Clinical Characteristics and Economic Burden of Asthma in China: A Multicenter Retrospective Study

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Research Article

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Abstract

Background: Asthma is a common chronic airway inflammation that produces a healthcare burden on the economy.

Objective: To obtain a better understanding of the clinical status and disease burden of patients with asthma in China.

Methods: A retrospective study based on the computerized medical records in the Jinan Health Medical Big Data Platform between 2011 and 2019 (n = 31,082) was carried out. The asthma severity of each patient was assessed retrospectively and categorized as mild, moderate, or severe according to GINA 2018.

Results: The results revealed that the majority (75.0%) of patients suffered from mild asthma. Patients treated with ICS/LABA at emergency department visits had lower frequencies of exacerbations in the following year compared with non-ICS/LABA treated patients.The incidence rates for 1 exacerbation are 14.49% vs 15.01 for the patients treated with ICS/LABA and without. The rates are 11.94% and 19.12% for 2 exacerbations above. The numbers are 6.51% vs 12.92% for 3 exacerbations above. The rates are 4.10% vs 9.35% for 4 exacerbations above. Also the difference got the statistical significance (p <0.001), COPD and GRED, two comorbidities related to asthma, were risk factors for asthma exacerbation. Finally, patients who suffered from exacerbations produced a heavier economic burden compared to the patients who never suffered exacerbations(mean costs are 3,339.67 vs 968.45 separately).

Conclusions: These results provide a reference for clinicians and patients to obtain a better treatment and therapy strategy management for asthma sufferers.

Background

Asthma is a common chronic airway inflammation, which presents in the clinic as symptoms such a shortness of breath, wheezing, tightness of the chest, and a persistent cough [1-3]. As a serious health problem worldwide, asthma affects about 300 million individuals globally[4]. It is estimated that 45.7 million individuals in China suffer from asthma[5]. Several studies investigated the prevalence of asthma(Table 1). The results published indicated the prevalence of Asthma in China is between 1.24% and 4.2%. Since asthma patients often have an associated reduced quality of life and an increased treatment burden [6, 7], it is a great public challenge to control asthma in China.

The trigger of asthma is driven by a complicated cascade of processes which include both genetic and environmental factors[8]. Regardless of its complex pathogenesis, asthma can be controlled effectively with proper treatment, especially when accompanied by monitoring during stable periods of the disease. Each patient is encouraged to construct a personalized action plan to reduce the risk of exacerbations[2]. Asthma exacerbation is reflected in an acute worsening of symptoms, which may need emergency treatment or hospitalization. Thus, asthma exacerbation might be the costliest problem for asthma

sufferers. Public education and proper self-management are essential for the patients to reduce the risk of exacerbations[1]. For this purpose, clinicians should be aware of the risks of exacerbation in patients with different degrees of asthma severity. It is also necessary for clinicians to evaluate the risk for future exacerbations in their patients. Several studies have reported the relationship between asthma and some risk factors, but the extent to which the risk factors affect acute exacerbation is still under intensive study. In addition, evidence is accumulating that the development of asthma involves a variety of factors that can vary with time. Acting in concert these factors can affect a number of biochemical processes that can drive asthma exacerbation. Modern information technology methods and data processing techniques provide new ways to study this disease and involve the collection of much globally available data provided globally and shared by many stakeholders.

As an asthma exacerbation is life-threatening, the patient is likely to visit the emergency department for acute medical care [9]. Inhaled corticosteroid (ICS) combined with long-acting β-agonists (LABA) is usually employed to treat asthma patients, either for the immediate relief of symptoms or asthma control [10]. Thus, an oral drug inhalation device combined with ICS plus LABA is preferable for the management of asthma [11].

In this study, we used longitudinal data from an asthma cohort in 11 hospitals in Jinan to examine the patient's proportions of different subtypes and the economic burden. With access to local databases, we also analyzed the potential risk factors for asthma exacerbation. This study will provide important information about the clinical status of asthma patients in Jinan, China.

