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EPIDEMIOLOGY AND GENETICS

Role of comorbid conditions in asthma hospitalizations in the south of France

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Keywords

asthma; comorbid conditions; diagnosis-related group; hospitalization.

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Abstract

Background: Reasons for asthma hospitalizations are dynamic and complex. Comorbid conditions are important contributors to most chronic diseases today. We aim to characterize and describe risk factors associated with hospitalizations due to asthma in the Languedoc-Roussillon region (France) in 2009.

Methods: Programme de Médicalisation des Systèmes d'Information (PMSI) data records from 2009 were sorted using selected International Classification of Diseases (ICD10) codes eliciting three groups of asthma hospitalizations according to acute severity. All available data including demographics, comorbid conditions, past hospitalizations either related or unrelated to asthma, seasonality and distance to medical facilities were used to compare the subjects within the three groups.

Results: One thousand two hundred and eighty-nine hospitalizations due to asthma exacerbation were found, concerning 1122 patients. We observed significant differences within the groups, using univariate analysis, concerning duration of hospitalizations (mean $\pm$ SD, 4.9 ± 5.9 days vs 6.4 ± 6.8 vs 15.8 ± 16.8 , $P < 0.001$), deaths (percentage, 0.03% vs 1.50% vs 9.20%, $P < 0.001$) and numbers of comorbid conditions (0.80 ± 0.95 vs 0.75 ± 0.97 vs 1.74 ± 1.36 , $P < 0.001$). Recurrent admissions for asthma during the period 2006–2008 were significantly more frequent in the more severe group (1.93 ± 3.91 vs 2.56 ± 4.47 vs 2.81 ± 3.97 , $P = 0.006$). In the multivariate model, age and number of comorbid conditions were independently associated with severe hospitalizations and deaths.

Conclusions: Asthma hospitalizations can be appropriately assessed using PMSI coding databases. In this study, age and the presence of comorbid conditions are the major risk factors for asthma hospitalizations and deaths.

The incidence of hospitalization due to asthma is decreasing worldwide (1–6). Over the last decade, exacerbations of asthma have been well managed in outpatient facilities in most of the cases (2). Therefore, understanding and monitoring triggers and risk factors related to hospitalizations for asthma appears to be a worthy task for public health advisors. The decision to admit a patient can rely on widely spread factors directly related to the disease (clinical severity of the exacerbation, near-fatal episode, recurrence of emergency department visit, known high level of airway hyper-responsiveness) or not (difficulty managing side-effects of the treatment on an outpatient basis, for example, diabetes, hypertension, or tachycardia (7)). However, admission

frequently relies on factors harder to identify using classical epidemiological data (psychiatric/psychosocial disorders, distance to medical facilities, season of admission (8–11), comorbid conditions, need for specific investigation (12), physician expertise). These last factors are difficult to explain and investigate and are not evidence based.

Understanding the patterns, rate, and risk factors for asthma hospitalizations is of tremendous interest for physicians and other healthcare providers as it is one major way to prevent future risks including new exacerbations.

Programme de Médicalisation des Systèmes d'Information coding (the French equivalent of the UK Caspe Healthcare Knowledge Systems (CHKS) is a wide and exhaustive

database likely to find out most of these criteria, especially since 2006 (13). The PMSI is a law commitment database coding performed by the clinicians at the end of every stay and then provides 100% of inpatient coverage in France. In this study, we aimed to describe several aspects directly and indirectly related to asthma hospitalizations in our district during the period 2006–2009. For that purpose, we hypothesized that a PMSI database sorting rule can efficiently identify three different kinds of hospitalization according to acute severity of the exacerbation. This process would allow a better description of risk factors for hospitalization and in hospital mortality. These results will help to identify risk factors related to most severe asthma exacerbations and deaths and to develop and implement new adapted health policies.

Materials and methods

Study design and population

We investigated standardized data from the PMSI which had been prospectively collected from 2006 to 2009. PMSI contains exhaustive medico-economic information about admissions based on the International Classification of Diseases (ICD-10) classification from both public and private hospitals. It includes all data provided by healthcare providers to the social welfare office.

