

Baker's asthma in bread factory workers

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ABSTRACT

Background: Baker's asthma (BA) is one of the most common causes of occupational asthma. Prevalence of BA varies from 3 to 24% in various studies; however, in our country, there are not enough data on its prevalence.

Objective: The aim of this study was to evaluate wheat flour sensitivity and to determine the rate of BA in workers at a large bread factory in Ankara.

Methods: All steps of the study were carried out in the workplace by the research team who made regular visits to the bread factory. A questionnaire was used to determine the presence of respiratory symptoms and its relation with the occupation. Skin-prick tests and specific immunoglobulin E measurements were performed. Pulmonary function tests and specific inhalation challenges (SIC) were performed to confirm the BA diagnosis.

Results: A total of 162 workers (women/men, 3/159; mean $\pm$ standard error age, 38.25 ± 7.8 years) were included in the study. Of the 99 workers who described symptoms, 88 (88.8%) had nasal and 57 (57.5%) had lower respiratory symptoms. Sensitivity to wheat flour was present in 23 of the workers (14.2%) among all the workers. Among all the workers, seven (4.32%) were diagnosed with BA and SICs were positive in four (2.46%).

Conclusion: Wheat sensitivity was high among the bakers who were exposed to wheat flour; however, the prevalence of BA was quite lower than the previous data in the literature.

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Baker's asthma (BA) is one of the most common types of occupational asthma. In bakers, the prevalence of asthma varies from 3 to 24% according to different studies.^{1–3} The main cause of asthma in bakers is wheat flour. Other flour sources, such as rye, oat, and barley, and enzymes that are used as additives, e.g., α -amylase, can also cause BA.⁴ In previous studies, the prevalence of wheat and α -amylase sensitization was between 4 and 47%, and 4.6 and 24%, respectively, and the main determinants of sensitization to bakery-related aeroallergens were atopy, exposure to these allergens, and work seniority.^{5–8}

In Turkey, the bakery industry is a widespread industry across the entire country. It is estimated that there are ~25,000 bakeries in Turkey. The annual bread production was reported to be 9 million tons, and Turkey was in first place in terms of daily consumption of bread in Europe, with 86 million loaves of bread per day. However, there is insufficient evidence for the prevalence of BA in our country. In our daily practice, we found that allergic rhinitis and asthma are common among bakers and/or patients who are exposed to wheat

flour. It is important to determine the frequency of the disease because widespread measures will have positive effects on workers' health at the population level. In this study, we aimed to evaluate wheat flour sensitivity and to determine the rate of BA in workers of a large bread factory in Ankara.

METHODS

Study Design

This was a cross-sectional study conducted in November 2017 in a bread factory in Ankara. Ankara, the capital city of Turkey, hosts many baking industries, including bakeries, patisseries, and several factories. This was the largest bread factory, producing bread, cakes, and other pastries, in Ankara. The research team (four physicians, three nurses) made regular visits to the factory. The visits were scheduled according to the 8-hour shifts of the workers. All steps, except specific inhalation challenge (SIC), were conducted in the workplace during these visits. The study was approved by the local ethics committee of Ankara University (approval 13–627-16).

Subjects

All the factory workers ages > 18 years were invited to participate in the study. There were a total of 180 workers in the factory. Among them, 18 were office workers, and these workers were excluded from the study. The rest of the workers (N = 162) were making bread dough, cooking, or packing the products. The workers mostly made bread with wheat flour, but rye

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wheat was also used, albeit rarely. They worked in three shifts of 8 hours each. All 162 workers were enrolled in the study in the morning between 8 A.M. and 12 P.M. Written informed consent was obtained from all the subjects.

Data Collection

Data collection was performed with a two-step approach. First, a survey, which consisted of 25 questions, was conducted through face-to-face interviews. The questions evaluated demographic features, medical history, work details, the presence of lower respiratory and/or nasal symptoms, and the relation of the symptoms with the workplace. Skin-prick tests with inhalant allergens (house-dust mites, storage mites, grass pollen mix, *Aspergillus*) and food allergens (wheat flour, rye flour, oat flour, barley flour, egg white, egg yolk) were performed (ALK, Copenhagen, Denmark) on all the subjects. In addition, a 5-mL blood sample was taken for specific immunoglobulin E (IgE) measurements of wheat flour, rye flour, oat flour, barley flour, and α -amylase (Pharmacia CAP, Uppsala, Sweden).

