

## ORIGINAL ARTICLE

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# Gastroesophageal Reflux Disease and Asthma in Pregnant Women with Dyspnea

*Katayoon Bidad<sup>1</sup>, Hassan Heidarnazhad<sup>2</sup>, Zahra Pourpak<sup>1</sup>, Giti Shayestefar<sup>3</sup>, Heshmat Moayeri<sup>4</sup>,  
and Nasrin Zendehtdel<sup>5</sup>*

<sup>1</sup> Immunology, Asthma and Allergy Research Institute, Tehran University of Medical Sciences, Tehran, Iran

<sup>2</sup> Tobacco Prevention and Control Research Center, National Research Institute of Tuberculosis and Lung Disease, Shahid Beheshti University of Medical Sciences, Tehran, Iran

<sup>3</sup> Department of Obstetrics, Arash Hospital, Tehran University of Medical Sciences, Tehran, Iran

<sup>4</sup> Department of Endocrinology, Imam Khomeini Hospital, Tehran University of Medical Sciences, Tehran, Iran

<sup>5</sup> Department of Internal Medicine, Shohada Hospital, Shahid Beheshti University of Medical Sciences, Tehran, Iran

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## ABSTRACT

Asthma and gastroesophageal reflux disease (GERD) are two common problems in pregnancy and they affect pregnancy in several ways. In this study, we aimed to evaluate GERD and asthma in pregnant women who referred for prenatal care visits.

One-hundred and seventy three pregnant women with a complaint of dyspnea were included in the study. A questionnaire was filled and lung function tests were performed. All patients were visited by a respiratory specialist and questionnaires were evaluated by a gastroenterologist.

Out of the total number of women studied, 37% were diagnosed to have asthma and 36.4% were non-asthmatics. Twenty six percent of the pregnant women who had symptoms and signs of asthma with normal spirometry were classified as probable to have asthma. GERD was diagnosed in 80.9% of the pregnant women, but it was not significantly higher in asthmatic or probable asthmatic women compared to non-asthmatic ones. However, severity of GERD was significantly higher in asthmatic pregnant women compared to the others.

In conclusion, the prevalence of GERD was quite high in pregnant women, irrespective of the fact that they were asthmatic or non-asthmatic. Further studies evaluating women throughout pregnancy will inform us more about this relationship.

**Keywords:** Asthma; Dyspnea; Gastroesophageal Reflux; Pregnancy

## INTRODUCTION

The prevalence of reflux symptoms in general

population seems to be variable and it ranges from 5 to 58% depending on the population studied and methods used.<sup>1</sup> Major symptoms of gastroesophageal reflux disease (GERD) are reported in up to one-third of the adult population in the United States of America<sup>2</sup> and 18.4 -39.7% of population in Tehran, capital of Iran.<sup>3,4</sup> GERD and its symptoms are also more prevalent in

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**Corresponding Author:** Nasrin Zendehtdel, MD;  
Department of Internal Medicine, Shohada Hospital, Shahid Beheshti  
University of Medical Sciences, Tehran, Iran. Tel/Fax: (+98 21) 2271  
8000, E-mail: zendehtdel@ams.ac.ir

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pregnant women, worsening by the increase in gestational age. The cause of GERD in pregnancy is believed to be multifactorial. Decreased pressure of lower esophageal sphincter (LES) pressure parallel to the increase in intragastric pressure and the effect of sex hormones on LES pressure have been shown as possible mechanisms.<sup>5</sup>

Asthma, as a public health problem world-wide, especially in affluent countries,<sup>6</sup> seems to be significantly associated with GERD. GERD occurs in 45-89% of patients with asthma and GERD management results in asthma improvement.<sup>2</sup> Aspiration of gastric contents into the trachea and vagal reflexes stimulated by low pH of esophagus and the distention have been proposed to explain incredible incidence of asthma in GERD. On the other hand, high prevalence of GERD in asthma can be attributed to increased negative intrathoracic pressure in asthma exacerbations, asthma medications which decrease LES tone and autonomic imbalance in asthma.<sup>2</sup>