Methods

Sources data and the cohort of patients studied

This was a retrospective study based on the computerized medical records stored in the Jinan Health Medical Big Data Platform. This database is administered by Shandong Health Medical Big Data Co., Ltd.and contains data extracted from 38 hospitals in Jinan, the capital of Shandong Province, China (the city with more than 8.9 million inhabitants). As the aim was to analyze the clinical status of asthma patients, only thepatients have asthma diagnosis were selected. We included adults aged ≥ 18 years of age, who had been diagnosed at least once as having asthma by physicians in the included hospitals. Individuals were excluded if their age were missing or had undergone surgery, anesthesia, pathological tests, delivery, nuclear medicine, interventional therapy, oral therapy, vaccination, IUD removal, transfusion, hemodialysis, or early education by the same visit. The screening process was indicated in Figure 1.

The cases with an established diagnosis of asthma were based on respiratory symptoms and tests for expiratory airflow limitations. Different types of ashma were determined and screened. Asthma severity was categorized as mild, moderate, or severe according to GINA2018. In brief, asthma severity was assessed retrospectively from the medication and dosage recorded at the last visit during a 6-month observation period (from July 1 to Dec 30 of the first year). Asthma exacerbations were evaluated during

the measurement period (from Oct 1 of the first year to Sept 30 of the next year). In addition, the degree of asthma severity of the patients was reviewed by an asthma specialist.

Primary endpoint: The proportion of the patients with different degrees of asthma severity in each year of the study.

Secondary endpoints: The risk factors for asthma exacerbation, the effect of ICS/LABA usage during the emergency department visits on asthma exacerbation, and the economic burdens on patients with different severities of asthma. The exacerbation has been determined by three situations, if the patient went to emergency room or admit to the hospitality or as outpatients were given intravenous corticosteroids or theophylline for the asthma flare-up then this patient has been defined as the exacerbation occurred.

Statistical analysis

Data are given as the mean ± standard deviation (SD) for normally distributed continuous variables, the median and interquartile ranges for non-normally distributed continuous variables, and proportions for categorical variables. Potential differences between the two groups were assessed using a *t*-test for normally distributed continuous variables, the Wilcoxon test for non-normally distributed continuous variables, and a chi-squared or Fisher's test for categorical variables. Logistic regression analysis was used to evaluate potential risk factors for asthma exacerbation. Potential risk factors with a *P*-value ≤ of 0.05 in the univariate analysis were considered and included in the multivariate analysis afterwards. The odds ratio (OR) and the 95% confidence interval (CI) were also determined.

Results

Patient characteristics

Patients' characteristics are summarized in **Table 2**. In total, there were 36,505 individuals documented having t least once diagnosis with asthma. Of these eligible patients, 31,082 were identified with typical asthma and 1,600 with cough variant asthma (CVA). In addition, 3,823 of the total patients were identified as suffering from asthmatic bronchitis, pneumonia asthma, cardiac asthma, mixed asthma, or asthmatic eosinophilia. Of the asthmatic patients, 14,177 (45.6%) were males and 16,900 (54.4%) were females; 5 (< 0.1%) of the people's gender were unknown. The asthmatics were generally middle-aged (50.7 ± 16.5 years old). The majority (71.0%) of them were between 18-60 years old and the remainder are > 60 years old. The total number of clinic visits for asthma patients was 78,103, and thus, the average visits for each patient were 2.5 ± 5.1 (Mean ± SD). Among the total visits, 69,894 (88.3%) were outpatients, 4,164 (5.3%) were inpatients and 5,068 (6.4%) were emergency cases.

Characteristic of patients with different severities of asthma

The characteristics of patients with different severity of asthma are shown in **Table 3**. Of 36,505 patients, only 14,264 patients got the severity information. The mean age of a total of 14,264 patients was 50.43 ±

16.3 years old. Most patients 10,691 (75.0%) were mild asthmatics, with a mean age of 50.0 ± 16.2 years. While 3,488 (24.5%) were moderate asthmatics with a mean age of 51.2 ± 16.4 years and 85 (0.6%) were severe asthmatics with a mean age of 58.3 ± 15.0 years. The average age of patients with different degrees of asthma severity showed a statistically significant difference ($P < 0.001$).

