, n=139).

Table 3: Details on HODS usage among users (n=153)

Item	n / n (%)
Who suggested to take HODS, n (%) [a]	
Friends / Relatives	105 (68.6)
Doctor / Dietitian / Pharmacist / Nurse	56 (36.6)
Social media/Website	47 (30.7)
Sources of HODS, n (%) [a]	
Pharmacy	91 (59.5)
Online purchase	45 (29.4)
Home	42 (27.5)
HODS taken, n [b]	
Vitamin C	76
Cloves	50
Honey	49
Lemon	22

[a] Patients were allowed to provide more than one response.
[b] Only the top four products / substances were presented. Patients were permitted to provide multiple responses on the HODS.
Abbreviation: HODS = Herbal/Oral Dietary Supplements

In responding to the question on who suggested HODS, friends and relatives (68.6%, n=105) were the primary motivators for patients to try HODS. Purchase from the pharmacies was the main source of HODS (59.5%, n=91), while nearly one-third of the users obtained HODS from online shopping platforms (29.4%, n=45) and acquiring it from their homes (27.5%, n=42). When asked about the types of HODS they had used, 76 respondents reported taking vitamin C, followed by cloves (n=50) and honey (n=49) (Table 3).

Regarding patients' beliefs about the use of HODS as a protective measure, 76.3% of the patients believed that consuming vitamin C, which is found in citrus, played a role in treating or reducing COVID-19 symptoms, while 50.9% believed that HODS could treat or reduce COVID-19 infection. Nevertheless, 61.4% of respondents disagreed that HODS can prevent the spread of COVID-19 better than social distancing (Table 4).

Table 4: Patients' belief on HODS (n=341)

Item	Yes	No	Maybe	Not sure
Drinking cloves / ginger / garlic helps to increase immunity and reduce the risk of COVID-19 infection	42.7%	24.0%	22.8%	10.5%
The consumption of vitamin C found in citrus has a role in treating / reducing the symptoms of COVID-19	76.3%	7.3%	13.5%	2.9%
Vinegar plays a role in treating or protecting against COVID-19	11.1%	55.0%	12.6%	21.3%
Taking herbal products/ health supplements can prevent the spread of COVID-19 better than social distancing	17.5%	61.4%	11.7%	9.4%
Vitamins and herbs / supplements can treat / reduce COVID-19 infection	50.9%	24.6%	17.0%	7.6%

Abbreviation: HODS = Herbal/Oral Dietary Supplements

The logistic regression analysis is presented in Table 5. Variables with a $p<0.25$ from the simple logistic regression, such as age ($p=0.131$), gender ($p=0.002$), employment status ($p=0.007$), and chronic illness ($p=0.032$), were further analysed using multiple logistic regression.

The multiple logistic regression model showed a statistically significant association between age, gender, and employment status with HODS usage. No interactions or multicollinearity were found among the independent variables in this study; thus, a preliminary final model was obtained. The Hosmer-Lemeshow test, classification table, and area under the curve were also tested for the model, and the assumption was met.

Males, younger individuals, and employed persons were more likely to use HODS as preventive measures against COVID-19 ($p<0.05$) during the pandemic. From this table, we concluded that an increase in age by one year will reduce HODS usage by 3.2% (adjusted OR: 0.97; 95% CI: 0.94-0.99; $p=0.013$). Compared to females, males are 2.8 times more likely to use HODS (adjusted OR: 2.87; 95% CI: 1.66-4.97; $p<0.001$). Employment status is also a predictor of HODS usage. Compared to those who are employed, unemployed individuals are 60% less likely to use HODS (adjusted OR: 0.39; 95% CI: 0.23-0.69; $p=0.001$).