Moreover, physiologic changes in pregnancy (decrease in functional residual capacity, increase in ventilation and nasal congestion) affect the pulmonary function and asthma.<sup>7</sup> Asthma course can worsen in about one-third of pregnancies especially those with more severe asthma before pregnancy, and can equally improve, or remain unchanged in the rest of pregnancies.<sup>8</sup>

This study aimed to evaluate GERD and asthma in pregnant women in Tehran, Iran with dyspnea referring for prenatal care visits.

### MATERIALS AND METHODS

This study was part of a larger study on asthma and pregnancy.<sup>9</sup> One-hundred and seventy three women referring for prenatal care visits in a university hospital of Tehran University of Medical Sciences in Tehran, Iran with a complaint of dyspnea were included in this study.

All included pregnant women were visited by a single trained physician. All demographic data were recorded. A previously-validated and symptom-oriented GERD questionnaire<sup>10</sup> was filled via face-to-face interview and all patients' forms were evaluated by a gastroenterologist later. Height and weight were measured barefoot with minimal clothing.

A respiratory specialist evaluated patients afterwards. For asthma diagnosis, a medical history on

symptoms of asthma (dyspnea, cough, wheezing and post exercise symptoms) was collected and the duration of each symptom was asked. Physical examination was performed and pulmonary function tests were conducted using a Jaeger Master Screen in a sitting position, with the use of nose clips, according to manufacturer's instructions and ATS/ERS task force guidelines.<sup>11</sup> After a baseline spirometry measurement, salbutamol (2 puffs, 200µg) was administered by a metered-dose inhaler via a spacer device. Fifteen minutes later, all tests were performed again. The diagnosis of asthma was made on the basis of the Guidelines for the Diagnosis and Management of Asthma developed by the National Asthma Education and Prevention Program (NAEPP).

As challenge tests are not recommended in pregnancy, a group of patients were classified as probable-asthmatics. They were the cases in whom symptoms and signs were suggestive of asthma but the spirometry did not meet the criteria for asthma diagnosis.<sup>9</sup>

Because the initial diagnosis of GERD in pregnancy can reliably be made based on symptoms alone,<sup>12</sup> each patient was asked about the typical symptoms of GERD including heartburn (burning sensation in the stomach or lower chest) and acid regurgitation (spontaneous return of gastric or esophageal contents towards the mouth) before and after pregnancy. The frequency of GERD symptoms (daily, weekly, monthly or less than once a month) were recorded and categorized as mild, moderate and severe. Subjects were also asked whether the symptoms interfered with their normal life, work and/or sleep. Severity of symptoms was scored as mild, moderate, severe and very severe. The presence and absence of globus and pillow change were also reported by patients. Patients were also questioned if they had received medical treatment for their asthma and/or GERD.

Statistical Package for Social Sciences (SPSS) software (version 17.0) was used for data analysis. Descriptive values were presented as mean  $\pm$  standard deviation (SD). Qualitative variables were analyzed by cross-tabulation. Quantitative variables were compared by independent T test or Anova between or among groups, respectively. *P*-values less than 0.05 were considered statistically significant.

The study was approved by the ethical board of Tehran University of Medical Sciences. All study protocols were explained to all subjects and informed

consent was obtained.

## RESULTS

One-hundred and seventy three pregnant women were included in the study. The mean age and mean gestational age of them were  $28.8 \pm 5.3$  years and  $24.8 \pm 9.2$  weeks, respectively. Mean body mass index of the subjects was  $27.4 \pm 4.1$  kg/squared meters. Of all women included, only one reported alcohol consumption once in a while and no woman reported smoking. Allergies were reported in 61.8 % of the subjects, 48.3% of whom were allergic rhinitis patients and 41.9% suffering from allergies including food allergies, eczema, urticaria and drug allergies. Family history of asthma and allergies was reported to be positive in 44.8% of women.

