APJAI
Asian Pacific Journal of
Allergy and Immunology

ORIGINAL ARTICLE

Factors associated with poor asthma control in children: A prediction model

Wanaporn Anuntaseree, Kanokpan Ruangnapa, Araya Yuenyongviwat, Kantara Saelim, Pharsai Prasertsan

Abstract

Background: Inhaled corticosteroids (ICS) are the first-line therapy for pediatric asthma. However, very few studies have developed simple tools for predicting treatment outcomes in pediatric asthma.

Objective: This study aimed to construct a predictive model for poor asthma control in children after 6 months of ICS therapy.

Methods: This retrospective study included children with asthma, aged 6-15 years, who received ICS with complete follow-up for 6 months. The potential factors associated with poor asthma control were assessed. Poor control was considered if the child had partial or uncontrolled symptoms according to the Global Initiative for Asthma guidelines.

Results: Among the 165 eligible children, 33 (20%) had poor symptom control. The factors associated with poor control were a history of more than four exacerbations in the 12 months before ICS treatment (odds ratio [OR], 3.39 [1.06, 10.83]), the presence of moderate to severe allergic rhinitis symptoms at the 6-month follow-up visit (OR, 21.93 [2.97, 162.05]), and poor adherence to asthma medications (OR, 4.16 [1.32, 13.12]). By incorporating these factors, a model for predicting poorly controlled asthma was constructed and converted into a nomogram with a total score of 200, with prediction risk ranging from 0 to 100%. The area under the receiver operating characteristic curve of the developed model was 0.737, indicating a moderate performance level.

Conclusions: We developed a predictive tool for poor asthma control. The model has a good discriminatory ability and is simple to use, which could facilitate the individualized management of children with asthma.

Key words: asthma, child, inhaled corticosteroids, prediction model, therapy

Citation:
Anuntaseree, W., Ruangnapa, K., Yuenyongviwat, A., Saelim, K., Prasertsan, P. (0000). Factors associated with poor asthma control in children: A prediction model. *Asian Pac J Allergy Immunol*, 00(0), 000-000. https://doi.org/10.12932/ap-170724-1894

Affiliation:
Department of Pediatrics, Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla, Thailand

Corresponding author:
Wanaporn Anuntaseree
Department of Pediatrics, Faculty of Medicine, Prince of Songkla University
15 Kanjanawanich Road, Hat Yai, Songkhla 90110, Thailand
E-mail: awanapor@medicine.psu.ac.th, wanaporn.a@psu.ac.th

Introduction

Asthma is a chronic illness that is highly prevalent in children. Epidemiological data show a high worldwide burden of asthma over the past three decades, with a mean global prevalence of current wheezing of 9.9 and 10.4% and prevalence of severe asthma symptoms of 4.3 and 4.9%, in children and adolescents, respectively.[1] The exacerbation of asthma symptoms increases the risk for emergency department visits and hospitalizations.[2] The Global Initiative for Asthma (GINA) guidelines provides new asthma classifications based on asthma control levels (controlled, partly controlled, or uncontrolled). Appropriate asthma treatment aims to improve disease control and reduce the disease burden by minimizing the risk of exacerbations.[3] Strategies for the treatment of asthma include early detection and effective therapy. Asthma is characterized by chronic airway inflammation and hyperresponsiveness

that lead to recurrent episodes of wheezing, and inhaled corticosteroids (ICS) are the recommended first-line treatment. Corticosteroids can suppress airway inflammation and control asthma symptoms. Leukotriene receptor antagonists (LTRA) and long-acting beta-2 agonists (LABA) are recommended as add-on therapies for the anti-inflammatory treatment of patients with asthma.[3,4] Despite the availability of asthma medications and treatment guidelines, a significant proportion of patients fail to achieve asthma control, resulting in intermittent or persistent symptoms and exacerbation. Previous studies have shown several barriers in achieving symptom control with ICS therapy in children with asthma, including treatment- and patient-related factors. Treatment-related factors, including inadequate medication, poor adherence, and poor inhaler techniques are important causes of poor control asthma.[5] However, even in children who adhere to asthma medication, 17.9–33% still fail to control their symptoms.[6,7] Several studies have found that multiple patient factors are related to poor response to treatment, such as increased asthma severity, long disease duration,[8] comorbid allergic rhinitis (AR),[9] and obesity.[10]

Although several studies have attempted to identify the risk factors for poor asthma control, very few have provided a simple tool to predict response to asthma treatment. A study of Taiwanese children with asthma receiving ICS treatment found that male sex, age at diagnosis of asthma > 5 years, and exhaled nitric oxide < 35 ppb are risk factors, and the author developed a model for predicting the response to ICS.[7] However, all risk factors in that study were non-modifiable, which did not help much in patient management. Herein, we sought to construct a prediction model for asthma control failure after 6 months of ICS therapy among pediatric patients and focused on both modifiable and non-modifiable factors. These findings will provide a risk assessment, improve the individualized management of patients with asthma, and increase the proportion of patients with good asthma control.

