ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 18, Issue 6, 2025

Online - 2455-3891
Print - 0974-2441

Research Article

RISK FACTORS, DIAGNOSTIC CHALLENGES, AND MANAGEMENT OUTCOMES IN PEDIATRIC ASTHMA (AGES 1–12 YEARS): A PROSPECTIVE COHORT STUDY ALIGNED WITH THE GINA GUIDELINES

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Received: 04 March 2025, Revised and Accepted: 19 April 2025

ABSTRACT

Objective: To identify risk factors for uncontrolled asthma, to evaluate diagnostic alignment with the Global Initiative for Asthma (GINA) criteria, and to assess management outcomes in children aged 1–12 years.

Methods: A prospective cohort study enrolled 378 children (1–12 years) diagnosed with asthma at SVBCH Hospital, Silvassa, from January 2022 to December 2023. GINA criteria defined asthma and uncontrolled disease. Multivariate logistic regression was used to identify risk factors, and management outcomes were analyzed using Cox proportional hazards models.

Results: Of 378 children (57% male, median age 6 years), 36% (n=136) had uncontrolled asthma. Significant risk factors included tobacco smoke exposure (adjusted odds ratio [aOR] 2.2, 95% confidence interval [CI]: 1.4–3.5, p<0.001), medication non-adherence (aOR 3.0, 95% CI: 1.8–4.9, p<0.001), and atopic dermatitis (aOR 1.7, 95% CI: 1.1–2.8, p=0.01). Use of controller medications reduced exacerbation risk by 42% (Hazard ratio [HR] 0.58, 95% CI: 0.42–0.79, p<0.001), and asthma action plans were associated with a 28% reduction in emergency visits (HR 0.72, 95% CI: 0.53–0.97, p=0.03).

Conclusion: Strengthening GINA-compliant diagnosis, caregiver education, and environmental modifications are critical to improving outcomes in young children with asthma.

Keywords: Asthma, Global Initiative for Asthma guidelines, Spirometry, Forced expiratory volume in one second 1.

 DOI: http://dx.doi.org/10.22159/ajpcr.2025v18i6.54354. Journal homepage: https://innovareacademics.in/journals/index.php/ajpcr

INTRODUCTION

Pediatric asthma is a prevalent chronic respiratory disorder affecting 5–10% of children globally, contributing to frequent hospitalizations, school absenteeism, and diminished quality of life [1]. Asthma is a chronic respiratory condition characterized by persistent inflammation of the airways, often leading to airflow limitation. Individuals with asthma typically exhibit reduced lung function. A review of previous research indicates that asthma symptoms follow a distinct circadian rhythm, with fluctuations in severity throughout the day [2]. Notably, approximately 42% of individuals with active asthma report symptom onset before the age of 16. This condition poses unique diagnostic and management challenges, particularly in children aged 1–12 years, due to overlapping symptoms with transient viral wheezing and the limited applicability of objective diagnostic tools such as spirometry in younger populations [3]. The Global Initiative for Asthma (GINA) guidelines aim to standardize care by recommending symptom-based assessments (recurrent wheezing, cough, or dyspnea) and bronchodilator reversibility testing (≥12% improvement in forced expiratory volume in one second [FEV1] post-bronchodilator) for children aged 6 years and older [4]. However, adherence to these guidelines remains inconsistent, particularly in resource-constrained regions, leading to delayed diagnoses and suboptimal management [5].

Children under 5 years of age face heightened diagnostic uncertainty, as spirometry – a cornerstone of asthma confirmation in older children – is often impractical due to technical and cooperative limitations [6]. As a result, health-care providers often depend on caregiver-reported symptoms and observed treatment response when initiating asthma management in young children. However, this approach carries the risk of both overdiagnosis – potentially leading to unnecessary medication use – and underdiagnosis, which can delay essential therapy. For example, wheezing caused by viral infections, a frequent occurrence in preschool-aged children, is sometimes incorrectly labeled as asthma, resulting in extended use of corticosteroids without proven benefit. On the other hand, failing to accurately diagnose asthma can postpone the initiation of controller medications, increasing the risk of complications and a higher health-care burden [7,8].

Compounding these challenges are modifiable risk factors strongly associated with uncontrolled asthma. Exposure to environmental tobacco smoke is reported in 20–40% of cases, exacerbates airway inflammation, and increases the frequency of exacerbation [9]. Pediatric asthma medication development faces unique challenges due to physiological differences across age groups, concerns about excipient safety, and the need for age-appropriate delivery devices. Limited profitability, ethical constraints in clinical trials, and unclear regulatory guidelines further hinder progress. Inhaler techniques require caregiver involvement, especially in younger children. In addition, poor adherence to controller medications – often driven by caregiver fears, misunderstandings, or difficulty administering treatment – remains a major barrier to effective asthma control. Addressing these issues requires a multifaceted approach involving tailored drug formulations, caregiver education, and supportive policies to ensure safe, effective, and accessible treatment for children with asthma [10,11].

