Risk factors for emergency department visit in a prospective open cohort of asthmatic children

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Research Article

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Abstract

Background

Risk factors of emergency department (ED) visits have mainly been obtained from hospital cohorts.

Objective

To evaluate risk factors for ED visits in asthmatic children in an out-of-hospital cohort.

Methods

We led a prospective study in an open cohort of 933 asthmatic children followed-up by a specialized pediatrician. We measured the annualized rate of ED visits since age two and described their characteristics at last visit.

Results

Mean age (± SD) at last visit was 11.1 ± 3.3 years, and the annualized rate of ED visit was 0.194 ± 0.356. Two groups were defined: one with no ED visits (n = 463), and the other with at least one ED visit (n = 470). The latter group included younger children, with multiple sensitizations and more frequent early atopic dermatitis, who reported having more inhaled corticosteroid (ICS) treatment and a more severe exacerbation rate in the three months prior to the last visit. Socioeconomic status did not influence the rate of ED visits. In a logistic regression, the absence of hospitalization before 2 years of age and of atopic dermatitis had odds ratios of 0.38 (95% confidence interval: 0.23–0.65) and of 0.57 (95% confidence interval: 0.42–0.79) respectively to predict at least one ED visit. When an asthmatic child had no early hospitalization and no atopic dermatitis, the relative risk of ED visit was decreased by 28%.

Conclusion

Asthmatic children with an absence of atopic dermatitis and hospitalization before two years of age are less prone to emergency department visit after age two.

What Is Known – What Is New

What is known: Risk factors for emergency department visit have been determined in asthmatic patients who previously visited the emergency department, which introduces biases. Significant impact of age, sex, disease severity, and socio-economic status on asthma morbidity have been demonstrated.

What is new: In an open cohort of asthmatic children followed-up in an out-of-hospital clinic, children with an absence of atopic dermatitis and hospitalization before two years of age are less prone to emergency department visit after age two.

Introduction

Emergency department (ED) visits are common in asthmatic children and ED visit rates have been related to hospitalization rates [1]. Along this line, ED visit count is a reliable predictor of future asthma hospitalization risk [2]. In a retrospective cohort study identifying factors associated with asthma exacerbation causing ED visits or hospitalizations in 490 asthmatic children, Ungar *et al.* showed that younger age, previous ED visits, nebuliser use, pet ownership and receipt of asthma education were significantly associated with more frequent exacerbations [3]. In this study, children with high income adequacy had 28% fewer exacerbations than children with low income adequacy, and children who were recruited from a physician's office or an asthma clinic had significantly fewer exacerbations [3]. These findings supported previous research demonstrating the significant impact of age, sex, disease severity, and socio-economic status on asthma morbidity [4]. In the latter study, the socioeconomic gradient of the likelihood of an inhaled corticosteroid prescription was most evident among children with mild-moderate asthma who were not under the care of an asthma specialist.

As it has been shown that 38% of ED visits for asthma exacerbation in children are potentially avoidable [5], identifying patients at higher risk of ED visits would allow healthcare resource utilization to decrease. An evidence-based clinical pathway for children and adolescents with moderate to severe exacerbations of acute asthma markedly has been shown to decrease the rate of hospitalization without an increased return to emergency care [6]. The determination of risk factors for ED visits may help to identify those that are modifiable and which could be implemented into a clinical pathway. Risk factors for ED visit have mainly been determined among patients who already visited the ED [1–3], which may introduce biases. Moreover, the health care system of the country may also introduce some bias. The main objective of this prospective study was to evaluate the risk factors of ED visits in an open cohort of asthmatic children followed-up in an out-of-hospital clinic by an asthma specialist. The secondary objective was to describe the risk factors of hospitalization.

Methods

This longitudinal study complied with The Strengthening the Reporting of Observational studies in Epidemiology (STROBE) guidelines (cohort study).

Participants

La Berma Cohort: This open cohort existing since 2009 is composed of children with asthmatic symptoms consulting in the La Berma out-of-hospital clinic. For this study, we included only children with a confirmed diagnosis of asthma: suggestive symptoms and a significant bronchodilator response (based on either sRaw [7] or FEV_1 [8]) during follow-up (at any time). The characteristics of each visit have been standardized [9] and are given in Table 1. All of the children had a written action plan for exacerbation management. Early wheezing was defined by the occurrence of at least three wheezing episodes before age two.

Table 1
Description of the 933 asthmatic children according to ED visit frequency.