Materials and Methods

Study design

This retrospective study was conducted at the Pediatric Pulmonology and Allergy Clinic of Songklanagarind Hospital, Prince of Songkla University, Southern Thailand. Patient information was collected from the hospital database using International Classification of Diseases (10th Revision) codes. Children who visited the clinic between 2015 and 2020 with one of the following diagnoses were recruited for the initial review: J45 asthma, J459 unspecified asthma, J458 mixed asthma, J451 non-allergic asthma, and R062 wheezing. Following the initial review, children who met the following criteria were enrolled as study participants: (1) aged 6–15 years with asthma diagnosed by a pediatric pulmonologist or an allergist based on a typical history of recurrent wheezing and bronchodilator response; (2) started treatment with ICS with or without LTRA and LABA; and (3) completed follow-up after 6 months of treatment. Children were excluded from the study if they had any underlying chronic disease (heart, lung, renal, neuromuscular, and primary or secondary immunodeficiency).

Ethics approval was obtained from the Ethics Committee of the Faculty of Medicine, Prince of Songkla University, Thailand (approval no. REC 65-123-1-1) prior to study initiation. The authors did not receive any funding support.

Data collection

Potential predictive factors were collected as follows: sex, weight, height, asthma onset, asthma presentation, comorbidities, atopic history, aeroallergen sensitization, exposure to smoking, pet ownership, asthma treatment including the type and dosage of ICS, and adherence to ICS.

Asthma control measurement

The main outcome of treatment was asthma symptom control at 6 months follow-up. The control level was evaluated according to the GINA guidelines.[3] The patient was considered "well-controlled" when none of the four following criteria were present in the previous 4 weeks: 1) daytime asthma symptoms more than twice a week, 2) nighttime asthma symptoms more than once a week 3) symptoms disturbing normal activity more than once a week, and 4) use of rescuer more than twice a week. The patient was considered "partly controlled" if 1–2 symptoms were present and "uncontrolled" if 3–4 symptoms were present. The combination of the latter two groups was classified as "poorly controlled." The primary outcome was the factors associated with poorly controlled asthma 6 months after the initiation of ICS.

Definitions

Asthma characteristics were determined at the initial stage before ICS treatment and were defined as (1) intermittent if the child had recurrent wheezing symptoms requiring bronchodilator rescue treatment and was symptom-free during episodes or (2) persistent if the child still had symptoms of cough or wheezing between exacerbation episodes.

Atopic history and asthma comorbidities, including food allergy, atopic dermatitis, AR, and obstructive sleep apnea, were defined based on physician diagnostic records.

AR was considered if the child had symptoms of rhinitis (sneezing, runny or blocked nose, and nasal itching) and was diagnosed by a physician. AR severity was classified according to the Allergic Rhinitis and Its Impact on Asthma guideline.[11]

Data of medication adherence was extracted from the follow up record forms for asthma patients attending the asthma clinic. In the record form, caregivers were asked how many doses were missed per month. Then, the missed doses were divided by the prescription dose per month. Adherence was defined as poor if < 80% was used.

A skin prick test involving common aeroallergens was performed with Uni-test devices (ALK-Abello, Royston Lane, Round Rock, Texas, USA) and 12 standardized aeroallergen extracts from Greater Pharma (Phutthamonthon, Nakhon Pathom, Thailand) and AllerTech (Lumphini, Pathum Wan, Bangkok). The aeroallergen included: grass pollen (Johnson grass, acacia, careless weeds), molds (Alternaria, Aspergillus mix, *Candida albicans*), pets (cat pelt, dog epithelium), and insects (*Dermatophagoides pteronyssinus* [*Dp*], *Dermatophagoides farinae* [*Df*], American cockroach, German cockroach). Histamine for positive control and glycerin for negative control were also performed for each patient. A mean wheal diameter of 3 mm greater than that of the negative control was considered test-positive. Polysensitization was defined as sensitization to two or more allergens.

Statistical analysis

Data were analyzed using R software version 4.1.4 (R Foundation for Statistical Computing, Vienna, Austria). Descriptive data are presented as percentages, means (standard deviations), and medians (interquartile range [IQR]). Participant characteristics were compared between the two groups (well- and poorly controlled) using the chi-square or Fisher's exact test for the proportion of each categorical variable (sex, obesity, atopic status, exposure to smoking, pet ownership, and asthma presentation). Continuous data (age at first wheezing and at receiving ICS) were compared based on the distribution of the data using the mean (Student's t-test) and median (Mann–Whitney U test). Multiple logistic regression analysis was performed to examine factors associated with poorly controlled asthma. Variables with $p < 0.2$ in the univariate analysis were initially included, and model reduction was performed using the backward elimination variable selection method. Statistical significance was set at $p < 0.05$.