As shown in **Table 4**, the majority of patients with different severities of asthma did not experience asthma exacerbation during the measurement period. 1.9% of the patients with mild asthma had 1 exacerbation during the measurement period and 1.2% had two or more. The average interval time between exacerbations was 33.0 ± 54.5 days. Similarly, 2.8% of the patients with moderate asthma had 1 exacerbation during the measurement period and 1.3% had more than two. The average interval time between the exacerbations was 61.3 ± 83.0 days. 3.5% of patients with severe asthma had 1 exacerbation during the measurement period and 2.4% had more than two. The average interval time between exacerbations was 91.1 ± 29.5 days.

ICS/LABA usage at exacerbation index reduces the attacks in the next year

The treatment records were reviewed for the documentation of asthma exacerbations. A record of exacerbation means an asthma patient visited the emergency department or was hospitalized or as outpatients were given intravenous corticosteroids or theophylline for the asthma flare-up. Among the 31,082 asthma-coded patients, a total of 12,566 exacerbations were documented, as shown in **Table 5**. While 10,630 exacerbation records were occurred more than 1 year before the last day of the audit, this is allowed us to analyze the frequency of exacerbations the recurred in the following year. As shown in **Table 6**, among the 10,630 patients, 2,195 were treated with ICS/LABA and 8,435 with non-ICS/LABA. Of the ICS/LABA treated patients, 1,615 (73.58%) did not experience repeat attacks in the next year after the index exacerbation, 318 (14.49%) experienced 1 repeat attack and 262 (11.94%) were re-attached at least twice. Of the non-ICS/LABA treated patients, 5,548 (66.77%) were never experienced a repeat attack in the next year after the index date, 1,274 (15.10%) had 1 attack, and 1613 (19.12%) had at least 2 attacks. More importantly, the proportion of patients without recurrence in the next year was much higher in the ICS/LABA treated group than that in the non-ICS/LABA treated group ($P < 0.001$). Furthermore, whether or not the index exacerbation was excluded, the ICS/LABA-treated patients experienced a significant longer mean interval between repeat attacks than the non-ICS/LABA-treated patients (index excluded: 69.0 ± 63.2 days *vs* 41.3 ± 57.4 days, $P < 0.001$; index included: 98.5 ± 91.1 days *vs* 46.0 ± 67.2 days, $P < 0.001$). These results revealed a better control of asthma exacerbations following ICS/LABA treatment, which indicates that ICS/LABA therapy of the exacerbation is more effective than non-ICS/LABA for the prevention of exacerbation recurrences in the following year.

Risk factors for asthma exacerbation

Since asthma is a common condition, the purpose of asthma management is to achieve asthma control and prevent exacerbation. It is important for clinicians to bear in mind the risk factors for exacerbation. **Table 6** presents the potential risk factors for asthma exacerbation. In the present study, the demographic variables included gender, age, and age grouping. As a result, a strong association between age and

exacerbation was found (odds ratio 1.012, 95% CI: 1.006-1.017, $P < 0.001$). Next, the comorbidities variables that might have modified the exacerbations were evaluated. The comorbidities presented here were derived from existing variables, such as COPD, rhinitis, nasosinusitis, nasal polyposis, GERD, anxiety, depression, and obesity. As a result, significant comorbidities association with exacerbation were COPD (odds ratio 2.618, 95% CI: 1.945 to 3.459, $P < 0.001$) and GERD (odds ratio 2.101, 95% CI: 1.131 to 3.57, $P = 0.016$).