Dyspnea was present in all subjects, cough was reported in 47.7% of women and wheezing was a complaint of 41.9% of women. Previous diagnosis of asthma before pregnancy was made in 20.9% of women included in the study. According to the symptoms, physical examination and spirometry, asthma was diagnosed in 37% of the included women and 26.6% were probable to have asthma, while 36.4% were non-asthmatics. In asthmatic group, 80.4% were diagnosed to have mild asthma, 16.6% had moderate asthma and 3.1% had severe asthma. Two of asthmatic women were diagnosed to have obstructive and restrictive patterns and FEV1 was improved in 1 of

these women after administering bronchodilators.

Heartburn before and after pregnancy, was reported in 29.1% (66% mild, 22% moderate and 12% severe) and 57.6% (37.3% mild, 1.01% moderate and 61.6% severe) of cases, respectively. Acid regurgitation before and during pregnancy, was present in 30.4% and 85.5% (68.7% since the first trimester, 20.4% since the second trimester and 10.8% since the third trimester) of the women included in the study. GERD was present in 80.9% of the pregnant women. Age distribution, BMI groups, trimesters of pregnancy and prevalence of GERD in each group are shown in table 1.

As shown in Table 2, GERD was not significantly higher in asthmatic or probable asthmatic women compared to non-asthmatic ones, but in pregnant women who had asthma, GERD was significantly more severe compared to women who did not have asthma ( $p=0.02$ ). There was no significant association between frequency or severity of GERD symptoms and severity of asthma. In women who reported globus, post bronchodilator percent of FVC was significantly lower than the women who did not report globus ( $89\% \pm 12$  vs  $97 \pm 11$ ,  $p=0.04$ ).

The risk of GERD and heartburn was greater in high multiparous women but it was not statistically significant. The patients with moderate, severe and very severe heartburn and acid regurgitation complained significantly more about sleep disturbances of any type caused by their symptoms.

**Table 1. Age distribution, BMI, trimester of pregnancy and prevalence of GERD.**

		Total	GERD		Asthma	
			(n)	(%)	(n)	(%)
Age	Total	172	139	80.8%	64	37.0%
	18-24	34	27	79.4%	11	32.4%
	25-34	110	92	83.6%	40	36.4%
	35-44	28	20	71.4%	12	42.9%
BMI	Total	163	131	80.4%		
	18.6-24.9	50	40	80.0%	15	34.1%
	25-29.9	74	59	79.7%	25	34.7%
	30-39.9	39	32	82.1%	13	33.3%
Trimesters of pregnancy	Total	165	132	80.0%		
	First Trimester, Weeks 1-12	19	14	73.7%	8	42.1%
	Second Trimester, Weeks 13-27	71	53	74.6%	31	43.7%
	Third Trimester, Weeks 28-42	75	65	86.7%	20	26.7%

NS: Nonsignificant

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**Table 2. prevalence and severity of GERD in asthmatic, probable asthmatic and non-asthmatic pregnant women.**

	Asthmatic pregnant women	Probable asthmatic pregnant women	Non-asthmatic pregnant women	P value
Prevalence of GERD	75.4%	87%	79.7%	0.32
Severity of GERD	2.69±1.11	2.22±1.13	2.25±1.24	0.04

Pregnant women who increased the number of their pillows had significantly higher BMIs (BMI: 29±4 in the group that increased their pillows and 26±3 in the group that did not increase the number of pillows,  $p=0.02$ ) and pregnant women with worsening wheezing more significantly ( $p=0.02$ ) tended to increase the number of their pillows. In the women who increased the number of their pillows, the heartburn ameliorated significantly.

Pregnant women with more severe GERD more significantly were referred to physician and more significantly used medication for their condition.