A nomogram was developed for predicting poor asthma control. The performance of the nomogram in the training set was evaluated using the area under the receiver operating characteristic curve (AUC). A calibration plot with bootstrap samples was used to show the agreement between the predicted probabilities of the model.

Results

Patient characteristics

A total of 2,540 patient records were initially reviewed, and 165 eligible patients were included in the study (**Figure 1**). The median age (IQR) of the participants was 8.5 (7, 10.4) years, and 59.4% were males. Among the patients, 117 (71.8%) presented with intermittent asthma and the remaining had persistent asthma. The frequency of asthma exacerbation requiring bronchodilator rescue treatment in the year before treatment was 1–2 times in 52.5%, 3–4 times in 28.7%, and more than four times in 11.9% of the children; 6.9% had no exacerbation. All patients with no exacerbation in the past year had previous history of exacerbation (but not within 12 months, ie., 13 months) and the presenting symptoms before ICS prescription were persistent daytime or nighttime cough or wheezing. Hospital admission in the past 12 months was observed in 36% of patients. A history of severe exacerbation requiring intensive care unit admission and endotracheal intubation was found in 1.8% and 1.2% of patients, respectively. The rates of AR at the initial visit and 6 months after ICS treatment were 80.5% and 84%, respectively. Skin prick tests were performed in 123/165 (74.5%) patients, and 108 (87.8%) were positive for at least one aeroallergen. Of the 108 patients with a positive test result, monosensitization and polysensitization were found in 9.3% and 90.7% of the patients, respectively. The first four common allergens were *Df* (78%), *Dp* (77.2%), German cockroaches (44.7%), and American cockroaches (41%).

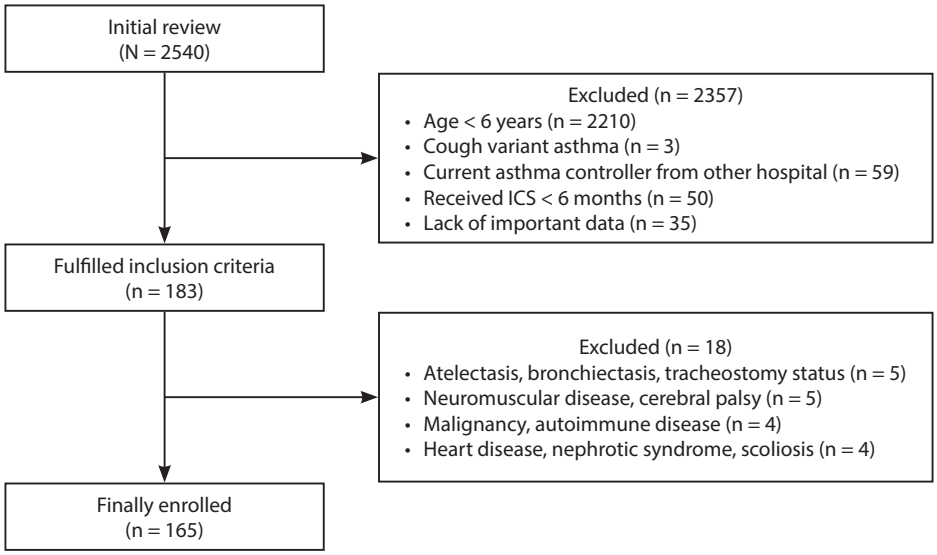

Figure 1. Study design and flow diagram.

Abbreviations: ICS, inhaled corticosteroid

Treatment outcomes and associated factors

After 6 months of asthma treatment, poor medication adherence (< 80% used) was observed in 19 (11.5%) patients. Of the total, 132 (80%) patients had well-controlled asthma symptoms, and 33 (20%) patients had poorly controlled symptoms. To compare the well-controlled and poorly controlled groups, various characteristics that were considered as potentially associated factors were examined. The variables that differed significantly between the well-controlled and poorly controlled groups were a history of more than four exacerbations in the 12 months before ICS treatment, presence of moderate to severe AR symptoms at the 6-month follow-up visit, and poor adherence to asthma medications. There were no significant differences in other variables, including patient and asthma characteristics, type of medication used (**Table 1**), or type of sensitization (**Table 2**).

