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## CASE SERIES

# Predictive Factors of Non-Control of Asthma in Moroccan Women about 50 Cases Using a Regression Logistic Model

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## ABSTRACT

Asthma is a chronic lung affection, caused by inflammation and a narrowing of the airways, leading to a variable combination of shortness of breath, cough, wheeze and chest tightness. Known as a benign disease, but can severely affect patient's quality of life and might be fatal if not controlled. As mentioned by the World Health Organization, asthma affected an estimated 300 million people and caused 455 000 deaths. All ages and gender may have asthma. Nonetheless literature data suggest that asthma has a higher incidence in females, particularly at certain stage of pubertal development. Besides, women are more likely to have severe asthma and a later onset of asthma compared to men. Numerous hypotheses have tried to explain this fact. There are not yet final data available in the literature on the role of gender in the pathogenesis of asthma and different behavior in females.

The purpose of this study is to describe then analyze the different factors influencing asthma control in women. This is a retrospective, analytical and descriptive study over a period of 3 years (between 2020 and 2022), involving 50 women with asthma followed in allergology consultation at the Pulmonology Department 20 August 1953, University Hospital Center IBN ROCHD, Casablanca, Morocco.

The age range was between 14 years and 41 years old. 54% of patients were postmenopausal compared to 46% women in young age. As characteristics of our patients, 84% had atopy, 72% had gastroesophageal reflux disease, 32% had vitamin D deficiency, and 13% had Fernand Widal syndrome. Asthma was controlled in 48% of cases and uncontrolled in 52%. Univariate analysis of predictors of asthma control showed that there was a significant association between menopause, vitamin D, gastroesophageal reflux disease, psychiatric disorders, and medication adherence with asthma control. Menopause increases the risk of having uncontrolled asthma with an OR of 12.6. Women with normal vitamin D level had a lower risk of having uncontrolled asthma with an OR of 0.125. Multivariate analysis of predictors of asthma control showed that there is a significant association between menopause and asthma control. Postmenopausal women are more likely to have uncontrolled asthma with an OR equal to 0.005 adjusted for vitamin D, gastroesophageal reflux disease, psychiatric disorders, and medication adherence. Compliant patient has a lower risk to develop an uncontrolled asthma with an OR equal to 0.08 adjusted for menopause, vitamin D, gastroesophageal reflux disease and psychiatric disorders.

The control of asthma in women is peculiar and may be influenced by hormonal and environmental factors. This notion is important to consider in the follow-up and management of female asthma.

**Keywords:** Asthma in women, asthma control, hormonal factors, Gastroesophageal reflux disease, menopause.

## Introduction

Asthma is a heterogeneous disease characterized by chronic inflammation of the bronchial tubes, which leads to recurrent episodes of shortness of breath, chest tightness and cough often associated with wheezing. It presents a global public health problem in women. Throughout life, from birth to middle age, women with asthma differ from men, both in terms of epidemiology and the evolution of the disease. Thus, sex hormones intervene in the inflammatory phenomenon of the respiratory mucosa which may interrupt asthma control. Sex steroids modulate the structure and function of bronchial and immune cells. Understanding their role in asthma pathogenesis is complicated by the ambivalent effects of bronchodilating and pro-inflammatory oestrogens as well as the diversity of response to their association with progesterone. Women with asthma are at high risk of exacerbations and of severe asthma. In this work, we are interested in the particularities of women's asthma and to analyze the different factors influencing asthma control in Moroccan women.

## Method and patients

A retrospective analytical study was carried out between 2020 and 2022 in the Department of

Pulmonology 20 August in 1953, University Hospital Center IBN ROCHD, Casablanca, Morocco. The study included women followed for asthma in allergology consultation. The data was collected from medical records of patients.

We used descriptive analysis for patient's characteristics and logistic regression analysis to identify factors associated with asthma control. Asthma control was the dependent variable and independent variables were: Menopause, Vitamin D, Gastroesophageal reflux disease, Fernand Vidal syndrome, Psychological disorder, Therapeutic compliance

All factors with a p-value < 0.05 in the univariate analysis were included into a multivariate analysis. Statistical analysis was performed using Jamovi Software.

## Results

The age range was between 14 years and 41 years old. 54% of patients were postmenopausal compared to 46% in genital activity. For asthma control predictors, 84% had atopy, 72% gastroesophageal reflux disease, 43% psychiatric disorder, 32% vitamin D deficiency, and 13% Fernand Vidal syndrome (table I).

**Table I:** Different past medical history of patients included in this study

Past medical history	%
Atopy	84
Gastroesophageal reflux disease	72
Vitamin D3 deficiency	32
Psychological disorder	43
Fernand Vidal syndrome	13

Asthma was controlled in 48% of cases and uncontrolled in 52%. Univariate analysis of predictors of asthma control showed that there was a significant association between menopause, vitamin D, gastroesophageal reflux disease, psychiatric disorders, and medication adherence with asthma control. Menopause increases the risk of having uncontrolled asthma with an OR of 12.6. Women with normal d saw had a lower risk of

having uncontrolled asthma with an OR of 0.125. Women with gastroesophageal reflux disease are more likely to have uncontrolled asthma with an OR of 12. Women with psychiatric disorders are more likely to have uncontrolled asthma with an OR of 6.5. Women with good adherence to treatment have a lower risk of developing uncontrolled asthma with an OR of 0.217 (Table II).

