

FACTORS ASSOCIATED WITH A SEVERE ASTHMA IN ASTHMATIC ADOLESCENT PATIENTS

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Abstract

Introduction: The present study aims to determine the frequency of severe asthma in asthma patients followed at the National Hospital of Pneumo-Phtisiology (CNHPP) of Cotonou and to identify the risk factors associated with it

Methods: The cross-sectional, descriptive and analytical study focused on 213 asthmatic patients in the 2013 active file of the CNHPP. The data were collected through the use of files and individual interviews with patients. They were processed and analyzed using EPIINFO7 and STATA11 software. Pearson's Chi 2 test, unvaried and multivariate logistic regression were used at the significance level of 0.05

Results: A total of 154 asthmatic patients, ie 72.7%, answered the questionnaire. Among them 20.8% (95% CI: (14.67; 28.05)) suffered from severe asthma. Patient ages ranged from 10 to 76 years with a median of 41 years; 51.3% were female, 79.9% had a history of allergy, 61.7% started their asthma after the age of 12, and only 11% had used or consumed tobacco. The factors associated with the onset of severe asthma were: age 46 to 55 years ($p = 0.04$); the third and fourth quintiles of economic well-being ($p = 0.01$) and the onset of asthma after the age of 12 ($p < 0.001$)

Conclusion: The study showed a high frequency of severe asthma in Benin and will improve its management at the CNHPP.

Keywords: Severe asthma, patients, associated factors, Benin

Introduction

Severe asthma is an uncontrolled asthma that can pose a risk of frequent severe exacerbations, death, adverse drug reactions or chronic morbidity [1]. The past 40 years have seen an increase in the prevalence of severe asthma worldwide and the associated economic burden, especially among children [2 , 3]. Globally, it is estimated that severe asthma affects between 1 and 3% of the general population in children and adults, ie around 5 to 10% or even 20% of asthma patients [4 , 5]. Patients with the most severe asthma take more drugs, seek more medical attention, and are hospitalized more often. Severe asthma therefore generates a heavy economic burden for individuals and their families and also for countries [6 , 7]. It alone represents 80% of asthma-related health expenditure [8]. Hospitalization is responsible for more than half of the costs [3]. Several recent studies have correlated asthma-related expenses with the severity of the disease and the quality of medical control, clearly showing that a

significant portion of the costs is due to sub-optimal disease control [3 , 6].

In Benin, there are few data on asthma and few epidemiological studies have focused on severe asthma. Asthma is one of the pathologies taken into account by the National Program for the Fight against Non-Communicable Diseases (PNLMNT). In addition, since 2009 it has been set up at the National Hospital of Pneumo Phtisiologie (CNHPP) a care unit for asthma patients in order to improve the care of patients with persistent asthma by facilitating their treatment. access to care and better follow-up. Despite these efforts, some subjects continue to be uncontrolled after a long period of follow-up. A study carried out at the CNHPP in 2012 to assess the management of persistent asthma revealed that 83.2% of cases of 9]. The severity of asthma is one of the main reasons that make it difficult to control the disease. The objectives of the present study were to determine the frequency of severe asthma in asthma patients followed at the National Hospital of

Pneumo-Phthisiology (CNHPP) in Cotonou and to identify the risk factors associated with it.

Methodology

Study setting: the CNHPP in Cotonou (Benin) is the national health structure for the care of tuberculosis patients and other lung diseases. It is located east of Cotonou in Akpakpa in the Abokicodji district about 300 m from the 2nd Cotonou bridge going towards the Akpakpa cemetery. The CNHPP is structured into three medico-technical services which are the clinical management service, the radiology service and the reference laboratory for Mycobacteria. It also has a pharmacy which dispenses asthma medication to patients at subsidized prices.

Type of study: this is a descriptive and analytical cross-sectional study carried out from April to July 2014.

Study population: The study targets were asthma patients in the 2013 CNHPP active file. The data sources were the medical records of patients in the active file 203 of the CNHPP and the consultation register of the asthma management unit.

Sampling techniques: calculation of the sample size with the Schwartz formula $n = z^2 \alpha * p * q / i^2$, for the proportion of severe asthma $p = 10\%$, the precision $i = 0,05$ and the risk $\alpha = 0.05$ with $Z\alpha = 1.96$ gave $n = 138$. This number was increased by 10% to predict the cases of non-response and we obtained $n = 152$. However, the 213 patient files received during the period considered were retained. Completeness was preferred to increase the power of the tests.