Pulmonary functions were measured by using a portable spirometer (Cosmed, Rome, Italy). If the forced expiratory volume in 1 second (FEV₁) to forced vital capacity ratio was lower than 70% in spirometry, a reversibility test with 400 μ g salbutamol was performed. The reversibility test was accepted positive if FEV₁ level increased at least 200 ml and 12% when compared to baseline. A methacholine challenge was performed if the spirometry was normal. A PC₂₀ (provocative concentration causing a 20% fall in FEV₁) level < 8 mg/mL was positive for asthma diagnosis.

Workers with a history of dyspnea, wheezing, and/or cough attributable to wheat flour exposure in the workplace; the appearance or worsening of symptoms at work and improvement of symptoms when away from work, with sensitization to any relevant allergens; and reversible airway obstruction were invited to the clinic. At the second step, workers underwent SICs with wheat flour. On the test day, we ensured that the subjects had controlled asthma with an FEV₁ > 70%. SICs were performed in a 7-m³ chamber that was impermeable to the passage of particles. The subjects brought their own samples and were exposed to the flour by sifting the samples while they were inside the chamber.

The subjects were exposed to a sham substance (lactose) on the first day, and, on subsequent days, they were exposed to wheat flour for 5, 10, 15, 30, and 60 minutes, consecutively. If there was a 20% fall in the FEV₁ from baseline, then SIC was considered to be positive. A threefold reduction in PC₂₀ values in the methacholine challenge between the baseline day and the day of wheat flour exposure was also considered

as a positive result if the SIC was negative.⁹ The BA diagnosis was based on a compatible history of occupational asthma, reversible airway obstruction, wheat flour sensitivity, and positive SIC.

RESULTS

A total of 162 subjects were included in the study. All the subjects except three were men. The mean $\pm$ standard error age was 38.25 $\pm$ 7.8 years. The mean $\pm$ working period at the factory was 11.23 $\pm$ 7.38 years. Eighty-four subjects (51.9%) were smokers. A family history of asthma was positive in seven subjects (4.3%) (Table 1).

Clinical and Occupational History

Ninety-nine subjects (61.1%) described symptoms while they were making dough and baking. Among the 99 subjects who described symptoms, 42 (42.4%) had nasal symptoms, 8 (8.1%) had lower respiratory symptoms, and 49 (49.4%) had both. The most frequent symptoms were sneezing 58.6% (n = 58), dyspnea 43.4% (n = 43), nasal obstruction 39.4% (n = 39), and rhinorrhea 34.3% (n = 34). In 71 subjects, the symptoms began after starting work, and 51 subjects described an increase in symptoms with flour exposure at the workplace.

The upper and lower respiratory symptom rates were 32 (38.1%) and 44 (52.4%) in current smokers, 18 (36%) and 29 (58%) in non-smokers, and 7 (25%) and 15 (53.6%) in subjects who had quit smoking. There were no significant differences in upper and lower respiratory symptoms among current smokers, ex-smokers, and non-smokers. Lower respiratory symptoms seemed to be more common than upper respiratory symptoms in all the groups, but this was not significant. Skin-prick tests were positive for wheat in 11 of 50 of non-smokers (22%), 10 of 84 of current smokers (11.9%), and 2 of 28 ex-smokers (7.1%). This difference was not significant.

Immunologic Testing

Among all the subjects, 43 (26.5%) were atopic according to skin-prick test results with common inhalant allergens and 23 (14.2%) were sensitive to wheat flour. Wheat flour specific IgE levels were positive in eight subjects (12.3%). Sensitization to wheat flour was shown by either skin test results or specific IgE levels in 13 of 51 subjects (25.5%) who stated increased symptoms with flour exposure.