### DISCUSSION

The prevalence of asthma is increasing in all populations and also asthma is one of the most common diseases associated with pregnancy.<sup>13</sup> However, the reported prevalence in pregnancy is low because in many mild cases, the asthma is undiagnosed.<sup>14</sup> In this study, the prevalence of asthma symptoms and asthma was quite high in pregnant women with the complaint of dyspnea and this was probably because of the tendency of women with more symptoms to be included in this study. This bias was also present in earlier studies of asthma and pregnancy.<sup>14</sup>

Optimal control of asthma results in improved maternal and fetal outcomes of pregnancy and depends on the proper treatment of asthma and its comorbid conditions.<sup>15</sup> One of the common comorbid conditions of asthma is GERD. The prevalence of GERD in asthmatic patients is reported to be 34-89% and this prevalence is higher than the normal population.<sup>16</sup> Actually it is believed that "GERD should be suspected in all patients with asthma"<sup>2</sup> and treatment of GERD in asthmatic patients especially patients with severe asthma and symptomatic GERD might improve asthma symptoms and decrease the need to use asthma medications.<sup>2,14</sup> GERD is also a frequent complaint in pregnancy.<sup>5</sup> In general, there are a few number of studies investigating GERD in pregnancy.<sup>17,18</sup> In this

study we aimed to assess if the prevalence of GERD was different in pregnant women with or without asthma.

In this study, we observed a high prevalence of GERD in pregnant women. GERD has been previously reported to affect less than one third of the population in Tehran<sup>3</sup> and in this study around 80 percent of pregnant women in Tehran were reported to have GERD and this was consistent with previous figures which reported that 40-80 percent of pregnant women complain of GERD sometime in pregnancy.<sup>19</sup>

However, in this study the prevalence of GERD was not different in pregnant women with or without asthma, contrary to the study by Bor et al. which investigated GERD in asthmatic non-pregnant population.<sup>20</sup> This difference could be explained by different methodologies to diagnose GERD, or different populations studied (pregnant vs non-pregnant) or the difference in countries. Similar to our results, Chunlertrith et al. also did not find any statistically significant difference in the prevalence of GERD in asthmatics vs controls.<sup>21</sup>

In our study the high prevalence of GERD was not related to the age of the participants, contrary to the study by Bor et al.<sup>22</sup> and this might have been because of the limited age groups investigated. On the other hand, similar to the study by Bor et al.,<sup>22</sup> we also found increasing chance of GERD with growing number of pregnancies but this difference was not significant in our study (maybe due to small sample size in comparison to the study mentioned). This finding indicates the permanent changes GERD could have in pregnant women and surely the importance of its prevention and treatment.

In accordance with the prospective study of Malferteiner et al.<sup>23</sup> and also Nouraei et al.,<sup>4</sup> we also observed that acid regurgitation is the most frequent symptom. Heartburn, which is reported to occur in 30-50% of pregnancies,<sup>24</sup> was present in around 51% of our subjects.

Our questions showed that life style modifications such as elevation of the head of the bed<sup>24</sup> can improve

the symptoms and have relieving effect.

Our study showed that reflux medications are only prescribed for cases with more severe symptoms and the drugs used are category B. Antacids, which were used for mild and moderate cases, are fast and effective treatments, being helpful in 30-50% of pregnant women with heartburn. Although there are limited data about their safety, most studies have reported them to be secure and efficient.<sup>24</sup> The Histamine 2 receptor antagonists are the most commonly used medications with excellent safety profile (being category B). For Omeprazole, the evidence suggests good safety.<sup>24</sup>

Our study had limitations such as small sample size and bias of selection. The strengths of our study was the visit of all patients by 3 doctors and evaluations made separately.

To the best knowledge of the authors, this study was the first study to evaluate GERD and asthma in pregnant women in Tehran, Iran, a developing country. We found high prevalence of asthma and also GERD in pregnant women with dyspnea. According to this study, we found no relationship between GERD and asthma in pregnant women, but due to low number of severe asthmatic patients, this result needs further studies.

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