Prospective cohort studies, although less common than retrospective analyses, provide dynamic insights into real-world asthma management by capturing longitudinal data on diagnosis, treatment adherence, and clinical outcomes. This prospective study, conducted at SVBCH Hospital, Silvassa, enrolled 378 children aged 1–12 years who

were diagnosed with asthma between January 2022 and December 2023. This study aimed to evaluate adherence to the GINA diagnostic criteria in a resource-limited setting, identify modifiable risk factors for uncontrolled asthma, and assess the impact of guideline-based interventions on reducing exacerbations and hospitalizations. By focusing on a prospective design, this research addresses critical gaps in understanding the barriers to effective asthma care while aligning with global efforts to prioritize evidence-based, equitable management strategies.

METHODS

Study design and setting

This prospective cohort study was conducted at SVBCH Hospital, Silvassa, a tertiary care center catering to urban and rural populations. The study enrolled children aged 1–12 years who were newly diagnosed with asthma between January 2022 and December 2023. These participants were followed for 12 months to assess their asthma control, exacerbation rates, and treatment adherence.

Sample size calculation

The sample size was determined using the standard formula for comparing two proportions, accounting for a 95% confidence interval (CI) ($Z\alpha/2 = 1.96$) and 80% statistical power ($Z\beta = 0.84$). Based on a reported prevalence of uncontrolled asthma (35%) and an expected reduction to 25% following intervention, the estimated sample size was 324 participants. To accommodate an anticipated attrition rate of 15%, the final sample size was set at 378 children.

The sample size was calculated using the following formula for two proportions:

$$n=(Z\alpha/2+Z\beta)2\cdot p(1-p)(p1-p2)2n=(p1-p2)2(Z\alpha/2+Z\beta)2\cdot p(1-p)$$

Where:

- $Z\alpha/2=1.96 Z\alpha/2=1.96$ (95% CI), $Z\beta=0.84 Z\beta=0.84$ (80% power)
- p1=35% (uncontrolled asthma prevalence [8])
- p2=25% (expected reduction).

This yielded n=324. Accounting for 15% attrition, the final sample size was 378.

Participants, variables, and data collection

Children aged 1–12 years were enrolled based on diagnostic criteria set by the GINA. Inclusion criteria included a clinical history of recurrent wheezing, cough, or dyspnea, and for children aged 6 years and above, a ≥12% improvement in FEV1 following bronchodilator administration was required, where spirometry was feasible. For younger children, a symptom-based diagnosis was made after ruling out differential diagnoses such as bronchiolitis and cystic fibrosis. Exclusion criteria included children with pre-existing chronic pulmonary diseases (e.g., cystic fibrosis and bronchiectasis) and those with incomplete follow-up, defined as fewer than three clinical visits during the 12-month study period. These criteria were established to ensure diagnostic accuracy and reduce potential confounding.

The primary outcome was uncontrolled asthma, identified using GINA standards as meeting at least one of the following: two or more exacerbations per year requiring systemic corticosteroids, frequent use of rescue inhalers (more than twice per week), or hospitalization due to asthma complications.

Exposure variables were categorized into four domains: Demographic factors: Age, sex, and socioeconomic status (measured through insurance type). Environmental factors: Tobacco smoke exposure as reported by caregivers. Clinical factors: Presence of allergic rhinitis, atopic dermatitis, and obesity (body mass index ≥95th percentile for age and sex). Management factors: Adherence to controller medications, evaluated using prescription refill records with a proportion of days covered ≥80%, and the use of asthma action plans (AAPs), based on caregiver reports.

Data were sourced from electronic health records, including clinical documentation, spirometry results, prescription history, and hospital records. To enhance validity, caregiver-reported tobacco exposure and adherence information were verified through structured interviews during follow-up, ensuring a thorough evaluation of asthma determinants.

Ethical approval

The study was approved by the Institutional Ethics Committee (IEC) of NAMO Medical Education and Research Institute and SVBCH Hospital (Approval Number: IEC/NMMC/2022/45). Written informed consent was obtained from the caregivers of all the participating children before enrollment.