Hospitalization was defined by at least one night stay in an institution. Children older than 4 years and adults with a permanent address in the Languedoc-Roussillon (France) were included even though they may have been cared for anywhere in metropolitan France.

The study focuses on admissions for asthma in 2009 (end of stay before January 1, 2010), and similar data obtained from 2006 to 2008 were used to highlight trends and past hospitalizations related and/or unrelated to asthma.

We reviewed anonymous and specific data for each patient including the chronological order of admission to various medical units during the hospitalization (e.g. intensive care unit (ICU), high dependency unit (HDU), monitoring, regular ward, etc.), initial admission or not through the emergency department (ED), the length of stay, living status on discharge, month of discharge, the primary diagnosis as reason for referral, the secondary diagnosis, medical acts performed during the stay, care center characteristics (geographic area, private or public institution, size), and the patient demographics (age, gender, residence).

The hospitalizations were sorted into three exclusive subgroups. Category definitions were chosen to include asthmatic patients only. They were strictly followed to improve the specificity of our analysis. Categories 1, 2, and 3 correspond to lowest, intermediate, and highest severity according to Table 1.

Definition of comorbid conditions

We defined twelve comorbid conditions according to the most frequently secondary comorbidity code in the PMSI for the selected stays: Smoking, Psychiatric conditions, Obesity,

Heart diseases, Pneumonia, Sinusitis, Gastroesophageal reflux disease (GERD), Diabetes mellitus, Sleep apnea, Dependence on respirator, Chronic respiratory failure, and Atopy.

Definition of hospitalization

Past admission history was tracked with a unique identification number (called 'MAGIC' number) that allowed chaining between 2006 and 2009 inclusive. Primary diagnosis recorded for those previous stays were used to identify stays related to asthma (classified as asthma relapses) or not (classified as other hospitalizations).

Moreover, the MAGIC number allowed potential identification of interhospital patient transfer. In this case, the stay in the health facilities in which the most serious exacerbation had been coded or the longest stay was always selected. Finally, if the two previous selection rules were the same, the stay was selected in which more comorbidities were listed. Then, the various transits by different medical units were summed to create the new stay, as the length of stay in each unit and the total length of stay.

Ethics and consent

According to French Law (Law 88-1138 relative to Biomedical Research of December 20, 1988, modified on August 9, 2004), this anonymous noninterventional study did not require approval by an ethics committee or informed signed consent from patients. The data set presented in this study was declared to the ATIH (Agence Technique de l'Information sur l'Hospitalisation) and approved by the CNIL (national commission for data processing and civil liberties).

Statistical analysis

Quantitative variables were expressed as means ($\pm$ SD) and compared using the parametric and nonparametric ANOVA. Qualitative variables were expressed as numbers (percent) and compared using the chi-square test. Distances to medical facilities were obtained using a specific application computing the distance in km between the residency address and the institution of admission.

A logistic regression was used to identify risk factors of category 3 stay and death. A multivariate model was established to predict category 3 stay and death. Variables were selected if *P*-value was <0.20 in the univariate analysis, and a stepwise procedure was used to select the final model. A two-tailed *P*-value of 0.05 was used to define statistical significance. The statistical analysis was performed by the medical statistical department of the Montpellier University Hospital with the help of statistical software (SAS, version 9.3; SAS Institute; Cary, NC, USA; and R, version 2.14.1).

Results

One thousand two hundred and eighty-nine hospital inpatient stays of 1122 different patients have been recorded for 2009 in our region (2 616 000 inhabitants in 2009). The general