The economic burden of asthma

The management of asthma undoubtedly increases the economic burden of healthcare and any exacerbation will likely impose a higher burden. It is necessary to analyze the costs for patients who experience exacerbations or not. **Table 7** provides a general summary of the expenditure on asthma management of patients who experienced exacerbations or did not. In our study, the analysis of the asthma economic burden included 468 patients who suffered exacerbations and 8,012 patients who never experienced a flare-up after filtering the patients with expenses records. The total mean expenditure of the patients who suffered exacerbations was ￥3,339.67 ±￥ 6,232.47 (Yuan), to which the fee for medicines made the most significant contribution (61.45%, ￥2,052.12 ± ￥4,258.97). To a lesser extent, fees for testing (13.53%, ￥451.93 ± ￥1,155.03) and others (25.02%, ￥835.62 ± ￥1,809.68) were smaller fractions of total costs. However, the total expenditure of the patients who never suffered an exacerbation was ￥968.45 ± ￥1,932.38, which was much lower than that of the patients who experienced attacks. In another aspect, the medication fee accounted for the highest proportion of the total fee (53.2%, ￥1,320.25 ± ￥1,983.20), and the next was the fee for testing (4.01%, ￥515.26 ± ￥1,305.81) and others (42.79%, ￥38.79 ± ￥150.93). More importantly, patients who never suffered exacerbations had significantly lower expenditure for either item compared to patients who experienced attacks ($P < 0.05$).

Discussion

Asthma is a common condition that is usually managed by drugs. It is worth noting that, in this ever-largest retrospective cohort study of patients with asthma in China, the asthma severity was assessed retrospectively from the level of treatment. We analyzed the proportion of the patients with different severities of asthma each year between 2011 and 2019, and the exacerbation frequencies of the patients with different severities during the study period. We also assessed the exacerbation frequencies in patients after emergency department visits who were treated with or without ICS/LABA. Then we evaluated the risk factors for exacerbations and the economic burden on patients who suffered from asthma exacerbations or not. Our results provide important information on asthma exacerbations and the economic burden in Jinan, Shandong Province, China.

Though a controllable disease, poor asthma management will increase exacerbations of asthma. It has been reported that the degree of asthma severity is highly correlated with likely exacerbations [12]. Here, we show that patients with any severity may suffer an exacerbation. Patients with mild asthma

experienced exacerbations less frequently compared to patients with moderate or severe asthma. A previous survey has reported that the exacerbation rate of patients in 6 cities of China with mild asthma was 17.8% [13], which is much higher than 3.3% (table 4) in this study. The different outcomes may be due to the different populations of the study cohort. In recent years, due to the continuous improvement of medical insurance policies and the increase of people's economic income, the proportion of Chinese asthma patients with standardized treatment has increased significantly, and more and more asthma patients can use ICS/LABA for long-term symptom control.[14] On the other hand, the current survey population was asthma patients in the urban area of Jinan, Shandong Province, with a per capita economic income and education level better than the Chinese average, which may also be a vital reason for the significantly lower rate of asthma exacerbations in this study. Alternatively, the survey methods may have differed. For example, in our study, asthma severity was assessed retrospectively according to the treatment. However, the previous study defined asthma severity based on self-reporting. Further, a study is required to investigate the potential risk factors associated with the change in the ratio of the patients with different degrees of asthma severity.

A previous report on asthma status in the United States showed that the highest asthma death rate was for adults aged ≥ 65 years old[15]. Therefore, more attention should be paid to asthma management in elderly patients.

Comorbidity is a modifiable risk factor for asthma exacerbation and is linked with greater healthcare use and a lower quality of life[16]. Thus, much attention should be paid to comorbidities during asthma management. Previous studies have reported several comorbid diseases associated with asthma, such as obesity, GRED, anxiety and depression, rhinitis, sinusitis, and nasal polyps. In this regional population-based cohort study, we found that either GRED (gastroesophageal reflux disease) or COPD (chronic obstructive pulmonary disease) was highly correlated with exacerbations of asthma. Both asthma and GERD are common causes of upper airway cough. As a chronic disease, GRED affects the upper gastrointestinal tract[17, 18]. However, it also coexisted with asthma in 80% of asthma patients without gastrointestinal symptoms[19]. Similar to asthma, COPD, inflammation of the airways, which is also treated with ICSs, LAMAs, and long-acting ß-agonists[20]. Thus, these results prompt us to suggest that COPD-asthma and GRED-asthma overlap during asthma management should be seriously considered.