Table 5: Factors associated with HODS use

Variables	Simple Logistic Regression			Multiple Logistic Regression		
	(b)	Crude OR (95% CI)	p-value	(b)	Adjusted OR (95% CI)	p-value[a]
Gender						
Female	0	1.00				
Male	0.78	2.18 (1.33-3.57)	**0.002**	1.06	2.87 (1.66-4.97)	**<0.001**
Age, year(mean)	-0.02	0.99 (0.96-1.00)	**0.131**	-0.32	0.97 (0.94-0.99)	**0.013**
Marital Status						
Unmarried	0	1.00				
Married	0.12	1.13 (0.74-1.73)	0.576			
Higher Education						
Yes	0	1.00				
No	-0.10	0.90 (0.50-1.64)	0.733			
Employment Status						
Yes	0	1.00				
No	-0.70	0.5 (0.30-0.823)	**0.007**	-0.93	0.39 (0.23-0.69)	**0.001**
Chronic Illness						
Yes	0	1.00				
No	0.64	1.90 (1.06-3.41)	**0.032**	0.60	1.81 (0.94-,3.51)	0.077
Number of COVID-19 Infection						
1	0	1.00				
More than 1	-0.04	0.96 (0.48-1.94)	0.915			
Vaccination Status						
No	0	1.00				
At least one dose	-0.29	0.752 (0.331,1.708)	0.496			

[a] Backward LR multiple logistic regression model was applied. Multicollinearity and interaction terms were checked and not found.

Constant 2.614

Hosmer-Lemeshow test, p=0.340; Classification table 64.2%; Area under the ROC curve 0.324.

Abbreviations: OR = odds ratio; CI = confidence interval; HODS = herbal/oral dietary supplements

Discussion

This research investigated the use of HODS for the management or prevention of COVID-19 symptoms among patients living in the suburban of Malaysia. Approximately 45% of our study population were HODS users, which is higher than the rates reported in neighbouring countries (Thailand: 28.6% & Indonesia: 24.4%) (22). Nevertheless, our findings aligned with a local study indicating that 41.9% of participants had used at least one HODS (7). In Saudi Arabia, reported HODS use was lower at about 15%, with a similar prevalence observed in Hong Kong at 19.3% (22). The variations in HODS prevalence across different regions may be attributed to differing sociodemographic profiles and the local cultures of the respondents.

Among the HODS users, 94% agreed that consuming HODS can strengthen their immune system, indicating their confidence with HODS. Patients also consumed HODS to alleviate COVID-19 symptoms, which was consistent with several studies conducted in various regions that have used HODS for general well-being and medicinal purposes for hundreds of years (23, 24). Vitamin C products

were popular food supplements during the COVID-19 outbreak due to their wide availability and favourable safety profile. Almost half of our respondents were convinced that consuming vitamin C, cloves, ginger, and garlic could help to increase immunity and reduce COVID-19 infection (16, 24) However, vitamin C consumption must remain within the recommended daily dietary dosage (25). Apart from vitamin C consumption, a study from Saudi Arabia also suggested that eating garlic may help to increase immunity and reduce the chance of contracting COVID-19 (22).

Despite the popularity of HODS use, our study found that around two-third of patients disagreed that taking herbal products or health supplements is more effective than social distancing in preventing the spread of COVID-19, which aligned with the findings from Alyami et al. (22). Data from 149 countries suggested that implementing different social distancing interventions was associated with an overall reduction in COVID-19 incidence by 13.0% (26). It was believed that maintaining a well-balanced diet and adhering to COVID-19 standard operating procedures would reduce the risk of infection and mitigate the severity of COVID-19 symptoms.

This study revealed that HODS consumption was largely influenced by the opinions from peers and relatives, followed by HCPs. Nonetheless, the information obtained from friends and relatives could be misleading, as they share advice based on their own experiences, which might not be applicable to the patients' unique situations. Consequently, this may nourish the culture of delayed treatment-seeking behaviours among patients and de-optimise the treatment outcomes. Our findings contradicted with those of a local study, which found that social media and websites were the most common sources for HODS (7). Comparatively, around 60% of patients turned to pharmacies for their routine HODS supply, suggesting that healthcare professionals could seize this golden opportunity to provide proper education and recommendations regarding HODS intake. Pharmacists play a key role in assisting patients to make better choices and avoid unnecessary harm.

Despite generally positive belief towards HODS, several safety concerns are important to highlight. In this study, 74.0% of respondents were concerned about the efficacy and side effects of HODS. All drugs carry risks, even though there were believes that HODS are safe and widely used. In Indonesia, with the spike in COVID-19 cases in 2020, people turned to herbal medicines to boost their immunity. The significant increase in HODS usage prompted the Public Health Department to warn that unproven treatment methods can create a false sense of security (26). Due to limited experimental data, the safety and efficacy of HODS cannot be guaranteed. According to a Cochrane systematic review, HODS combined with Western medicine may have improved symptoms and quality of life in SARS-CoV-2 patients, but it might contribute to high rates of polypharmacy and HODS-drug interactions (18). A local Malaysian survey also highlighted that the co-administration of HODS and conventional drugs might have led to interactions affecting the effectiveness or causing adverse effects, which could impact patient outcomes (7).