Table 1. Characteristics of participants according to the level of asthma control. (n = 165)

Characteristic	n	Well-controlled group (n = 132)	Poorly controlled group (n = 33)	*p* value
Sex, male, n (%)	165	79 (59.8)	19 (57.6)	0.97
BMI (kg/m^2), median (IQR)	165	16.5 (14.7, 21.4)	16 (15.2, 18.4)	0.34
Age at first wheezing, years, median (IQR)	165	4 (2, 6.3)	2.5 (1, 5.8)	0.12
Age at asthma diagnosis, years, mean (SD)	165	6.3 (2.7)	5.6 (2.4)	0.20
Age at asthma treatment, years, median (IQR)	165	8.5 (6.9, 10.6)	8.7 (7.3, 9.6)	0.69
Asthma presentation	163			0.61
Intermittent		95 (73.1)	22 (66.7)	
Persistent		35 (26.9)	11 (33.3)	
Asthma exacerbations in the past year	160			0.03*
≤ 4		116 (91.3)	25 (75.8)	
> 4		11 (8.7)	8 (24.2)	
Allergic rhinitis at 6 months of ICS therapy	162			< 0.001*
No		22 (16.9)	4 (12.5)	
Mild		106 (81.6)	20 (62.5)	
Moderate to severe		2 (1.5)	8 (25)	
Atopic dermatitis	72	8 (14.5)	5 (29.4)	0.28
Food allergy	135	12 (11.1)	2 (7.4)	0.73
Obstructive sleep apnea	89	19 (26.8)	8 (44.4)	0.24
Passive smoking	102	24 (31.2)	10 (40)	0.57
Pet ownership	87	24 (36.9)	9 (40.9)	0.94
Maternal asthma	129	7 (6.9)	3 (11.1)	0.44
Paternal asthma	129	12 (11.8)	2 (7.4)	0.73
Sibling asthma	128	14 (13.9)	7 (25.9)	0.15
Maternal allergic rhinitis	120	16 (16.7)	7 (29.2)	0.24
Paternal allergic rhinitis	120	19 (19.8)	2 (8.3)	0.24
Sibling allergic rhinitis	120	8 (8.3)	1 (4.2)	0.68

Table 1. (Continued)

Characteristic	n	Well-controlled group (n = 132)	Poorly controlled group (n = 33)	*p* value
Medication	165			
Type of ICS				0.49
Fluticasone MDI		14 (10.7)	4 (12.1)	
Fluticasone DPI		11 (8.3)	3 (9.1)	
Budesonide MDI		32 (24.2)	4 (12.1)	
Budesonide DPI		75 (56.8)	22 (66.7)	
ICS level	165			0.15
Low		52 (39.4)	8 (24.2)	
Medium		77 (58.3)	23 (69.7)	
High		3 (2.3)	2 (6.1)	
LABA	165	26 (19.7)	6 (18.2)	1
Montelukast	165	14 (10.6)	5 (15.2)	0.54
GINA treatment	165			0.35
Step 2		43 (32.6)	6 (18.2)	
Step 3		68 (51.5)	21 (63.6)	
Step 4		21 (15.9)	6 (18.2)	
Intranasal corticosteroid	165	90 (68.2)	27 (81.8)	0.18
Time of complete 6- month asthma controller use	165			0.33
January–March		28 (21.2)	3 (9.1)	
April–June		34 (25.8)	12 (36.35)	
July–September		42 (31.8)	12 (36.35)	
October–December		28 (21.2)	6 (18.2)	
Poor adherence to ICS	165	10 (7.6)	9 (27.3)	0.004*

The total value may vary because of missing values.
IQR, interquartile range; SD, standard deviation; BMI, body mass index; ICS, inhaled corticosteroid; MDI, metered-dose inhaler; DPI, dry powder inhaler; LABA, long acting beta-2 agonist; GINA, Global Initiative for Asthma

Table 2. Type of sensitization and aeroallergens according to the level of asthma control. (n = 123)

	Well-controlled group (n = 94)	Poorly controlled group (n = 29)	*p* value
Type of sensitization			0.42
No sensitization	12 (12.8)	3 (10.3)	
Monosensitization	6 (6.4)	4 (13.8)	
Polysensitization	76 (80.8)	22 (75.9)	
Type of common aeroallergen			
Dermatophagoides farinae	75 (79.8)	21 (72.4)	0.56
Dermatophagoides pteronyssinus	73 (77.7)	22 (75.9)	1
German cockroach	41 (43.6)	14 (48.3)	0.82
American cockroach	41 (44.1)	9 (31)	0.30
Johnson grass	21 (22.3)	5 (17.2)	0.74

Table 3. Multiple logistic regression analysis of factors associated with poor asthma control.