Characteristics	Whole population N = 933	ED visit = 0 N = 463 (50%)	ED visit > 0 N = 470 (50%)	P value
Sex, female/male, n	330/603	164/299	166/304	0.974
Birth weight, g	3243 ± 556	3222 ± 567	3262 ± 547	0.328
Early wheezing, n (%)	424 (45)	196 (42)	228 (49)	0.058
Hospitalization before 2 years of age, n (%)	107 (11)	36 (8)	71 (15)	< 0.001
Skin prick tests, n	217	97	120	0.780
One positive test, n	340 (36)	143 (31)	217 (46)	< 0.001
More than one, n (%)	221	148	53	< 0.001
Negative, n	155	75	80	< 0.001
Non available, n	327 (35)	146 (32)	251 (53)	0.736
Atopic dermatitis before 2 years of age, n (%)	124	56	68	0.001
Maternal allergy excepting asthma, n	130	56	74	0.286
Paternal allergy excepting asthma, n	221	99	122	0.286
Maternal asthma, n	208	108	100	0.100
Paternal asthma, n	-48 ± 11 (918)	-48 ± 10 (455)	-48 ± 11 (463)	0.452
Best sRaw response (n tested)	+ 18 ± 12 (683)	+ 17 ± 11 (313)	+ 20 ± 12 (370)	0.303
Best FEV_1 response (n tested)	50	30	20	0.004
Universal health coverage, n	55	27	28	0.131
100% covered by social security, n	5 ± 4	6 ± 4	8 ± 5	0.935
Asthma specialist visits, n	**0.194 ± 0.356**	**0**	**0.386 ± 0.422**	< 0.001
Annualized rate of ED visit	**0.055 ± 0.161**	**0**	**0.110 ± 0.213**	
Annualized rate of hospitalisation				
Last follow-up visit	11.1 ± 3.3	10.8 ± 3.5	11.5 ± 3.2	0.002
	147.0 ± 19.8	145.4 ± 20.7	148.5 ± 18.9	0.020
	41.7 ± 15.8	40.2 ± 15.7	43.1 ± 15.9	0.007
	18.5 ± 3.4	18.2 ± 3.1	18.8 ± 3.6	0.007

sRaw is the specific airway resistance; FEV_1 is the forced expiratory volume in 1 s; BMI is the body mass index; LABA is long acting beta-agonist; ICS is inhaled corticosteroid; FVC is the forced vital capacity; TLC is the total lung capacity; FRC is the functional residual capacity and RV is the residual volume

Characteristics	Whole population N = 933	ED visit = 0 N = 463 (50%)	ED visit > 0 N = 470 (50%)	P value
Age, years	144 / 475 / 517	67 / 196 / 217	77 / 277 / 300	0.419 / < 0.001 / < 0.001
Height, cm	371 ± 200	357 ± 197	408 ± 243	0.006
Weight, kg	84	30	54	0.542
BMI, $kg.m^{-2}$	210 ± 51 (880)	211 ± 47 (444)	209 ± 54 (436)	0.008
Obesity (> 97.5th percentile), n	95 ± 14 (727)	94 ± 13 (345)	95 ± 14 (382)	0.546
LABA, n	100 ± 13	100 ± 13	100 ± 13	0.440
ICS, n	0.79 ± 0.07	0.79 ± 0.07	0.80 ± 0.08	0.980
Beclomethasone Equivalent Dose, µg	102 ± 11 (720)	102 ± 11 (343)	103 ± 12 (377)	0.295
Days with symptoms of last 3 months, n	100 ± 17	100 ± 17	100 ± 18	0.582
Severe exacerbation within last 3 months, n	110 ± 24	111 ± 23	109 ± 26	0.648
Baseline pulmonary function	146 ± 31 (554)	143 ± 27 (294)	149 ± 35 (260)	0.380
sRaw, % predicted, (n tested)	100 ± 13 (503)	99 ± 13 (249)	100 ± 13 (254)	0.039
FEV_1, % predicted, (n tested)	101 ± 13	100 ± 13	101 ± 14	0.614
FVC, % predicted	0.83 ± 0.06	0.83 ± 0.06	0.83 ± 0.06	0.670
FEV_1/FVC				0.662
TLC, % predicted, (n tested)				
FRC, % predicted				
RV, % predicted				
Post-bronchodilator pulmonary function				
sRaw, % predicted, (n tested)				
FEV_1, % predicted, (n tested)				
FVC, % predicted				
FEV_1/FVC				

sRaw is the specific airway resistance; FEV_1 is the forced expiratory volume in 1 s; BMI is the body mass index; LABA is long acting beta-agonist; ICS is inhaled corticosteroid; FVC is the forced vital capacity; TLC is the total lung capacity; FRC is the functional residual capacity and RV is the residual volume