Diagnosis of BA

As mentioned in the clinical and occupational history section, there were 51 subjects who described increased nasal and lower respiratory symptoms at the workplace. When the subjects who had only nasal symptoms were excluded, there were 18 subjects who

Table 1 Characteristics of subjects (N = 162)

Men, <i>n</i> (%)	159 (98.1)
Age, mean $\pm$ SE, years	38.25 $\pm$ 7.8
Work seniority, mean $\pm$ SE, years	11.23 $\pm$ 7.38
Current smoker, <i>n</i> (%)	85 (51.9)
Comorbidities, <i>n</i> (%)	
Hypertension	14 (8.6)
Thyroid disease	10 (6.1)
Diabetes	8 (4.9)
Other	9 (5.5)
Lower respiratory symptoms, <i>n</i> (%)	
Dyspnea	43 (26.5)
Cough	29 (17.9)
Wheezing	20 (12.3)
Nasal symptoms, <i>n</i> (%)	
Sneezing	58 (35.8)
Nasal obstruction	39 (24.1)
Rhinorrhea	34 (20.1)
Skin-prick test result positivity, <i>n</i> (%)	
Wheat flour	23 (14.2)
Oat flour	24 (14.8)
House-dust mites	19 (11.7)
Grass pollens	19 (11.7)
Rye flour	16 (9.9)
Wheat flour + grass pollen	15 (9.3)
Barley flour	12 (7.4)
Storage mites	10 (6.2)
Specific IgE level positivity, <i>n</i> (%)	
Wheat flour	20 (12.3)
Rye flour	20 (12.3)
Oat flour	15 (9.3)
Alfa-amylase	10 (6.2)
Pulmonary function indices	
FEV ₁ , min-max (mean $\pm$ SD), L	1.71–5.62 (3.68 $\pm$ 0.67)
FEV ₁ , min-max (mean $\pm$ SD), % predicted	53–134 (94.89 $\pm$ 13.37)
FEV ₁ /FVC, min-max (mean $\pm$ SD)	41–92 (79.05 $\pm$ 6.77)
FEV ₁ /FVC < 70, <i>n</i> (%)	9 (5.5)

SE = Standard error; IgE = immunoglobulin E; FEV₁ = forced expiratory volume in 1 second; min = minimum; max = maximum; SD = standard deviation; FVC = forced vital capacity.

described lower respiratory symptoms with or without nasal symptoms that were aggravated at work and improved on days off. Two subjects already had a diagnosis of asthma that started before employment, so these were considered as work-aggravated asthma. Five subjects had reversible spirometry. Thirteen subjects underwent a bronchial challenge with methacholine and two results were positive. In total, seven subjects were diagnosed as having probable BA. The diagnostic flowchart of the subjects is given in Fig. 1.

Further investigations were made to confirm whether asthma was occupational in the seven subjects. Skin-prick test results and/or specific IgE levels for flour were

positive in all of them (Table 2). Three of them were smokers. Serial peak expiratory flow (PEF) measurements could not be performed during at-work and off-work periods because the shifts were 8 hours for work and 16 hours for rest per day, and there was no option to change the exposure time. Because of their working schedule, they could not get permission for a continuous off-work time during the study period. We invited the subjects who were diagnosed as having suspected BA to our clinic for SICs with wheat flour. For the SICs, all seven patients had rhinitis symptoms in 30 minutes after the test started, and four had a 20% decrease in FEV₁ compared with baseline (Table 2).