**Table II:** Univariate analysis of asthma control predictors

Variables	OR	95% CI	P value
Menopause	12,6	3,288 - 48,287	< .001
Vitamin D	0,125	0,0214 - 0,731	0,021
Gastroesophageal reflux disease	12,00	2,305 - 62,456	0,003
Fernand Vidal syndrome	5,57e+7	0,00 - Inf	0,994
Psychological disorder	6,500	1,712 - 24,677	0,006
Therapeutic compliance	0,217	0,050 - 0,936	0,040

Multivariate analysis of predictors of asthma control showed that there is a significant association between menopause and asthma control because  $p$  value=0.005. Postmenopausal women are more likely to have uncontrolled asthma with an OR equal to 0.005 adjusted for vitamin D, Gastroesophageal reflux disease, psychiatric disorders, and medication adherence. After adjusting for menopause, Gastroesophageal reflux disease,

psychiatric disorders, and adherence there is no association between vitamin D and asthma control. There is a significant association between asthma adherence and control because  $p$  value = 0.034. Women with good adherence are less likely to have uncontrolled asthma with an OR equal to 0.08 adjusted for menopause, vitamin D, Gastroesophageal reflux disease and psychiatric disorders (Table III).

**Table III:** Multivariate analysis of asthma control predictors

Variables	OR	95 % CI	p value
<b>Menopause</b>	30,84	2,764 - 344,106	<b>0,005</b>
<b>Vitamin D</b>	0,622	0,052 – 7,356	0,707
<b>Gastroesophageal reflux disease</b>	5,727	0,615 – 53,262	0,125
<b>Psychological disorder</b>	7,063	0,999 – 49,919	0,051
<b>Therapeutic compliance</b>	0,080	0,007 – 0,826	<b>0,034</b>

## Discussion

The natural history of asthma by gender has been well described in the literature: asthma is more common in boys before adolescence; more frequently affects girls after adolescence <sup>(1)</sup>. Cross-sectional studies stated that about two-thirds of asthmatics before adolescence are boys and one-third are girls <sup>(2)</sup>.

After puberty, the process changes and asthma become more common in girls. Among the hypotheses put forward in an attempt to explain these differences, an anatomical factor can be distinguished: girls have smaller lung volumes than boys, suggesting that they have smaller bronchial tubes. However, they have higher expiratory flows, which leads to the conclusion that they actually have wider airways and lower bronchial resistance <sup>(3)</sup>. In adulthood, asthma is more common in women. It is often a late-onset non-atopic asthma. Certain factors, such as obesity, especially in childhood <sup>(4)</sup>, early menarche, or irregular menstrual cycles are associated with the development of asthma symptoms in women <sup>(5)</sup>.

The European cohort ECRHS, showed that the prevalence of asthma was higher among women, going hand in hand with an increase in bronchial hyperreactivity obtained by the methacholine test <sup>(6)</sup>. More recent results of four British cohorts found a higher prevalence of asthma in women after 18 years, with an increased risk of exacerbations over 55 years old <sup>(7)</sup>. Sex disparities in asthma assumed the involvement of sex hormones on the onset and the severity of asthma; it was noted that symptoms get worse in the pre-ovulatory period and luteal phase <sup>(1)</sup>.

Approximately one-third of pregnant women suffer from a worsening of their bronchial asthma during pregnancy; in another one-third, asthma severity remains without change; while in the remaining third, their bronchial asthma shows improvement from the basal condition. The explanation of this variability remains unexplained<sup>(2)</sup>. Symptoms of asthma peak in the late second or early third trimester, but exacerbations are rare during labor and the peripartum period.

Menopausal asthma is defined as new cases of asthma occurring at this time of life. However, the distinction with the worsening of pre-existing asthma during menopausal is not always clear in the literature. The incidence of menopausal asthma, in a cohort of 98,995 women, is estimated at 1.15 cases/1000 women/year <sup>(8)</sup>. Current evidence shows an increased risk of asthma in postmenopausal women, especially for those receiving hormone replacement therapy <sup>(9)</sup>, as our study showed in both univariate and multivariate analyses. Late-onset asthma in women is most often non-atopic, associated with obesity, and difficult to treat <sup>(10)</sup>. Pregnancy is often considered a period of asthma instability, increasing the risk of exacerbation by half <sup>(11)</sup>. The role of the increase in estrogen and progesterone levels, which are highest in the 3rd trimester, is of course mentioned, but it should not obscure the fact that immune changes are also profound during pregnancy <sup>(12)</sup>. As well as a lack of management, in particular the absence of disease-modifying treatment with inhaled corticosteroids, is a major factor in the loss of control observed during pregnancy <sup>(13)</sup>. Multiple studies have shown that adults with asthma with low vitamin D levels are more likely to receive urgent medical care for asthma and have poor asthma control, which is consistent with the results of our univariate study. Clinical trials are needed to determine the

role of vitamin D supplementation in asthma management <sup>(14)</sup>. The role of gastroesophageal reflux disease in poorly controlled asthma is often mentioned, but published studies have presented conflicting results. A recent study of 102 children with poorly controlled asthma, 59 of whom (57.8% had acid reflux has shown the possible benefit of effective treatment in improving asthma control <sup>(15)</sup>. Our study also objectified a high prevalence of gastroesophageal reflux disease, hence the interest of specialized management for asthma control.

Most studies suggest that obesity predisposes adult women more than men to develop asthma <sup>(16)</sup>. Other studies have highlighted an association between obesity and severe asthma with in particular an increase in the rate hospitalizations and number of

asthma exacerbations in asthmatic obese patients <sup>(17)</sup>. The pathophysiological mechanisms of this association of obesity and severe asthma are not well understood and probably multifactorial. Certain respiratory symptoms such as dyspnea in obese people can mimic asthma <sup>(18)</sup>.

### **Conclusion**

This study showed that non-control of asthma in women is associated with obesity, menopause, gastroesophageal reflux disease, poor adherence to treatment and psychiatric disorders. The control of asthma in women is peculiar by hormonal and environmental factors. Knowledge of the latter is important in the follow-up and proper management.

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