Table 1 Sorting rule for stays

	Main diagnoses	Associates diagnoses		Remark
Category 1: lowest severity	J45: asthma	+	...	Excluding: J46 (acute severe asthma), J96.0 (acute respiratory failure), J80 (acute respiratory distress syndrome in adults), Acts of assisted ventilation (GLLD-) Stays containing ICU/HDU/CCU code medical unit (MU 01, 02, 03, 13, 14)
	J20: acute bronchitis	+	J45	
	J44: other obstructive pulmonary conditions	+	J45	
Category 2: intermediate severity	J45	+	J96.0	Excluding: GLLD-MU 01, 02, 03, 13, 14
	J45	+	J80	
	J20	+	J45+ J96.0	
	J20	+	J45+ J80	
	J44	+	J45+ J96.0	
	J44	+	J45+ J80	
	J96.0	+	J45	
	J80	+	J45	
	J46	+	...	
	...	+	J46	
Category 3: highest severity	J45	+	J96.0	GLLD-MU 01, 02, 03, 13, 14
	J45	+	J80	
	J20	+	J45+ J96.0	
	J20	+	J45+ J80	
	J44	+	J45+ J96.0	
	J44	+	J45+ J80	
	J96.0	+	J45	
	J80	+	J45	
	J46	+	...	
	...	+	J46	

+: and (if and only if both codes are verified).

...: whatever code.

Codes are as follows: J45: asthma; J20: acute bronchitis; J44: other obstructive pulmonary conditions; J46: acute severe asthma; J96.0: acute respiratory failure; J80: adult respiratory distress syndrome in adults; GLLD-: acts of assisted ventilation; MU 01, 02, 03, 13, 14: stays containing ICU/HDU/CCU code medical unit.

trend showed a reducing incidence of asthma hospitalizations between 2006 and 2009 (see Table 2).

Demographic characteristic for patients during the year 2009 are presented in Table 3. In 2009, 591, 412, and 119 patients corresponded to category 1, 2, and 3, respectively. 55.1% of the admitted patients had at least one comorbidity, and the mean number of comorbidities was 0.88 ± 1.05 . Age, mortality, length of stay, and number of comorbidities were all higher in category 3. Details of comorbidities were assessed in each category. Results are presented in Table 4. Overall, the comorbidities were more found in category 3 except for atopy, which was more associated to category 1.

All were significantly different between steps. Past medical histories of hospitalizations for asthma (relapses) and for other reasons are detailed in Table 5.

Among patients admitted in 2009 for asthma corresponding to category 3, 65% were admitted at least once in the past 3 years (*vs* 54% and 63% in categories 1 and 2, respectively, $P = 0.004$). The number of previous admissions for other reason than asthma was significantly higher in the category 3 when compared with categories 1 and 2 (1.60 ± 3.58 *vs*

Table 2 Incidence of asthma hospitalizations and deaths between 2006 and 2009

	2006	2007	2008	2009
Number of hospitalizations (N)	1443	1372	1276	1289
Patients (N)	1330	1269	1190	1122
Percentage of total admission (%)	0.357	0.340	0.314	0.320
Number of deaths (N)	18	16	22	19

2.00 ± 3.83 *vs* 2.26 ± 3.37 , $P = 0.028$). The number of previous admissions for asthma was significantly lower in the category 1 when compared with categories 2 and 3 (0.33 ± 1.04 *vs* 0.55 ± 1.62 *vs* 0.55 ± 1.75 , $P = 0.013$).

Seasonality of admissions and deaths are represented in Fig. 1. 2009 data distribution was similar to 2006–2008 and cumulative incidences were considered. A nonuniform distribution of annual admissions is observed ($P = 0.007$).

Table 3 Demographic characteristics of hospitalizations in 2009 in Languedoc-Roussillon for asthma. SD indicates standard deviation

	All	Category 1	Category 2	Category 3	P-value
Number of hospitalizations (N)	1289	704	459	126	
Patients (N)	1122	591	412	119	
Age (years, mean $\pm$ SD)	47.6 $\pm$ 28.0	44.6 $\pm$ 28.7	48.7 $\pm$ 28.2	59.6 $\pm$ 18.8	<0.001
Gender (% of female)	62.4	59.9	66.9	60.3	0.050
Deaths (n (%))	19 (1.7)	2 (0.03)	6 (1.5)	11 (9.2)	<0.001
Duration of hospitalization (days, mean $\pm$ SD)	6.5 $\pm$ 8.5	4.9 $\pm$ 5.9	6.4 $\pm$ 6.8	15.8 $\pm$ 16.8	<0.001
Institution (public/private, %)	1023/266 (79/21)	556/148 (79/21)	370/89 (81/19)	97/29 (77/23)	0.630
Number of associated diagnoses/patient (mean $\pm$ SD)	0.88 $\pm$ 1.05	0.80 $\pm$ 0.95	0.75 $\pm$ 0.97	1.74 $\pm$ 1.36	<0.001