Statistical analysis

Data were analyzed using STATA 17.0. Continuous variables (e.g., age) were summarized as medians with interquartile ranges (IQRs), whereas categorical variables (e.g., sex, comorbidities) were reported as frequencies and percentages. Multivariate logistic regression identified independent risk factors for uncontrolled asthma, adjusting for age, sex, and socioeconomic status. Results were expressed as adjusted odds ratios (aORs) with 95% CIs. The impact of medication adherence was assessed using Kaplan–Meier survival analysis, comparing exacerbation-free survival between adherent and non-adherent groups, with significance tested through the log-rank test ($p<0.05$). Sensitivity analyses validated model assumptions. The methodology adhered to STROBE guidelines, ensuring statistical rigor, reliability, and reproducibility of study findings.

RESULTS

Table 1 presents the demographic and clinical characteristics of the 378 children included in this study, with a median age of 6 years (IQR: 3–9 years), 57% of whom were male. Among the participants, 36% (n=136) had uncontrolled asthma. The majority (68%, n=257) resided in urban areas. Common comorbidities included allergic rhinitis (38%, n=144) and atopic dermatitis (22%, n=83). In addition, 27% (n=102) of children were exposed to tobacco smoke.

Table 2 outlines the significant risk factors associated with uncontrolled asthma in the study population. Tobacco smoke exposure was a strong predictor, with an aOR of 2.2 (95% CI: 1.4–3.5, $p<0.001$). Medication non-adherence was most strongly associated with uncontrolled asthma (aOR 3.0, 95% CI: 1.8–4.9, $p<0.001$). In addition, atopic dermatitis was identified as a significant risk factor (aOR 1.7, 95% CI: 1.1–2.8, p=0.01).

Table 3 presents the impact of management strategies on asthma outcomes. The use of controller medications significantly reduced the risk of exacerbations by 42%, with a Hazard ratio (HR) of 0.58 (95% CI: 0.42–0.79, $p<0.001$). In addition, the implementation of AAPs was associated with a 28% reduction in emergency room visits (HR 0.72, 95% CI: 0.53–0.97, p=0.03).

DISCUSSION

This prospective cohort study provides critical insights into the risk factors, diagnostic adherence, and management outcomes of pediatric asthma in children aged 1–12 years, aligning with the GINA guidelines. Our findings underscore the persistent challenges in asthma care, particularly in resource-limited settings, while highlighting actionable strategies to reduce morbidity. Below, we contextualize our results within existing literature, discuss their clinical implications, and outline future research directions. This study identified a subset of children with severe, uncontrolled asthma despite guideline-based therapy, a finding consistent with Fitzpatrick *et al*., who characterized severe pediatric asthma as a heterogeneous condition influenced by environmental, immunological, and genetic factors [12]. Fitzpatrick's work within the

Table 1: Demographic and clinical characteristics (N=378)

Characteristic	Total	Uncontrolled asthma	Controlled asthma	p-value
Age, median (IQR)	6 (3–9)	5 (2–8)	7 (4–10)	<0.001
Male, n (%)	216 (57)	78 (57)	138 (57)	0.92
Urban residence, n (%)	257 (68)	98 (72)	159 (66)	0.04
Tobacco exposure, n (%)	102 (27)	58 (43)	44 (18)	<0.001

Data are presented as median (IQR) or number (percentage). Sample size for each variable: n=378. Statistical comparisons are based on the Mann–Whitney U test or the Chi-square test. IQR: Interquartile range

Table 2: Risk factors for uncontrolled asthma

Risk factor	aOR	95% CI	p-value
Tobacco smoke exposure	2.2	1.4–3.5	<0.001
Medication non-adherence	3.0	1.8–4.9	<0.001
Atopic dermatitis	1.7	1.1–2.8	0.01

Data are based on multivariate logistic regression. aOR with 95% CI are presented. All analyses adjusted for age, sex, and socioeconomic status.
aOR: Adjusted odds ratio, CI: Confidence interval

Table 3: Management outcome

Strategy	Outcome	HR	95% CI	p-value
Controller medications	Reduced exacerbations	0.58	0.42–0.79	<0.001
Asthma action plans	Reduced ER visits	0.72	0.53–0.97	0.03

Data are presented as HR with 95% CI, based on the Cox proportional Hazards model. Exacerbation-free survival and ER visits assessed over 12 months.
HR: Hazard ratio, CI: Confidence interval

National Heart, Lung, and Blood Institute's Severe Asthma Research Program highlights the importance of phenotyping to tailor therapies, particularly in cases refractory to standard inhaled corticosteroids (ICS). In our cohort, 15% of the children with uncontrolled asthma presented features of severe asthma (e.g., frequent exacerbations despite high-dose ICS), underscoring the need for advanced therapies such as biologics, as recommended by Duncan *et al*. [13].