ICS-formoterol, is a treatment choice in the emergency department to relieve acute asthma bronchoconstriction, which is also recommended by GINA 2020[21]. One previous study has compared budesonide plus formoterol (LABA) with salbutamol (SABA) therapy for the treatment of exacerbations of asthma in the emergency room and found that a high dosage combination of budesonide and formoterol is effective[22]. Also our study found a significantly lower frequency of re-exacerbations after ICS/LABA therapy in emergency visits compared to non-ICS/LABA usage. Due to the continuous improvement of China's health insurance policy, we found that the financial burden of asthma patients is significantly lower than that of developed countries such as the United States. Similar results were obtained from several related studies in mainland China[23, 24]. A study found that the annual per-person incremental medical cost of asthma in the United States was $3,266, of which $1,830 was attributable to prescription

medication, $640 to office visits, $529 to hospitalizations, $176 to hospital-based outpatient visits, and $105 to emergency room visits in 2015[25]. In addition, we found that asthma patients who ever suffered exacerbation had higher medication costs and lower screening costs relative to patients without previous acute asthma exacerbations. Our research team speculates that this phenomenon may be more related to patient compliance. Patients with poorly controlled asthma tend to have poor compliance and are unable to complete the regular pulmonary function and nitric oxide tests and control their symptoms with medication alone. This result also suggests that we should focus on health education for asthma patients in the future and emphasize the need for pulmonary function and other tests so that more asthma patients can be effectively controlled in the long term.

Unfortunately, this study also has some shortcomings. Since the clinical data of all patients were obtained from the outpatient electronic medical record system of 10 tertiary care hospitals, the vast majority of the hospitals could not directly connect the pulmonary function results to the outpatient system, so the investigators had some difficulties in the later data collection, resulting in missing pulmonary function results in more than 80% of the patients. Secondly, the classification of asthma was not reflected in the medical records of patients in eight of the hospitals, so the investigators were only able to make the corresponding judgments through the description of clinical information such as patient history, symptoms, and signs, and thus there may be some discrepancies with the true classification of patients.

Conclusions

From the study findings, we first established a detailed overview of asthma in the Jinan province of China by analyzing the medical records of 31, 082 asthma patients using real-world medication data. Patients with mild asthma exhibited the highest rate of asthma exacerbations. Age, COPD, and GERD were unequivocally identified as risk factors for asthma exacerbations, and ICS/LABA therapy at the exacerbation stage is more effective than non-ICS/LABA. This study provides more detailed and exact information about the clinical status of asthma patients in Jinan, China that can be used for their further medical management and therapy strategy.

Abbreviations

CI: Confidence interval; CVA: Cough variant asthma;GERD: Gastroesophageal reflux disease; GOLD: Global Initiative for Asthma; ICS: Inhaled corticosteroids; LABA: Long-acting beta agonists; LAMA: Long-acting muscarinic antagonists; OR: Odds ratio; SD: Standard deviation;

Declarations

Ethics approval and consent to participate

The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). This study was approved by the Committee on Ethics of Jinan Central Hospital affiliated to Shandong First Medical University, Shandong (No. JCH2020-136-01). Patient consents were waived due to retrospective study design.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests that could have influenced the present study.

Authors' contributions

Bin Shang and Xiangguo Li contributed equally to this article.

Jian Sun and Shujuan Jiang contributed equally to this article.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Tables

Table 1. Summary of studies published

Study	Objective of study	Number of patients	Regions covered	Method	Prevalence
Study 1(Huang et al, Lancet)	Estimate the national prevalence of asthma in a representative sample of the Chinese population	57779	Six geographical regions	Cross-sectional, survey	4·2% (95% CI 3·1–5·6)
Study 2(Lin, et al, Respiratory Medicine)	Demonstrate the prevalence and risk factors of asthma in mainland China	164215	Eight provinces/cities of seven areas in mainland China	Survey	2234(1.24%)
Study 3(Ding, et al, J Asthma)	Estimate the prevalence of mild asthma in urban China	59935	Data were from the China National Health and Wellness Surveys (NHWS)	cross-sectional assessment, Internet-based surveys of adults in urban China	1,191 (1.99%)
Study 4(Qing-Ling Fu et al, International Journal of Environmental Research and Public Health)	Assess the prevalence and risk factors of asthma in Chinese adults	9974	Seven major Chinese cities	Cross-sectional survey. All participants were interviewed face-to-face in their homes using a standardized self-administered questionnaire	2.46%