	Crude OR (95%CI)	Adjusted OR (95%CI)	*p*
> 4 exacerbations in the past year	3.45 (1.26, 9.5)	3.39 (1.06, 10.83)	0.04
Allergic rhinitis			
Mild	1.03 (0.32, 3.32)	1.15 (0.32, 4.14)	0.83
Moderate to severe	21 (3.2, 137.98)	21.93 (2.97, 62.05)	0.002
Poor adherence to ICS	5.04 (1.81, 14.08)	4.16 (1.32, 13.12)	0.02

OR, odds ratio; CI, confidence interval ICS, inhaled corticosteroid

Nomogram and predictive performance

Based on multivariate logistic regression, a nomogram for predicting the risk of poorly controlled asthma was developed by incorporating three variables: the number of exacerbations, AR, and adherence to ICS. The impact of each predictor on the risk of poor asthma control is presented using a nomogram (**Figure 2**). The final scoring system allowed the calculation of a predictive score (range, 0–200 points) to predict the risk. We stipulated that an AUC of 0.737 would guarantee discriminative ability of our scoring system (**Figure 3a**). In the calibration plot, the predicted probability is plotted against the actual probability of poor control. The calibration plot showed agreement with the predicted probabilities in our model, with a mean absolute error of 0.037, which represents perfect calibration (**Figure 3b**).

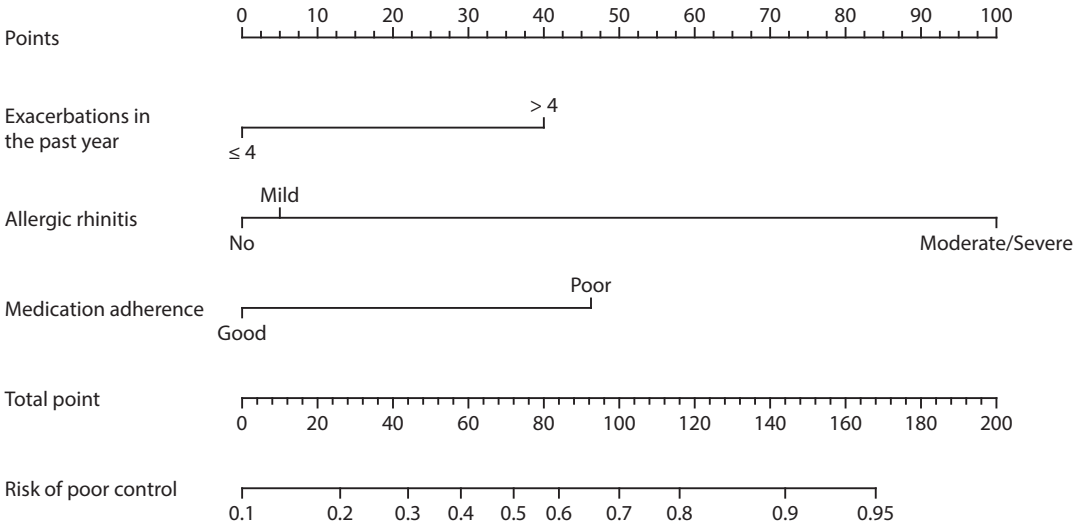

Figure 2. Nomogram to estimate the risk of poor asthma control after 6 months of inhaled corticosteroid therapy.

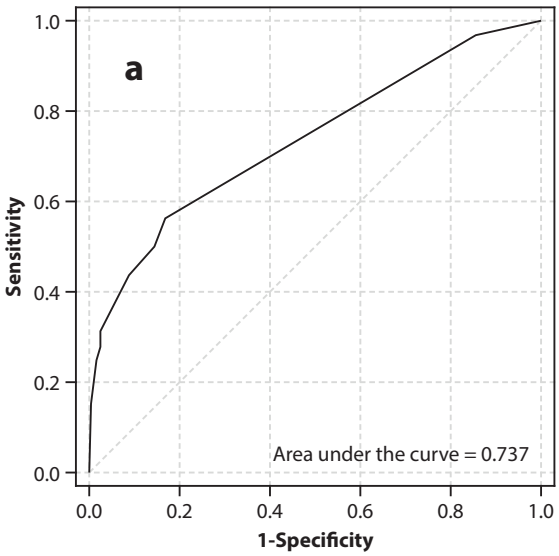

Figure 3. Predictive scores for poorly controlled asthma.

(a) Receiver operating characteristic (ROC) curve for the prediction tool and area under the curve (AUC) of 0.737.

(b) The calibration plot of the predictive tool (assessed using bootstrap validation) shows the predicted probability of 500 random-repetition samples (orange line). The ideal line (dashed line) indicates a perfect calibration. The corrected bias line (blue line) is locally weighted close to the line of equality, with a mean absolute error of 0.037.