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This open cohort has been declared to our regulatory agency for computer data collection (Commission Nationale Informatique et Libertés, n°1408710), and approval from the Ethics Committee of French Society of Pulmonology - SPLF was obtained (CEPRO 2009/019). All children and parents were informed of the prospective recording of clinical and physiological data and could request to be exempted from this study in accordance with French law regarding non-interventional research. Thus, formal oral or written informed consent was not required.

Measurements

The annualized rate of ED visits or hospitalizations (hospital contacts) for acute asthma was defined by the number of ED visits/hospitalizations between two years of age and the visit to the clinic. The term ED visit (hospital contact) was defined as going to the ED, with or without subsequent hospitalization. These rates were evaluated at each follow-up visit (minimum each year). A low socioeconomic status was defined by the benefit of universal health coverage due to low income, the effect of 100% rate of reimbursement by the French healthcare system due to asthma severity was also evaluated.

Pulmonary function tests (MasterScreen Body; Jaeger, CareFusion, San Diego, CA, USA) were performed without inhaled treatment (bronchodilator or LABA/ICS association) on the day of measurement by the same operator (BM). Spirometry and body plethysmography were performed according to international guidelines[10, 11] and as previously described [9]. The bronchodilator response to salbutamol 400 µg was assessed in children with airflow limitation. Reference values were those of Zapletal *et al.* [12], as frequently used in Europe [13]. Only Caucasian children were included due to the selection of these reference values.

Statistical analyses

Results were expressed as mean ± Standard Deviation. Intergroup comparisons were made using the *t* test. Linear correlations were evaluated using the Pearson test. Multivariate analyses: we used stepwise regression (forward) with ED visits or hospitalizations as dependent variables and the almost significant ($p < 0.10$) variables in the univariate analyses as independent variables, with the exception of number of asthma specialist visits due to collinearity with age. The other statistical analyses are described in the text. A P-value < 0.05 was deemed statistically significant. All statistical analyses were performed with Statview 5.0 software (SAS institute, Cary, NC, USA).

Results

Results from the overall cohort

The cohort is composed of 933 asthmatic children (330 girls); their characteristics are described in Table 1. Two groups of asthmatic children were differentiated: those with no ED visits (no hospital contact) and those with at least one ED visit (without or with hospitalization) after age two. It appears that asthmatic children with at least one ED visit had multiple sensitizations and more frequently suffered from atopic dermatitis; also, at their last visit, they were younger, received more inhaled steroids and LABA, and had more severe exacerbation in the previous three months, confirming the higher severity.

The annualized rate of ED visits was increased in preschool children (< 6 years, n = 84) compared to school children (≥ 6 years, n = 849): 0.302 ± 0.626 versus 0.184 ± 0.316, p = 0.004, respectively, whereas the annualized rates of hospitalization were not different: 0.054 ± 0.181 versus 0.055 ± 0.159, p = 0.925, respectively.

Children benefiting from universal health coverage due to a low household income or having a 100% rate of reimbursement by the French healthcare system due to asthma severity did not have a significantly different ED visit rate or hospitalization rate than the other children (data not shown).

Risk factors for ED visits and hospitalization

Results from univariate analyses are described in Table 2.

Table 2
Univariate analyses of factors linked to ED visit frequency.

	ED visit rate		**Hospitalization rate**	
Characteristics	R value	P value	R value	P value
Best sRaw reversibility	-0.064	0.052	+ 0.070	0.034
Last visit:	-0.150	< 0.001	-0.094	0.850
Age	+ 0.061	0.065	+ 0.124	0.004
Number of specialist visits	+ 0.115	< 0.001	+ 0.086	< 0.001
Number of days with symptoms	+ 0.150	< 0.001	+ 0.116	0.038
Beclomethasone dose	+ 0.101	0.023		0.009
FEV_1, after salbutamol	+ 0.110	0.026		0.400
FEV_1/FVC, after salbutamol				
ED visit and hospitalization rates were weakly related: $r^2 = 0.11$, $p < 0.001$.				