Table 2. Descriptive statistics of patients with asthma between 2011 and 2019 in Jinan at baseline

		Total	Asthma	Cough Variant Asthma	Others
Patient Numbers		36,505	31,082	1,600	3,823
Gender	Male	16,965 (46.5%)	14,177 (45.6%)	637 (39.8%)	2,151 (56.3%)
	Female	19,535 (53.5%)	16,900 (54.4%)	963 (60.2%)	1,672 (43.7%)
	Unknown	5 (< 0.1%)	5 (< 0.1%)	-	-
Age (Year)	Mean	51.2	50.7	44.5	58.2
	SD	16.6	16.5	14.4	15.7
	Q1	38.1	37.7	33.0	47.1
	Median	50.4	49.8	43.1	57.5
	Q3	62.4	62.0	54.7	69.0
Age Group (Year)	18-60	25,516 (69.9%)	22,063 (71.0%)	1,334 (83.4%)	2,119 (55.4%)
	>60	10,989 (30.1%)	9,019 (29.0%)	266 (16.6%)	1,704 (44.6%)
Visit Number		88,101	78,103	2,638	7,360
Average Visit Number (Mean ± SD)		2.4 ± 4.8	2.5 ± 5.1	1.7 ± 2.8	1.9 ± 2.7
Department	Outpatient	78,703 (89.3%)	69,894 (88.3%)	2,326 (96.1%)	6,483 (98.9%)
	Inpatient	4,249 (4.8%)	4,164 (5.3%)	51 (2.1%)	34 (0.5%)
	Emergency	5,149 (5.8%)	5,068 (6.4%)	43 (1.8%)	38 (0.6%)

Table 3. Characteristics of patients with different severities of asthma

	Total	Mild	Moderate	Severe
Patient Number	14,264 (100%)	10,691 (75.0%)	3,488 (24.5%)	85 (0.6%)
Gender				
Male	6,760 (47.4%)	4,956 (46.4%)	1,754 (50.3%)	50 (35.3%)
Female	7,502 (52.6%)	5,734 (53.6%)	1,733 (49.7%)	35 (41.2%)
Unknown	2 (< 0.1%)	1 (< 0.1%)	1 (< 0.1%)	0 (0.0%)
Age (Mean ± SD)	50.3 ± 16.3	50.0 ± 16.2	51.2 ± 16.4	58.3 ± 15.0

Table 4. Characteristics of asthma exacerbations in patients with different asthma severities

	Total	Mild	Moderate	Severe
Patient Number	14,264 (100%)	10,691 (75.0%)	3,488 (24.5%)	85 (0.6%)
Exacerbation Number				
Never	13,791 (96.7%)	10,366 (97.0%)	3,345 (95.9%)	80 (94.1%)
Ever	473 (3.3%)	325 (3.0%)	143 (4.1%)	5 (5.9%)
1	299 (2.1%)	200 (1.9%)	96 (2.8%)	3 (3.5%)
≥2	174 (1.2%)	125 (1.2%)	47 (1.3%)	2 (2.4%)
Average Interval of Exacerbation (d)*				
	41.3 ± 64.4	33.0 ± 54.5	61.3 ± 83.0	91.1 ± 29.5
Interval of Exacerbation [Median (Q1, Q3), (d)*]				
	13.1 (2, 52.6)	9.5 (2, 43.3)	27 (3, 76.2)	91.1 (80.7, 101.6)

* Patients suffered from exacerbations ≥ 2 times

Table 5. Analysis of the exacerbation frequency after ICS/LABA or non-ICS/LABA treatment at the exacerbation index