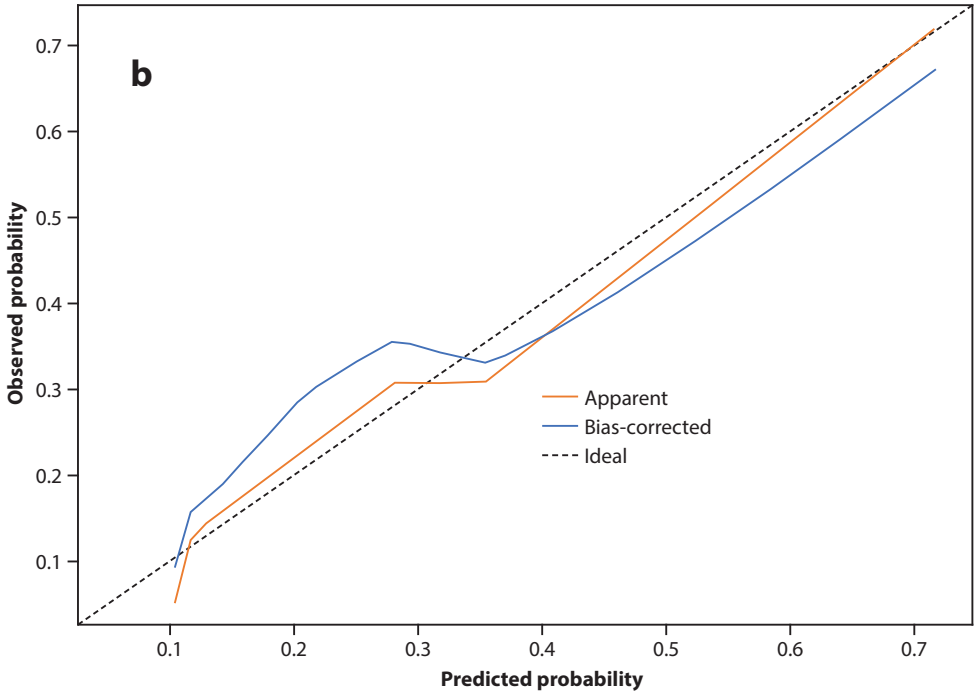

Figure 3. (Continued)

Discussion

This retrospective study presents data from a tertiary hospital concerning the rate of poorly controlled asthma after receiving ICS for 6 months in a sample of children aged 6–15 years. The rate of poorly controlled asthma was 20%. Previous studies reported varying rates of asthma control. Our findings were similar to those of a study in tertiary hospitals in China, which reported that asthma is uncontrolled in 19.9% of children aged 2–16 years[5] and to those of study in a pediatric chest clinic in Nigeria, which reported a rate of 17.9% in children aged 2–14 years.[6] Previous studies have shown that the rate of poor asthma control was high in studies performed in school-based settings using a questionnaire survey; for example, a study in Canadian children aged 5-13 years found that the rate of poor asthma control was 75%,[12] and in Ugandan children aged 5-17 years found the rate was 45.5%.[13] The factor responsible for the high rate of poor control in these studies was the low rate of asthma controller medication use, which was 62% in the Canadian study and 6.7% in the Ugandan study.

We identified three factors that were independently associated with poor asthma control: more than four exacerbations in the year before ICS treatment, the presence of moderate to severe AR, and poor medication adherence. The rational for using a cut point of four exacerbations in the 12 months was due to the initial analysis finding no difference for the rate of poor control asthma in children having one to four exacerbations; however, the rate was significantly different when the exacerbation was above four. The finding of frequent exacerbations before commencement of treatment as a risk factor for poor response to ICS could be explained by the severity of the disease. A previous study on adolescents and adults with asthma found that the frequency of asthma exacerbation increases with the severity of the disease.[14] Our findings suggest that more severe disease may be more difficult to control than less severe disease. The presence of asthma exacerbation indicates an accentuation of the existing inflammatory process. A recent systematic review of 26 eligible articles showed that asthma exacerbation in children is associated with an increased risk of future exacerbation.[15] This finding emphasizes the importance of early treatment in children with asthma before the development of repeated exacerbations. The benefit of early treatment in children with asthma is not only symptom control and reduction of the risk of severe exacerbations but also preservation of lung function. A previous study provided evidence that asthma exacerbations are associated with a decline in lung function, which is attenuated when patients are treated with ICS.[16]

In this study, the prevalence of AR in patients with asthma was 84.2%, which is slightly higher than those of previous studies in the Netherlands[9] and New York, USA,[16] which reported rates of 76.2% and 63%, respectively. The relation between AR and asthma has been highlighted that these often co-exist in the same patients.[11] Although our patients with both asthma and AR were treated with intranasal corticosteroids during the course of 6 months follow-up, we found that some patients still had

moderate-to-severe AR symptoms, which were identified as a strong predictor of poorly controlled asthma. Our findings support those of previous studies that found that children with concurrent AR are more likely to have poor asthma control.[13,17] AR is a disease of the upper airways, which consists of the nasal passages and paranasal sinuses, whereas asthma is a disease of the lower airways, which consists of the bronchi and bronchioles. A connection between upper and lower airway diseases has been observed, and the concept of a "united airway disease" has been highlighted. Patients with AR also have lower airway hyperresponsiveness, which increases in severity if the AR symptoms are uncontrolled.[18,19] Thus, controlling AR symptoms also helps asthma control.