Results from multivariate analyses

The independent contributors to the rate of ED visits were (at last visit): the age (coefficient − 0.028 per year of age), the ICS dose (coefficient 0.021 per 100 µg Beclomethasone Equivalent Dose) and the post-bronchodilator FEV_1 (coefficient 0.004 per % predicted). The model explained 11% of ED visit variance ($p < 0.0001$).

The independent contributors to hospitalization rate were the number of specialist visits (coefficient − 0.007 per visit) and the post-bronchodilator FEV_1 (coefficient 0.002 per % predicted). The model explained 6% of ED hospitalization variance ($p = 0.0002$).

From a practical point of view, for the physician in charge of a young asthmatic child, it is important to have predictors of future risk of ED visit; thus, we performed a logistic regression with ED visits (= 0 or > 0) as a dependent variable and early wheezing, hospitalization before two years of age, atopic dermatitis and atopic status (prick tests) as independent variables (n = 778 children). Early hospitalization ($p = 0.0003$) and atopic dermatitis ($p = 0.0006$) remained significant independent predictors of the future risk of ED visits (r^2 of the model = 0.03). The absence of early hospitalization had an odds ratio of 0.38 (95% confidence interval: 0.23–0.65) and the absence of atopic dermatitis had an odds ratio of 0.57 (95% confidence interval: 0.42–0.79) to predict at least one ED visit (hospital contact).

In the whole population (n = 933), when an asthmatic child had no early hospitalization and no atopic dermatitis, the relative risk of hospital contact was 0.72 (95% confidence interval: 0.64 to 0.82), $p < 0.0001$.

Discussion

The main result of this study is that two kinds of risk factors of ED visit are observed: early (before two years of age) risk factors such as multiple sensitization and atopic dermatitis, and *a posteriori* risk factors observed at the last follow-up: younger age, more inhaled treatment and more severe exacerbation in the previous months, suggesting more severe asthma. The independent contributors for ED visit were age, the dose of ICS and post-bronchodilator FEV_1, whereas the independent contributors for ED hospitalization were the number of specialist visits and post-bronchodilator FEV_1. From a practical point of view, the absence of hospitalizations and atopic dermatitis before two years of age decreased the risk of ED visits after two years by approximately one third. These two risk factors are not modifiable.

The first issue deals with whether an ED visit is a marker of severe exacerbation in children. ED visits and hospitalizations were supposed to be related to severe exacerbations in the TENOR study [14]. Nevertheless, this could be a shortcut. A prospective study in French ED assessed the number of ED visits for asthma exacerbation that would be avoidable [5]. An ED visit was deemed potentially avoidable when a child who had not received adequate pre-hospital treatment left the ED after a maximum of 3 nebulisations with a bronchodilator with no relapse within 48 hours; in total, 38% of children had an

avoidable ED visit, suggesting that some of the ED visits are not related to severe exacerbation in children. Feelings of fear/anxiety were the only independent risk factor for avoidable visits [5]. Thus, parents of younger children may be more prone to visiting the ED, explaining why younger asthmatic children had more ED visits. This increased frequency of ED visits in younger children was expected since it has previously been demonstrated a decrease in severe exacerbations with increasing age [15, 16].

Children with high respiratory resource use in early childhood are characterized by more frequent wheezing in infancy and continue to incur healthcare costs from 3 to 5 years of age [17]. Compared to older children with persistent asthma, preschool children with recurrent wheezing have nearly twice the rate of outpatient physician visits and ED visits for wheezing exacerbations and more than five times the rate of hospitalizations [18]. Accordingly, in our study, preschool children had nearly twice the rate of ED visits than school children.

The mean annualized rate of ED visits in our study was 0.194, which is quite similar to that observed in the USA in an older asthmatic population (6 to 21 years: 0.171) [19]. The mean annualized rate of ED hospitalizations (0.055) was nearly twice that observed in France in 2010 (30.1/10,000 children with ~ 10% asthmatics) [20], which may be related to the better hospital proximity in the suburbs of Paris or recruitment bias of a specialized pediatrician.