	ICS/LABA	Non-ICS/LABA	*P*-value
Patient Numbers	2,195	8,435	
Exacerbation Number			
Never	1,615 (73.58%)	5,548 (65.77%)	< 0.001
Ever	580 (26.42%)	2,887 (34.23%)	
1	318 (14.49%)	1,274(15.10%)	
≥ 2	262 (11.94%)	1,613 (19.12%)	
≥ 3	143 (6.51%)	1,090 (12.92%)	
≥ 4	90 (4.10%)	789 (9.35%)	
Interval of exacerbation (excluding the index asthma exacerbation, days)*			
Mean ± SD	69.0 ± 63.2	41.3 ± 57.4	< 0.001
Median (Q1, Q3)	50.3 (30.7, 91.9)	22.6 (3, 51.5)	< 0.001
Interval of exacerbation (including the index asthma exacerbation, days)			
Mean ± SD	98.5 ± 91.1	46.0 ± 67.2	< 0.001
Median (Q1, Q3)	65.2 (34.2, 134.6)	21 (2.5, 58.0)	< 0.001

* patients suffered from exacerbations ≥ 2 times

Table 6. Analysis of risk factors for exacerbation of asthma

		Patients suffered exacerbations	Patients never suffered exacerbations	*P*-value	Odds ratio
Patient number	**N**	473	13,791		
Gender	**Male**	223 (47.15%)	6,537 (47.41%)	0.948	0.99 (0.823,1.189)
	Female	250 (52.85%)	7,252 (52.59%)		
Age (years)	**Mean ± SD**	53 ± 14.625	49.85 ±1 6.186	< 0.001	1.012 (1.006,1.017)
	Median (Q1, Q3)	52.3 (42.9,61)	48.2 (37.3,60.3)		
Age group (years)	**18-60**	343 (72.52%)	10,259 (74.39%)	0.388	1. (0.894,1.348)
	>60	130 (27.48%)	3,532 (25.61%)		
Comorbidities	**COPD**	57 (12.05%)	686 (4.97%)	< 0.001	2.618 (1.945,3.459)
	Rhinitis	130 (27.48%)	3,695 (26.79%)	0.779	1.036 (0.841,1.268)
	Nasosinusitis	18 (3.81%)	473 (3.43%)	0.755	1.114 (0.665,1.746)
	Nasal polyposis	4 (0.85%)	37 (0.27%)	0.062	3.17 (0.946,7.943)
	GERD	13 (2.75%)	183 (1.33%)	0.016	2.101 (1.131,3.57)
	Anxiety	17 (3.59%)	384 (2.78%)	0.365	1.302 (0.764,2.068)
	Depression	9 (1.9%)	231 (1.68%)	0.844	1.139 (0.539,2.101)
	Obese	0 (0%)	70 (0.51%)	-	0 (0,0.073)

Table 7. Analysis of the costs of asthma management

		Total cost	Medicine fee	Testing fee	Fee for others
Asthma patients ever suffered exacerbation	Patient number (N)	468	468	468	468
	Patients with cost incurred□%□*	468 (100%)	365 (77.99%)	211 (45.09%)	358 (76.5%)
	Mean	3,339.67	2,052.12	451.93	835.62
	S.D.	6,232.47	4,258.97	1,155.03	1,809.68
	Q1	361.36	136.75	0	2
	Medium	1,074.34*	747.44*	0*	106.01*
	Q3	3,132.41	2,141.67	214	658.15
	Contribution to the total cost	100%	61.45%	13.53%	25.02%
Asthma patients never suffered exacerbation	Patient numbers	8,012	8,012	8,012	8,012
	Patients with cost incurred□%□*	8,012 (100%)	6,730 (84%)	1,025 (12.79%)	4,969 (62.02%)
	Mean	968.45	1,320.25	515.26	38.79
	SD	1,932.38	1,983.20	1,305.81	150.93
	Q1	197.89	385.38	75.84	0
	Medium	433.52	747.9	221	0
	Q3	948.37	1,483.07	484.66	0
	Contribution to the total cost	100%	53.2%	4.01%	42.79%

*All cost, fee, and payment are presented as RMB, and 1RMB approximately equal to 0.15USD.