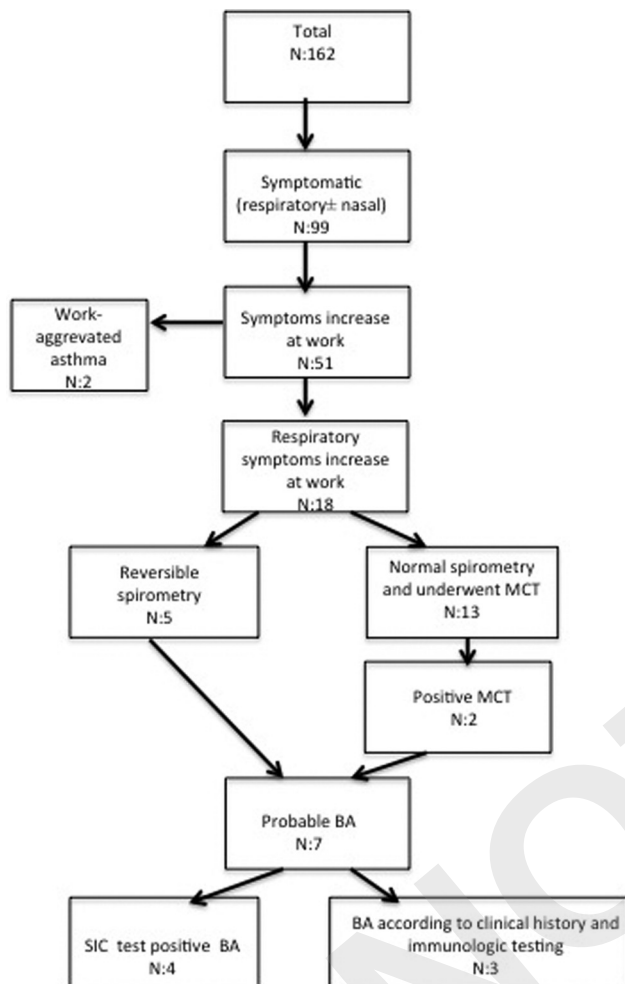


Figure 1. Diagnostic flowchart of the patients. BA = Baker's asthma; MCT = methacholine challenge test; SIC = specific inhalation challenge test.

DISCUSSION

In this study, we evaluated wheat flour sensitivity and asthma prevalence among workers in a bread factory in Ankara. Wheat flour sensitivity was positive in 25% of the subjects who described increased symptoms with flour exposure. Nearly two-thirds of the subjects described work-related symptoms, and BA was diagnosed in 2.4% of all the subjects. Although the prevalence of BA was reported to be in the range of 3–24% in previous studies, we found a lower rate (2.4%) in this study.^{1–3} SIC is recommended to make a definite diagnosis of BA.⁶ However, in recent years, immunologic tests with several allergens, *e.g.*, flour and latex, have been validated against SICs in the diagnosis of occupational asthma. The positive predictive value of the skin-prick test with flour is reported as > 90% in patients with possible BA.⁸

Accordingly, the diagnosis of BA was based on the sensitivity to flour and of having a compatible history without performing SIC in most of the studies that

found a higher prevalence. In our study group, there were seven subjects with a sensitivity to flour and compatible clinical symptoms. After performing SICs, the diagnosis was excluded in three of the seven subjects, even though they had sensitivity to flour and compatible clinical symptoms. We believe that performing SICs as the final step in the diagnosis was one of the reasons for obtaining a lower rate of BA in our study group.

When the subjects with negative SICs were evaluated, all of them had both grass pollen and wheat flour sensitization. Wheat flour sensitization may be due to cross-reactivity to grass pollen because wheat is a grass from the Poaceae family.¹⁰ Cross-reactivity rates vary according to disease conditions and age groups. It is reported that, to diagnose BA, occupational sensitization to wheat flour should be distinguished clearly from influences of co-sensitization, which may exist in patients with pollinosis. We thought that the negative challenge result in these subjects might be a result of cross-sensitization between wheat and grass pollen. However, in the four subjects who were diagnosed as having BA based on positive SICs, skin-prick tests, and flour specific IgE levels were positive, without any accompanying grass pollen sensitization. In view of these data, we think that a positive SIC could be more possible in patients with no accompanying pollen sensitivity.

It is well known that preventive strategies in the workplace play an important role in the prevention of occupational asthma.^{11–13} Although complete avoidance of flour dust exposure is not possible in BA, interventions that can reduce exposure are recommended. In a literature review, Heederik *et al.*¹⁴ reported an overall reduction in the incidence of new cases of symptomatic sensitization through an intervention, including exhaust ventilation, respiratory protection, education, respiratory health surveillance, and dust sampling among bakers. Another study revealed that exposure levels of wheat flour were reduced by 93–96% by using face masks; the investigators concluded that these respiratory system protectors might help to prevent BA.¹⁵ The factory in our study was monitored by Ankara Municipality, which periodically visited *via* occupational health and safety inspectors. It was a large, well-ventilated factory, and flour dust levels were below the occupational exposure limits. The workers were wearing uniforms, caps, and face masks. Concordantly, good hygienic precautions, such as a clean workplace, good air conditions, and use of preventive equipment in the factory might be another explanation for the lower prevalence of BA in our study.