Study variables: the dependent variable was severe asthma. Severe asthma was defined taking into account the WHO guidelines [1] for epidemiological studies on severe asthma. Three elements were taken into account for this definition: the level of control, the daily dose of corticosteroid therapy achieved and compliance with treatment. Asthma was classified as severe if during the last 6 months, despite good adherence to treatment, it was partially or not controlled despite a moderately or very high dose of inhaled corticosteroids with more than 500 μg of beclomethasone in adults and more than 200 μg in children or if it has been controlled at the cost of a high dose of inhaled corticosteroid therapy with more than 1000 μg of beclomethasone in adults and more than 400 μg in children. The data collected covered the following independent variables: sex, age, level of education, place of residence, level of socio-economic well-being, age of onset of asthma, history personal allergy, history of asthma or familial atopy, exposure to tobacco smoke or other fuels, history of drug reactions, place of residence, exposure to allergens in the workplace, history of illness, smoking status and weight status. The level of economic well-being of the household in which the patient lives was determined according to the model of the 2006 Benin demographic health survey based on criteria. A score is assigned to each criterion based on the patient's response. The latter is

classified in one of the quintiles of economic well-being according to the total score obtained [history of illness, smoking status and weight status. The level of economic well-being of the household in which the patient lives was determined according to the model of the 2006 Benin demographic health survey based on criteria. A score is assigned to each criterion based on the patient's response. The latter is classified in one of the quintiles of economic well-being according to the total score obtained [history of illness, smoking status and weight status. The level of economic well-being of the household in which the patient lives was determined according to the model of the 2006 Benin demographic health survey based on criteria. A score is assigned to each criterion based on the patient's response. The latter is classified in one of the quintiles of economic well-being according to the total score obtained [10]. In this study, thirteen criteria were retained which are: belonging to the house where one lives, possession of land, sources of energy for cooking, source of lighting, water supply, type of soil, type of toilet, roof of the house, construction materials, means of transport, source of information in the house, means of communication and number of rooms used by family members for sleeping. The weight status of the patients was classified as thin, normal, overweight and obese according to the criteria of the World Health Organization [11].

Data collection techniques and tools: Techniques were based on document use, questionnaire survey and observation. The collection tool consisted of a sheet for analyzing patient records, a questionnaire for patients, as well as measuring equipment such as a bathroom scale, a tape measure and a peak flow meter.

Data processing and analysis: the data were entered using the EPIINFO version 7 software and analyzed by the STATA11.0 software. The analysis focused on the descriptive aspect and the analytical aspect. The characteristics of the sample were described, the estimated proportions and the odds ratios (OR) were calculated with their 95% confidence interval (95% CI) to measure the strength of the association between the occurrence of severe asthma in patients and independent variables. The frequency comparison was made using Pearson's Chi2 test. A model was built using a top-down stepwise logistic regression analysis. The variables were entered into the multiple model from the uni-variate analysis between the dependent variable and the independent variables. 12]. The significance level for all tests was 0.05, but variables were introduced into the multiple regression model up to a cutoff of 0.20.

Results

Of the 213 asthma patients received in 2013 whose files were examined, 154 responded to the data collection and were interviewed or 72.3% of the expected number.

Socio-demographic characteristics of the subjects interviewed

They were aged between 10 years and 76 years with an asymmetric age distribution, the median being 41 years with an interquartile range ranging from 28.5 years (Q1) to 54.5 years (Q3). Fifty three percent were women. The subjects having reached the secondary level represented 32.5% of the respondents. More than one in three respondents found themselves at the level of the third quintile of economic well-being

Other characteristics of the subjects interviewed

A family history of asthma or atopy was frequent in asthmatics followed by the CNHPP (84.4%). Of the 154 respondents, 79.9% said they had a personal history of allergy and 38.3% started their asthma before the age of 12. Only 24.0% of the patients interviewed are not exposed in their living environment to tobacco smoke or other fuels. Almost half of them (44.2%) suffer from at least one of the following pathologies: gastroesophageal reflux disease, sinusitis, pneumonia, depression, anxiety and 13.6% have a history of known drug reaction to aspirin, nonsteroidal anti-inflammatory drugs, antibiotic or corticosteroid. One in four respondents (25.3%) said they were exposed to an allergen such as dust, smoke, odor, pollens and animals in his professional environment. Only 11% of the patients interviewed have used or still used tobacco, while 42.9% are overweight or obese.

Comparison of non-respondents to respondents

The study recorded 59 non-respondents, or 27.7% of patients in the 2013 active file. There were several reasons for non-response. Thirty patients were no longer reachable at their contact available at the CNHPP, 4 had died, 15 were absent from Cotonou during the data collection period for the study and 10 patients did not respond to the invitation for the questionnaire. despite the many reminders. This proportion was high and required the comparison of respondents with non-respondents based on the independent variables available in the files, which were age, sex, place of residence and smoking status, there was no significant difference between the group of respondents and that of non-respondents according to these variables. The group of respondents and that of non-respondents were therefore comparable.