Tobacco smoke exposure emerged as a significant predictor of uncontrolled asthma (aOR 2.2, 95% CI 1.4–3.5), consistent with meta-analyses by Wang *et al*., who reported a 1.7-fold increased risk of exacerbations in children exposed to secondhand smoke [9]. Our findings align with global data emphasizing the need for public health interventions targeting household smoking, particularly in low-income communities where exposure rates remain high [10,13].

Medication non-adherence was the strongest predictor of poor outcomes (aOR 3.0, 95% CI 1.8–4.9), mirroring Grant et al. (2015), who identified adherence as a cornerstone of asthma control, with non-adherence rates exceeding 50% in preschoolers due to caregiver concerns about side effects and dosing complexity [13]. Our study extends these observations by demonstrating that adherence barriers are magnified in children aged 1–5 years, where only 38% of caregivers maintained ≥80% adherence, compared with 77% in older children. This disparity echoes Paracha *et al*., who linked poor adherence in preschoolers to logistical challenges in administering inhalers and fragmented care [14].

Comorbid atopic dermatitis (aOR 1.7, 95% CI 1.1–2.8) further exacerbates asthma severity, reinforcing the "atopic march" hypothesis explained by Hill and Spergel, wherein early allergic manifestations predict subsequent respiratory morbidity [15]. Similar trends were reported by Castro-Rodríguez *et al*., whose asthma predictive index highlighted the prognostic value of atopic comorbidities in young children [16].

Only 30% of children ≥6 years underwent spirometry, reflecting systemic barriers such as limited access to pulmonary function testing and training gaps among clinicians. This aligns with Dombkowski *et al*. [17], who noted that spirometry remains underutilized in primary care, leading to over-reliance on symptom-based diagnosis. While symptom-based approaches are pragmatic in younger children, they risk misdiagnosis, as viral wheezing – common in this age group – can mimic asthma.

Regular controller medication use reduced exacerbations by 42% (HR 0.58, 95% CI 0.42–0.79), corroborating GINA's emphasis on ICS as first-line therapy [5]. However, our adherence rates lag behind clinical trial benchmarks, where adherence often exceeds 80% under controlled conditions. Real-world studies, such as those by Levy *et al*., attributed this gap to socioeconomic disparities and inadequate caregiver education [18].

According to a review by Pegoraro *et al*. [19], AAPs reported improvement in asthma control and reduced emergency visits; pediatric-specific plans are scarce and inconsistent, often omitting critical instructions for caregivers and essential therapies. Despite this, only 55% of our cohort had AAPs, suggesting implementation gaps similar to those reported in low-resource settings globally.

Limitations in generalizability and need for multicenter validation

This study was conducted in a single tertiary care hospital, which may limit the generalizability of findings to populations with different health-care infrastructures. While the results align with previous studies, regional variations in health-care access, environmental exposures, and adherence behaviors may affect asthma control. A multicenter study involving diverse geographic locations (urban vs. rural, low-income vs. high-income settings) would enhance external validity. In addition, the 12-month follow-up period may not fully capture long-term asthma control trends or seasonal variations. Future studies should consider longer follow-up durations (2–5 years) to assess long-term medication adherence and disease progression.

Clinical and policy implications and future directions

Clinical and policy implications emphasize structured caregiver education on inhaler techniques, smoke avoidance, and AAP use, augmented by digital tools such as mobile apps to improve adherence. Expanding spirometry access and clinician training in GINA criteria, supported by community health workers, can reduce diagnostic errors in underserved areas. Policy reforms, such as subsidizing medications and AAPs, are vital to mitigate disparities. Future research should prioritize longitudinal studies to assess long-term outcomes, evaluate telehealth and digital adherence monitors, and conduct multicenter trials to validate scalable interventions across diverse global settings.

CONCLUSION

Our findings reaffirm the importance of GINA-guided asthma management while highlighting systemic and socioeconomic barriers to its implementation. By prioritizing caregiver education, equitable access to diagnostics, and policy reforms, health-care systems can reduce the global burden of pediatric asthma.

AUTHORS' CONTRIBUTIONS

The manuscript was written by Pushparaj Patil, and the data collection and analysis were done by Pushparaj Patil. Research was reviewed and edited by Zubair Khan, and a statistical analysis was done by Pushparaj Patil and Zubair Khan. The manuscript was finalized, edited, and submitted for publication by Pushparaj Patil.

CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

AUTHORS' FUNDING

None.

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