Occupational rhinitis often precedes and is more common than occupational asthma among bakers. The prevalence of baker's rhinitis was reported between the range of 18–29% in previous studies.^{5,16,17} In our study group, half of the subjects had nasal symptoms.

Table 2 Features of the subjects who underwent a SIC

Age, Gender	Work Seniority, years	Symptom Duration, years	Symptom	Positive Skin-Prick Test Result	Specific IgE Level	Specific Inhalation Challenge
44, E	17	10	Lower respiratory, nasal, eye	Wheat flour, oat flour, house-dust mites, storage mites	Wheat flour, rye flour, oat flour, amylase	Positive (24% fall in FEV ₁ after 1 hr, nasal symptoms after 10 min)
40, E	8	2	Lower respiratory, nasal	Wheat flour	Wheat flour	Positive (22% fall in FEV ₁ after 30 min, nasal symptoms after 5 min)
48, E	20	18	Lower respiratory, nasal, eye	Wheat flour, pollen	Negative	Negative
37, E	10	5	Lower respiratory, nasal	Wheat flour, pollen	Negative	Negative
33, E	12	6	Lower respiratory, nasal, eye	Wheat flour, pollen	Amylase	Negative
23, E	3	1	Lower respiratory, nasal, eye	Wheat flour, rye flour, oat flour, barley flour	Wheat flour, rye flour, oat flour	Positive (20% fall in FEV ₁ after 30 min, nasal symptoms after 15 min)
39, E	17	14	Lower respiratory, nasal, eye	Wheat flour, rye flour, oat flour	Wheat flour, rye flour	Positive (25% fall in FEV ₁ after 30 min, nasal symptoms after 15 min)

SIC = Specific inhalation challenge; IgE = immunoglobulin E; FEV₁ = forced expiratory volume in 1 second.

All the subjects who were diagnosed as having BA also developed nasal symptoms preceding the decline in FEV₁ during the SIC. We did not perform specific nasal provocation tests in 27 subjects with nasal workplace symptoms and strong sensitivity to flour because it was not the primary aim of our study. However, if the diagnostic approach in BA is considered, then we may accept these subjects as having probable baker's rhinitis.¹⁸

Our study had some limitations. In the diagnosis of occupational asthma, PEF monitoring is suggested for 2 weeks of at-work and off-work periods. First, we could not perform PEF monitoring to the workers because the shifts were 8 hours for work and 16 hours for rest per day. According to their working schedule, they could not get permission for a continuous off-work time during the study period. However, because the SIC was available, we believed that this did not have a negative impact on the diagnostic approach. Second, cross-reactivity between wheat flour and grass pollens could be confirmed by component-resolved diagnosis in cases of both grass pollen and wheat flour

sensitivity. Third, most of the workers were men. This could be misperceived as a bias, but, in our country, factory workers are generally men, thus this disparity was unavoidable. The strength of our study was that we were able to screen a high number of participants because it was a field study. To the best of our knowledge, this was the first study to perform SICs in a large number of bakers in Turkey. For this reason, we think that the results of this study will fill a gap in the data of the national prevalence for BA.

CONCLUSION

Wheat sensitivity was high among bakers who were exposed to wheat flour, but the prevalence of BA was somewhat lower than in previous studies. The diagnostic steps in this study included occupational history, evaluation of sensitivity to flour, and SICs with wheat flour. We think that SIC-based diagnosis and good industrial hygiene measures taken in the factory explained the lower rate of BA in our study group. Furthermore, our results showed that a compatible

occupational history and the presence of true wheat allergy may work to predict a positive SIC in workers with BA.

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