Table 4 Most frequently coded secondary diagnosis (comorbidities) of asthma patients admitted in 2009

Comorbidities	Total	Category 1	Category 2	Category 3	P-value
N	1122	591	412	119	
Smoking (%)	6	5	6	16	<0.001
Psychiatric disorder (%)	5	4	5	10	0.036
Obesity (%)	6	4	6	18	<0.001
Heart disease (%)	11	9	10	22	<0.001
Pneumonia (%)	9	6	9	23	<0.001
Sinusitis (%)	4	5	2	5	0.014
GERD* (%)	2	4	1	2	0.054
Diabetes (%)	8	8	7	16	0.005
Sleep apnea (%)	4	3	4	8	0.015
Dependence on respirator (%)	3	1	3	8	<0.001
Chronic respiratory failure (%)	9	4	9	30	<0.001
Atopy (%)	21	27	14	17	<0.001

*Gastroesophageal reflux disease.

We observed an increase in incidence during fall–winter season for categories 1 and 2 only while admission rate was more or less constant in category 3.

No significant differences were observed for distances to medical facilities between steps. Patients admitted in category 1, 2, and 3 were living at a distance of 18.8 ± 25.5 , 20.9 ± 27.4 and 19.7 ± 27.3 kms, respectively ($P = 0.34$), from the institutions. The transportation time was similar in the three categories (20.9 ± 22.8 minutes vs 22.5 ± 22.9 minutes vs 21.5 ± 24.0 minutes, $P = 0.79$). Maps displaying dwelling places and cities of admission are presented in the Fig. 2.

In the multivariate model built with all the data available, the main predictors of category 3 were related age (OR = 1.013 [1.005–1.022], $P = 0.002$) and the number of comorbidities (OR = 1.838 [1.562–2.163], $P < 0.001$). A specific multivariate analysis on comorbidities identified Smoking (OR = 3.24 [1.72–6.11], $P < 0.001$), Obesity (OR = 2.91 [1.58–5.35], $P < 0.001$),

Heart disease (OR = 2.17 [1.27–3.72], $P = 0.004$), Pneumonia (OR = 3.10 [1.80–5.32], $P < 0.001$), Dependence on respirator (OR = 3.01 [1.23–7.37], $P = 0.016$), Chronic respiratory failure (OR = 3.86 [2.31–6.47], $P < 0.001$) as independent factors associated with a category 3 stay.

Similarly, the multivariate model built to identify factors predicting death was age (OR = 1.048 [1.018–1.080], $P = 0.002$) and the number of comorbidities (OR = 1.714 [1.236–2.377], $P = 0.001$).

Discussion

In this study, we observed a decreasing incidence of asthma-related hospitalizations in our region between 2006 and 2009. Using strict rules for sorting PMSI data, we delimited three relevant levels of severity.

Age and number of comorbidities were independent risk factors for asthma hospitalization of patients falling in category 3. Patients with a previous history of hospitalizations over the past 3 years were frequently readmitted (59%) but more often due to comorbid conditions (53%) rather than new exacerbations (19%). Winter was found to be an ‘at-risk season’ except for the most severe cases where seasonality disappeared. Distance between place of residence and medical facilities did not seem to account for any parameter including the severity of acute exacerbation.