Frequency of severe asthma

Among the 154 respondents, 20.8% (95% CI: (14.67; 28.05)) suffered from severe asthma.

Factors related to severe asthma

Of the fourteen variables studied, three were significantly associated with the onset of severe asthma at a varied analysis: age and level of economic well-being and age of onset of the first attack. Thus, subjects with asthma aged 46 to 55 were 5.46 times significantly more likely to develop severe asthma than those aged 35 or younger ($p < 0.01$). People aged 36 to 45 were less likely to have severe asthma than those aged 35 and under, and subjects 56 and older were 2.91 times more likely than those aged 35 or younger but these differences were not significant (respectively $p = 0.66$ and $p = 0.05$). Subjects belonging to the third and fourth economic well-being quintiles ran 2, 75 times significantly more risk of developing severe asthma than those belonging to the first and second quintiles ($p < 0.01$). Subjects who started their asthma after the age of twelve had 2.65 times (CI95% : (1.07; 6.6)) significantly more risk of developing severe asthma. Two variables had p -values < 0.20 : personal allergy history and level of education. These five variables were introduced into the multiple regression model. (Table 1). By adjusting for age, level of economic well-being, level of education and personal history of allergy, subjects who started their asthma after the age of twelve had 2.97 times (95% CI : (1.03; 8.57)) significantly more risk of developing severe asthma ($p = 0.04$). When adjusted for level of economic well-being, age of onset of asthma, level of education and personal history of allergy, asthma subjects aged 46 to 55 were 4.45 times (95% CI: (1.4; 14.15)) significantly more risk of developing severe asthma than those aged 35 years or less ($p = 0.01$). When taking into account the age of the subjects, the age of onset of asthma, the level of education and the personal history of allergy, subjects belonging to the third and fourth quintiles of economic well-being ran 3.80 times (95% CI : (1.53; 9.39)) significantly more risk of developing severe asthma than those belonging to the first and second quintiles ($p < 0.001$).

Table 1:

Variables	Modalities	GOLD	95% CI	p-value
Age of onset of asthma	<12 years	1		
	> 12 years	2.97	1.03 - 8.56	0.04
Age	≤35 years	1		
	36-45 years	.43	0.09 - 1.98	0.28
	46-55 years	4.45	1.40 - 14.15	0.01
	≥56 years	1.95	0.60 - 6.36	0.26
Level of economic well-being	The richest and the second	1		
	The middle and the fourth	3.8	1.53 - 9.39	
Educational level	Primary or out of school	1		
	Secondary	.97	0.31 - 3.04	0.96
	Superior	1.24	0.37 - 4.18	0.72
Personal history of allergy	No	1		
	yes	.86	0.31 - 2.40	0.78

Discussion:

Comparison of results with those of other studies

Studies on the severity of asthmatic disease use varieties of definitions of severe asthma that differ in their specification in terms of frequency and severity of symptoms and exacerbations, ventilatory function, and corticosteroid doses [13 - 15] For the discussion of the results of this study, comparisons were made with the results of studies exploring asthma control and also those of studies that used various definitions of severe asthma.

The frequency of severe asthma

The proportion of asthmatic subjects with severe asthma in this study is 20.8%. This frequency is high compared to the prevalence of 5-10% worldwide [4 , 5]. It is also high compared to 6% of asthmatics presenting severe persistent clinical signs obtained by the Institute for Research and Documentation in Health Economics (IRDES) in France [16]. The frequency of severe asthma at CNHPP is close to the 16% frequency of severe persistent asthma found by Aissa *et al* [17] in Tunisia in a cross-sectional study, carried out in an allergology consultation. This difference could be explained by the fact that the IRDES carried out a population survey while the present study and that of Aissa *et al* were carried out in a hospital environment. SARP [13] and ENFUMOSA [18] noted higher frequencies of severe asthma, 46.6% and 50.8%, respectively.

Factors associated with severe asthma

Age has been associated with severe asthma. This association has been documented by most studies. Thus, in the SARP study [13 , 19], subjects suffering from severe asthma were older and had suffered from the disease for a longer period of 25 ± 14 years on average compared with 17 ± 11 years at 20 ± 14 years for those suffering from mild asthma and moderate asthma respectively. The study carried out by IRDES [16] among asthmatics in the French population showed that subjects aged 40 to 64 years were 1.47 times significantly more likely to have uncontrolled asthma than those aged under 40 years old. Godard *et al* [20], in metropolitan France, found that the percentage of patients with unacceptable control of their asthma increased significantly with age. However, among subjects with severe asthma, those having 3 or more exacerbations per year were significantly the youngest [21]. Contrary to our results, Yildiz [22], in a study carried out in Turkey to assess the profiles of asthma patients and their inhaler treatment devices for asthma control did not find that age was linked to asthma control. It is the same for ENFUMOSA [18 , 19] who found no age-related difference between subjects with severe asthma and those with mild or moderate asthma. Gender was not associated with severe asthma in our study. Our result is consistent with that of Varraso *et al* [23], in the Epidemiological Study on Genetics and Environment of Asthma (EGEA), who noted that the severity of asthma was not related to sex when the clinical score, inhaled steroids, or lifetime