The third factor associated with poor asthma control was poor medication adherence. In our study, the rate of poor medication adherence was 11.5%, which was lower than that reported in a tertiary pediatric asthma outpatient clinic in Denmark (54%).[20] Previous studies have demonstrated the effect of medication adherence on asthma outcomes in terms of poor asthma control[5] and severe asthma exacerbation.[21] This finding indicates that health care providers must be aware of medication adherence when treating children with asthma, particularly those with uncontrolled asthma symptoms. The parents are the key people that take responsibility for making sure that the medication is administered to their child. When the child grows up to an adolescent and; furthermore, an adult, there is a shift of responsibility for administering their own medication. A recent study found that younger age at diagnosis of asthma < 16 years was a significant risk factor for poor medication adherence in adults with moderate to severe asthma.[22] The authors mentioned the possibility that established poor adherence in patients with childhood-onset asthma might be carried over to adulthood. The result of this study emphasizes that promoting medication adherence should be conducted early during the childhood period and this should be regularly checked to identify specific barriers for each patient as well as adopting suitable techniques to overcome them.

In this study, a prognostic model was created by combining three associated factors that general physicians can use to predict response to treatment in children with asthma. The nomogram had a total score of 200, with a prediction risk ranging from 0 to 100%. The AUC of the developed model was 0.737, indicating a moderate performance level. The following is an example of the use of a nomogram. A doctor started ICS therapy to a child with asthma who had history of five episodes of asthma exacerbations in the past year (40 points); the patient also had moderate AR (100 points). During treatment, the patient showed good medication adherence (0 point). The total score calculated is 140 points; hence, the probability of poor asthma control observed in the nomogram is 90%. In this case, there is a very high risk of poor asthma control; therefore, early intervention, including intensive management of comorbid allergic rhinitis, should be considered. However, if the child has poor medication adherence, an intervention to improve adherence should be considered.

Limitation

This study has several limitations. It is a retrospective study; thus, there was a presence of missing data for certain important factors. The sample size used in this study was relatively small, and this may have limited the power to detect other associated factors. This study included children aged 6-15 years; however, children aged 12-15 years might have different factors associated with poor asthma control. This is due to younger children may have higher rates of respiratory infections, which can affect asthma control symptoms. In addition, the prediction score was performed in a single center and external validation using an independent sample was not performed in this study. A validation study should be conducted to validate the predictive model in addition to further work being needed to confirm its use in different populations. As 70% of the participants in this study had intermittent asthma, the prediction model should be tested in other setting with different asthma severities to find out whether there is a difference in the predictive score. However, as there is no practical tool available to predict the outcome of ICS treatment in children with asthma, our model could be a basis for further studies.

Conclusions

A nomogram for predicting symptom control in children with asthma receiving ICS therapy was developed by including three associated factors. The model is simple and inexpensive, and can help clinicians evaluate the chances of poor asthma control, which could facilitate the management of each individual child with asthma.

Acknowledgements

none

Funding

The authors did not receive any funding support.

Conflicts of Interest

The authors declare no conflicts of interest.

Author Contributions

- Wanaporn Anuntaseree, conceptualized and designed the study, collected data, carried out the analyses, drafted the initial manuscript, reviewed and revised the manuscript.
- Kanokpan Ruangnapa, conceptualized and designed the study, and providing critical revisions.
- Araya Yuenyongviwat, conceptualized and designed the study, and providing critical revisions.
- Kantara Saelim, conceptualized and designed the study, and providing critical revisions.
- Pharsai Prasertsan, conceptualized and designed the study, and providing critical revisions.

Ethics Approval

Ethics approval was obtained from the Ethics Committee of the Faculty of Medicine, Prince of Songkla University, Thailand (approval no. REC 65-123-1-1) prior to study initiation.

Consent to Participate

Not applicable.

Consent for Publication

Not applicable.