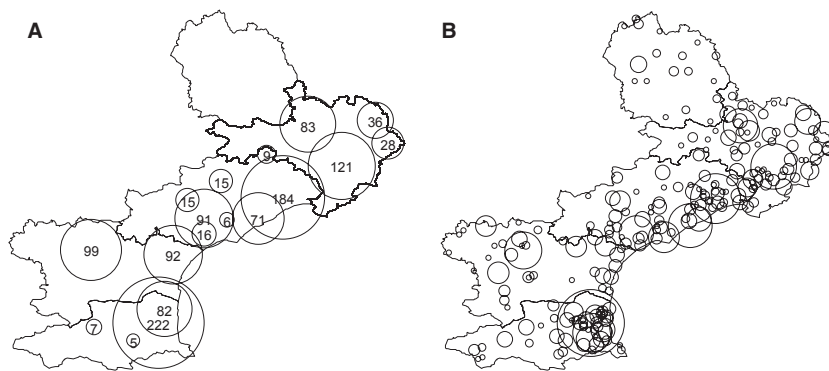
Risk factors for near-fatal asthma episodes are dominated by the importance of previous ICU admissions (10, 14–16). The present study did not confirm these data as it only covered 4 years.

The absence of seasonality in category 3 admissions is a possible indicator of a specific pathophysiological mechanism underlying these near-fatal or fatal episodes (17). This finding is in agreement with the lower prevalence of atopy reported in this category. We would suspect a lack of supervised adherence to current treatment during these periods (18) as it is frequently reported during patient interviews.

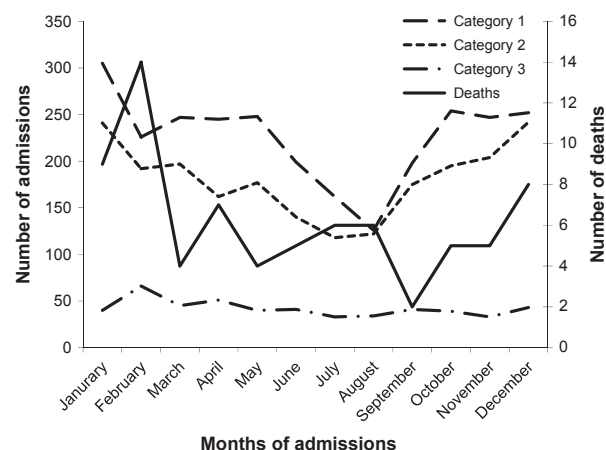
Previous studies have shown that patients living far from medical institution are at higher risk of severe asthma exacerbations (15); however, our study did not confirm this finding.

The role of comorbid conditions remains of major importance as previously reported (19–21). Using a similar methodology in

	Total	Category 1	Category 2	Category 3	P-value
Number of admissions in 2009	1289	704	459	126	
Number of patients admitted in 2009	1122	591	412	119	
Mean number of previous admissions between 2006 and 2008 (Mean $\pm$ SD)	2.25 $\pm$ 4.14	1.93 $\pm$ 3.91	2.56 $\pm$ 4.47	2.81 $\pm$ 3.97	0.006
% of patient admitted at least once between 2006 and 2008	59	54	63	65	0.004
Relapses					
% of patient admitted for asthma between 2006 and 2008	19	16	24	22	0.005
Mean number of previous admissions for asthma (Mean $\pm$ SD)	0.43 $\pm$ 1.37	0.33 $\pm$ 1.04	0.55 $\pm$ 1.62	0.55 $\pm$ 1.75	0.013
Other hospitalizations					
% of patient admitted for other reason than asthma (Mean $\pm$ SD)	53	49	56	61	0.017
Mean number of previous admissions for other reason than asthma (Mean $\pm$ SD)	1.82 $\pm$ 3.66	1.60 $\pm$ 3.58	2.00 $\pm$ 3.83	2.26 $\pm$ 3.37	0.028



of patients' place of residence distribution in our region (the area of each circle is proportional to the total number of patients of each dwelling place).



In the present study, more than half of the patients were previously admitted for reasons other than asthma in the past 3 years. Comorbid conditions related to behavior are clearly and independently associated with category 3: Obesity was reported in 18% of these patients and smoking in 16%. The lower prevalence of atopy in category 3 reflects what was already reported in the Severe Asthma Research Program (23), where the phenotype with the highest prevalence of ICU admissions and ED visits ('cluster 5') was associated with the lowest prevalence of atopy. In our study, atopy was probably underreported in PMSI because it did not enter in the final cost of the stay (no reimbursement). We acknowledge that the secondary diagnosis mostly reported did not perfectly correspond to the exact definition of comorbidity.

between asthma and obesity has already been largely reported (26, 27), but this is one original study to report its importance in ICU admission for asthma. In our study, ICU stays were classified in category 3.