hospitalizations are considered. The SARP [13 , 19] also did not find the gender associated with severe asthma between subjects with severe asthma and subjects with moderate asthma with similar lung function. On the other hand, Godard *et al* [20], both in bivariate and multivariate analysis, found that the probability of having optimal asthma control was significantly associated with gender.

The level of economic well-being was significantly associated with severe asthma in our study. Blanc *et al* [24], noted that asthmatics whose households come from low socioeconomic backgrounds had a significantly higher asthma severity score. For Eisner *et al* [25] the subjects with the lowest incomes were significantly more at risk of hospitalizations for asthma during the 18 months of follow-up in their study. This disparity between the different socioeconomic classes could result from greater exposure in less privileged neighborhoods to certain psychosocial and environmental risk factors that can induce or exacerbate asthma. Lower purchasing power and lower treatment adherence among the less advantaged classes could also account for this result. There was no significant association between education level and severe asthma in this study. Yildiz [18] and Blanc *et al* [24], did not demonstrate a link between education level and asthma control or asthma severity score. However, this relationship was found by IRDES [16]. In this study, the less educated subjects were more likely to have uncontrolled asthma than the more educated subjects. Eisner *et al* [25] observed in a cohort study carried out in Northern California that the more the number of years of instruction increases, the more the risk of hospitalization for asthma decreases. This divergence in results can be explained by local socio-geographic specificities.

A history of asthma or familial atopy and a personal history of allergy have not been identified as risk factors for severe asthma. The SARP [13 , 19], on the other hand, found that atopy confirmed by the skin test was significantly less frequent in subjects with severe asthma on univariate analysis than on multivariate analysis. This association has also been found by ENFUMOSA [18 , 19]. In a cross-sectional study by Amelink *et al* in the Netherlands [26] in subjects who developed their first asthma attack in adulthood, the absence of atopy was one of the factors associated with the severity from asthma to univariate analysis. For Ten Brinke *et al* [21], the family history of asthma was significantly associated with frequent exacerbations among subjects with severe asthma. The results obtained in the present study could be explained by the fact that the concept of atopy and allergy was sought by questioning and not by skin tests. People who started their asthma after the age of 12 were at greater risk of developing severe asthma. Yildiz [22] did not note a significant association between the age of onset of asthma and the level of control. The SARP [13] also did not find a difference between the groups according to the age of onset of asthma, however onset of asthma after the age of 12 was significantly associated with reduced lung function and

infections. sinusopulmonary in subjects with severe asthma. According to Pascual and Peters [27], in a review of articles, the association of the age of onset of asthma with the severity of the disease remains questionable because of the contradictory data found by the various authors.

In the present study, there was no significant relationship between smoking and severe asthma. The low proportion of current and former smoking subjects could explain this result because current and past smoking has been very often found to be linked to severe asthma and to non-control of asthma in several studies [14 , 20 , 22 , 28]. However, this result agrees with those of SARP [13] and IRDES [16] which did not find any association with smoking. Overweight and obesity were not significantly associated with severe asthma. This result agrees with that of the SARP [19] in the United States who did not find associated obesity. The ENFUMOSA [19] and EGEA [23] studies, for their part, found this association of obesity in female subjects. In the United States, a national asthma survey [29] that included 3095 adult subjects found that obese subjects were significantly more likely to be classified as severe persistent asthma. IRDES [16] noted that overweight and obese subjects were significantly more likely to have uncontrolled asthma than those of normal weight or lean. For Godard et al [20], the likelihood of having optimal asthma control was significantly higher in patients with normal body mass index compared to obese patients. These contradictory results in relation to body mass index should be the subject of further study.

Conclusion:

The present study made it possible to know the frequency of severe asthma among asthmatics monitored at the CNHPP, based on the new WHO guidelines for epidemiological studies on the severity of asthma. This frequency was 20.78%. Factors associated with severe asthma were also determined in this study population. Three factors have been associated with severe asthma. These are the high age and low level of economic well-being and the asthma onset age over 12 years. Severe asthma is a public health problem that is often not prioritized. It is important to take the measures in terms of organization of services at the CNHPP and communication for behavior change with patients to improve patient care. Furthermore, these results can be used for in-depth studies on severe asthma.

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