ED visits are mostly related to severe exacerbations, and these children remain symptomatic at their last visit despite increased ICS. This result is in agreement with that of the multicenter INSPIRERS study, showing that a phenotype was comprised of highly symptomatic asthmatic adolescents at baseline who presented the highest number of unscheduled healthcare visits per month and exacerbations per month, both at baseline and follow-up [21]. Lenhardt *et al.* showed that patients with asthma exacerbations most often had uncontrolled asthma before the ED visit that subsequently deteriorated, temporarily improved with ED treatment, and continued as uncontrolled asthma after the ED visit [22]. Thus, increased ED visits is a marker of severity of asthma, which was not related to the level of health insurance coverage in French children. Asthma exacerbation frequency in adults did not differ significantly between low and medium/high socioeconomic status patients in France, but differences were found in the management of asthma exacerbations since patients with a medium/high socioeconomic status were less likely to visit an ED or be hospitalized [23].

The main unexpected finding was that a higher post-bronchodilator FEV_1 was related to increased ED visit and hospitalization rates. Low pre-bronchodilator FEV_1 is a strong independent predictor of risk of exacerbations [24]. Nevertheless, in the TENOR study, a lower post-bronchodilator FVC and lower post-bronchodilator FEV_1/FVC were associated with a decreased risk of future severe exacerbations or steroid bursts, respectively [14]. Thus, our result may be in agreement with the results of the TENOR study.

In a patient with multiple sensitizations and early-onset disease, the prognosis of asthma is poor with a high risk of persistence and severity of disease during childhood [25]. Thus, our results are in agreement with this statement, further showing that the absence of atopic dermatitis decreased the rate of ED visits.

The results of the logistic model that show that atopic dermatitis but not atopic status remains an independent predictor of ED visits, which is in agreement with the concept of atopic march [26]. Interestingly, Yoon *et al.*, in a cluster analysis of the Korean childhood asthma study cohort, found a specific cluster of children (36.6%; mean age, 8.9 ± 2.1 years) that was characterized as having early-onset atopic asthma with atopic dermatitis and the least severe type of asthma [27]. Contrarily to our findings, the proportion of these patients requiring hospitalization or ED visit was the lowest among their four clusters, although the differences were not statistically significant among the clusters [27].

Unexpected ED visits and hospitalization rates were weakly related and their independent contributors were different, except for post-bronchodilator FEV_1. This may be related to the fact that a lot of ED visits are avoidable [5]. Visits to asthma specialists were associated with a decreased rate of hospitalization, which may be related to the increased ability of these families to manage exacerbations at home after the initial treatment.

Overall, our study shows that the absence of hospitalization before two years of age and of atopic dermatitis decreased the risk for further ED visits or hospitalizations by 28%, which should be taken into account when selecting candidates for a written action plan. It has been shown that the delivery of a comprehensive asthma education program after an ED visit may be effective in children [28]. Nevertheless, all children in our study had a written action plan. Finally, it has to be stated that the level of explained variance of the risk of ED visit was low and that the risk factors identified are non-modifiable. Overall, our study confirms in an out-of-hospital setting that younger age, increased asthma severity and early hospitalization are risk factors of subsequent ED visit.

Our study has some limitations. The interval between two visits to the specialised pediatrician was not standardized, thus it could be questioned whether the recall for ED visits may vary to some extent. Nevertheless, visits to the ED are undoubtedly events that are important enough to make an impression, facilitating the recall. In addition, these visits to the ED are generally noted in the child's health record, which is examined by the pediatrician. Due to the open cohort design, the follow-up duration of each child was different, which may introduce some bias. Finally, severe exacerbations leading to ED visits are only some of those experienced by asthmatic children, since most exacerbations are treated in an out-of-hospital setting. Our study also has clinical consequences. ED visitation rates and early hospitalization are markers of asthma severity that need to be taken into account.

In conclusion, in our out-of-hospital cohort of asthmatic children followed up by a specialized pediatrician, half of the children experienced emergency department visits and those with the absence of atopic dermatitis and hospitalization before two years of age are less prone to these visits.

List Of Abbreviations In Alphabetical Order

body mass index (BMI)

emergency department (ED)

forced expiratory volume in 1 s (FEV_1)

forced vital capacity (FVC)

functional residual capacity (FRC)

inhaled corticosteroid (ICS)

long acting beta-agonist (LABA)

residual volume (RV)

specific airway resistance (sRaw)

total lung capacity (TLC)

Declarations

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Code availability: Not applicable

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Ethics approval: Approval from the Ethics Committee of French Society of Pulmonology - SPLF was obtained (CEPRO 2009/019)

Consent to participate: All children and parents were informed of the prospective recording of clinical and physiological data and could request to be exempted from this study in accordance with French law regarding non-interventional research.

Consent for publication: all authors consented for publication.

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