Figures

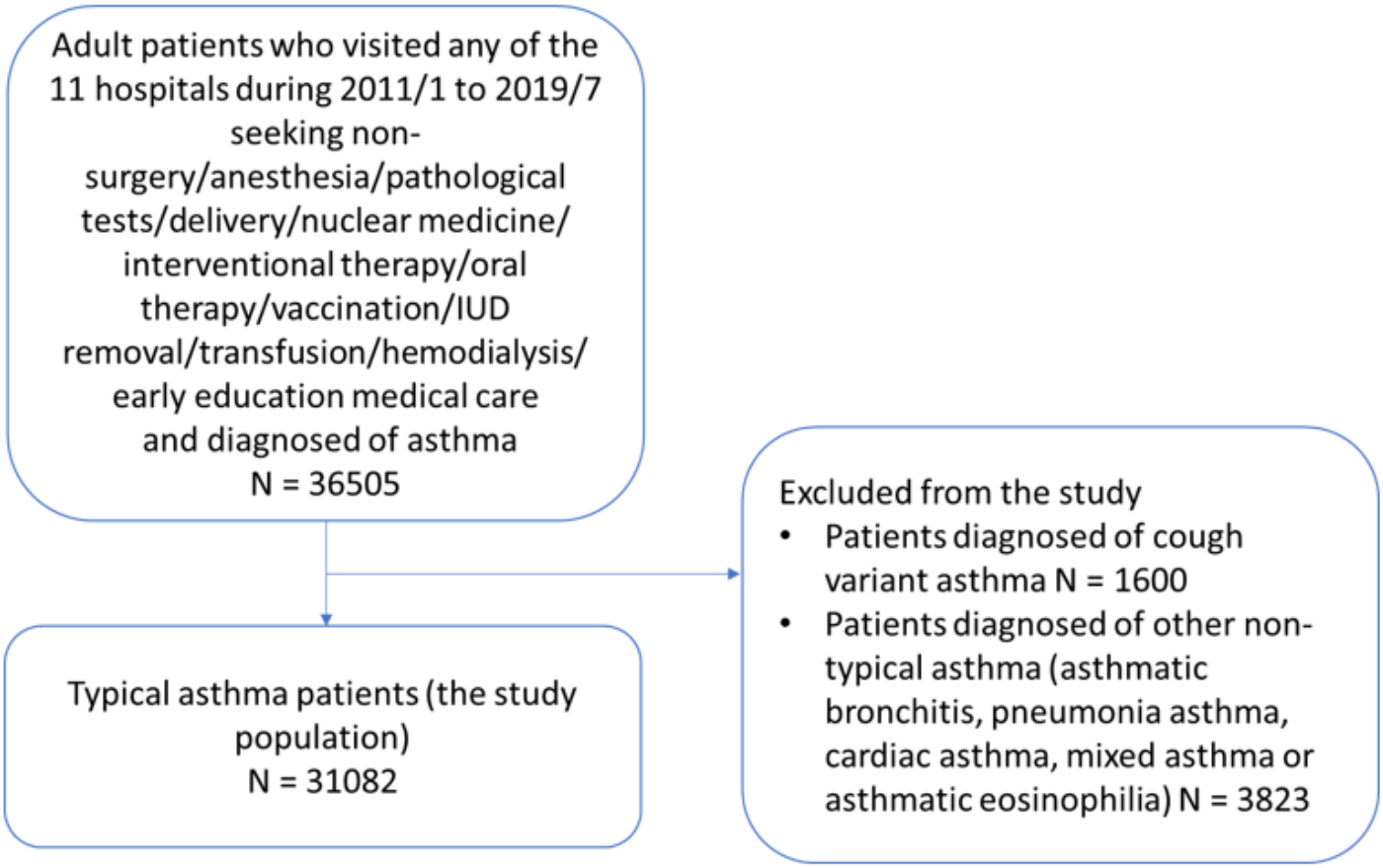

Figure 1

Screening scheme of patients enrolled