References

1. Asher MI, Rutter CE, Bissell K, Chiang CY, El Sony A, Ellwood E, et al.; Global Asthma Network Phase I Study Group. Worldwide trends in the burden of asthma symptoms in school-aged children: Global Asthma Network Phase I cross-sectional study. Lancet. 2021;398:1569–80.
2. Suruki RY, Daugherty JB, Boudiaf N, Albers FC. The frequency of asthma exacerbations and healthcare utilization in patients with asthma from the UK and USA. BMC Pulm Med. 2017;17:74.
3. Global Initiative for Asthma[Internet]. Fontana: Global Initiative for Asthma; c2024 [cited 2024 Jun 1]. Global Strategy for Asthma Management and Prevention 2024; [about 1 screen]. Available from: www.ginasthma.org.
4. Papi A, Blasi F, Canonica GW, Morandi L, Richeldi L, Rossi A. Treatment strategies for asthma: reshaping the concept of asthma management. Allergy Asthma Clin Immunol. 2020;16:75.
5. Xiang L, Zhao J, Zheng Y, Liu H, Hong J, Bao Y, et al. Uncontrolled asthma and its risk factors in Chinese children: a cross-sectional observational study. J Asthma. 2016;53:699–706.
6. Kuti BP, Omole KO, Kuti DK. Factors associated with childhood asthma control in a resource-poor center. J Family Med Prim Care. 2017;6: 222–30.
7. Wu YF, Su MW, Chiang BL, Yang YH, Tsai CH, Lee YL. A simple prediction tool for inhaled corticosteroid response in asthmatic children. BMC Pulm Med. 2017;17:176.
8. Hedlin G, Bush A, Lødrup Carlsen K, Wennergren G, De Benedictis FM, Melén E, et al. Problematic severe asthma in children, not one problem but many: a GA2LEN initiative. Eur Respir J. 2010;36:196–201.
9. de Groot EP, Nijkamp A, Duiverman EJ, Brand PL. Allergic rhinitis is associated with poor asthma control in children with asthma. Thorax. 2012;67:582–7.
10. Forno E, Lescher R, Strunk R, Weiss S, Fuhlbrigge A, Celedón JC; Childhood Asthma Management Program Research Group. Decreased response to inhaled steroids in overweight and obese asthmatic children. J Allergy Clin Immunol. 2011;127:741–9.
11. Brożek JL, Bousquet J, Agache I, Agarwal A, Bachert C, Bosnic-Anticevich S, et al. Allergic rhinitis and its impact on asthma (ARIA) guidelines-2016 revision. J Allergy Clin Immunol. 2017;140: 950–8.
12. McGhan SL, MacDonald C, James DE, Naidu P, Wong E, Sharpe H, et al. Factors associated with poor asthma control in children aged five to 13 years. Can Respir J. 2006;13:23–9.
13. Mpairwe H, Tumwesige P, Namutebi M, Nnaluwooza M, Katongole T, Tumusiime J, et al. Asthma control and management among schoolchildren in urban Uganda: results from a cross-sectional study. Wellcome Open Res. 2019;4:168.
14. Moore WC, Bleecker ER, Curran-Everett D, Erzurum SC, Ameredes BT, Bacharier L, et al. Characterization of the severe asthma phenotype by the National Heart, Lung, and Blood Institute's Severe Asthma Research Program. J Allergy Clin Immunol. 2007;119:405–13.
15. Lowden R, Turner S. Past asthma exacerbation in children predicting future exacerbation: a systematic review. ERJ Open Res. 2022;8: 00174-2022.
16. O'Byrne PM, Pedersen S, Lamm CJ, Tan WC, Busse WW; START Investigators Group. Severe exacerbations and decline in lung function in asthma. Am J Respir Crit Care Med. 2009;179:19–24.
17. Stern J, Chen M, Fagnano M, Halterman JS. Allergic rhinitis co-morbidity on asthma outcomes in city school children. J Asthma. 2023; 60:255–61.
18. Liu Y, Sha J, Meng C, Zhu D. Mechanism of lower airway hyperresponsiveness induced by allergic rhinitis. J Immunol Res. 2022; 2022:4351345.
19. Tenero L, Vaia R, Ferrante G, Maule M, Venditto L, Piacentini G, et al. Diagnosis and management of allergic rhinitis in asthmatic children. J Asthma Allergy. 2023;16:45–57.
20. Marckmann M, Hermansen MN, Hansen KS, Chawes BL. Assessment of adherence to asthma controllers in children and adolescents. Pediatr Allergy Immunol. 2020;31:930–7.
21. Engelkes M, Janssens HM, de Jongste JC, Sturkenboom MC, Verhamme KM. Medication adherence and the risk of severe asthma exacerbations: a systematic review. Eur Respir J. 2015;45:396–407.
22. Masaki K, Miyata J, Kamatani T, Tanosaki T, Mochimaru T, Kabata H, et al. Risk factors for poor adherence to inhaled corticosteroid therapy in patients with moderate to severe asthma. Asian Pac J Allergy Immunol. 2023;41:113-20.