Speaking of the non-HODS users, 80.9% reported being satisfied with modern treatments. In contrast, only 8.9% expressed satisfaction with modern medicine in a study conducted in Vietnam, where HODS usage was preferred over conventional treatments as they were trusted to be safer and more effective in minor ailments, given their long and rich history of practice among Vietnamese (28). Moreover, HODS had been listed in the National Essential Drug List under the Vietnam Ministry of Health whereby medical practitioners were permitted to legally prescribe these herbal medicines for patient use (28).

HODS use during the pandemic was common among women and the older population, as they were considered vulnerable groups to infection (29, 30). A local study reported that individuals aged 40 years and older were more likely to use HODS (7). In addition, Alhazmi et al. concluded that HODS use was a prevalent phenomenon in Asia region among middle aged (45 to 60 years) and older adults (60 years and over) (29). These findings contrasted with this study which unveiled that younger age was significantly associated with an increase in HODS use ($p=0.013$). Young people today are more health-conscious and may have used HODS to enhance their health during the pandemic. There was also a higher chance of HODS use, if an individual was of male gender and employed. The use of HODS by males and employed individuals could be attributed to health-related motivations, social influences, and financial considerations. Some HODS products available on the market were pricey and could only be afforded by certain social classes in society.

This study has several limitations. Self-reporting was used for data collection, which could introduce various response biases. These self-reported data might either overestimate or underestimate the actual use of HODS. Other than that, online surveys often rely on participants who have access to technology. Therefore, the sample may not represent the broader population, including older or rural demographics who tend to have lower digital literacy levels. This may act as a confounding factor when interpreting age as one of the factors affecting prevalence of HODS use. Another limitation is that this study did not examine the type and form of herbal medicine taken by patients. While the online survey method offers convenience and cost-effectiveness, researchers need to be aware of these potential consequences and take steps to mitigate them, such as enhancing survey design and considering appropriate sampling techniques to ensure the validity and reliability of their research.

Given the widespread use of HODS among COVID-19 survivors and the dependence on social circles for information, several policy and clinical recommendations can be made. Healthcare systems should include routine screening for HODS use during patient consultations. Implementing standardised protocols can assist healthcare providers in identifying unsafe or unnecessary supplement use and to intervene when appropriate. Public health authorities should prioritise developing evidence-based educational materials for both patients and HCPs. These resources should dispel myths about immunity-boosting products, encourage professional consultation, and promote safe usage. Integrating complementary medicine, including HODS, into healthcare training programs would further equip providers with the knowledge to offer informed, non-judgmental guidance. This approach can shift patients away from unreliable sources of information and thus adopt safer health practices.

Future studies should strive to include underrepresented groups, such as older adults, rural residents, and individuals with limited digital access, as the current reliance on online data collection might have led to sampling bias. It may be valuable to explore the role of informal information sources, motivations and satisfaction levels of both users and non-users to support the development of strategies in empowering healthcare providers to deliver accurate guidance, particularly in the community settings. Considering the potential interactions between HODS and modern treatments, future clinical and pharmacological studies are necessary to validate health claims and ensure patient safety. Additionally, the observed demographic trend, where younger, employed males are more likely to use HODS, that contrasted with findings from other regions, highlighted the need for broader sociodemographic research across diverse populations to better understand the influence of cultural, economic, and lifestyle factors on HODS usage.

Conclusion

This study revealed a high prevalence of HODS use among COVID-19 survivors, primarily driven by the desire to boost immunity and maintain overall wellness. HODS usage was significantly higher among younger, male, and employed individuals. Of concern was the reliance on non-professional advice for HODS consumption, despite the majority of products being sourced from pharmacies. These findings underscore a critical opportunity for healthcare professionals, particularly pharmacists, to bridge the information gap. Public health initiatives should prioritise evidence-based education to ensure the safe and rational use of supplements, mitigating the risks of self-medication based on anecdotal suggestions.

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Conflict of Interest Statement

The authors declare that there is no conflict of interest.

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