Efforts are still being made for this particular group of asthma patients through dedicated structures. Therapeutic education programs designed to improve the global adherence to the proposed management such as smoking cessation help and dietary expertise are also highlighted as important aspects of severe asthma follow-up (28, 29). A more specific management including original pharmacological approaches should be developed.

Our data indicated a large difference between category 1–2 and 3 for diabetes. Unfortunately, we could not address the critical question of early or onset diabetes which is known to be age dependent. Specifically, corticosteroid-induced diabetes (type 2) may be more present in the category 3 of asthma hospitalization (30).

Therefore, we believed PMSI-derived data can be a worthwhile source of information when using strict rules of sorting. Accordingly, we acknowledge that improving the specificity to reduce the major risk of bias and consequent confusion regarding clinical diagnosis will reduce the sensitivity. Using our method may have limited the major confounding condition of chronic obstructive pulmonary disorder (COPD) exacerbation, especially because we excluded stays with ICD10 codes, which correspond to acute exacerbation of COPD.

Nevertheless, codes used to define stays of patients belonging to category 3 correspond to comorbidities likely suggesting a COPD diagnosis (chronic respiratory failure, dependence on ventilator – an inaccurate word that can refer both to short term and long term). Clinically, the overlapping conditions (COPD exacerbations and near-fatal asthma) are very hard to distinguish, especially in an emergency context where clinical signs and symptoms and therapeutic management are very similar. We excluded children under 4 years old to avoid the risk of confusion with viral bronchiolitis.

Optimization of PMSI coding with the aim of improving institution funding may cause another bias as different levels of funding are assigned to different codes. For example, it is clear that atopy is underreported in our study as it does not lead to any subsequent increase in reimbursement (what is already true for asthma). However, PMSI is an exhaustive database, where coding by a clinician is enforced by law in France. So, all admissions were reported. Moreover, French social welfare inspectors are regularly checking cohesiveness between codes and clinical reports with the ability to impose penalties for mistakes.

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Other strengths of the PMSI are all the available demographic characteristics linked with the codes that allowed us to compute original variables such as the distance and transportation time to medical facility.

The definitions we used gathered three groups that showed significant differences for most relevant outcomes. We expect these categories to correspond to potential real clinical entities. Thus, in category 1, we considered mild exacerbations that cannot be managed at home because of social or other conditions indirectly related to asthma, and/or to patients admitted for diagnostic consolidation in the context of difficult-to-treat asthma (7), therapeutic education and/or psychiatric condition. Category 3 may describe fatal or near-fatal asthma episodes, while category 2 may correspond to severe exacerbations without clinical evidence of acute respiratory failure at admission.

Observed deaths directly related to asthma in categories 1 and 2 are surprising. This can reveal difficult conditions in the hospital organization, for example a possible lack of available ICU rooms. In the future, hospital admission guidelines may rely more on ambulatory care and ICU rather than large wards.

We expect that this study in addition to previous reports will help physicians to identify patients at risk of hospitalizations. We especially support the idea that this study may help health-care advisors to plan out the structure of hospitalizations.

In conclusion, asthma hospitalizations can be appropriately assessed using PMSI coding databases. In this study, age and the presence of comorbid conditions are the major risk factors for asthma hospitalizations and deaths.

Authors' contributions

All authors approved the manuscript submitted. Aubas C conceived the study, analyzed and interpreted the data, and drafted the manuscript. Bourdin conceived the study design and drafted the manuscript. Aubas P collected the data and critically reviewed the manuscript. Gamez and Halimi critically reviewed the manuscript. Vachier drafted and reviewed the manuscript. Malafaye collected the data and reviewed the manuscript. Chanez conceived the study design and drafted the manuscript. Molinari contributed to the study design, statistical methods, statistical data analysis, and critical review of the manuscript.

Conflict of interest

The authors declare no conflict of interest.

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