

Respiratory Morbidity Induced by Occupational Inhalation Exposure to High Concentrations of Wheat Flour Dust

Masoud Neghab

Department of Occupational Health and Research Center for Health Sciences, Shiraz University of Medical Sciences, Shiraz, Iran

Ahmad Soltanzadeh

Abbas Alipour

Jafar Hasanzadeh

School of Health and Nutrition, Shiraz University of Medical Sciences, Shiraz, Iran

Hamzeh Alipour

Research Center for Health Sciences, Shiraz University of Medical Sciences, Shiraz, Iran

Introduction. The main purpose of this study was to investigate the respiratory effects of exposure to high airborne concentrations of wheat flour dust. **Methods.** This cross-sectional study was carried out at a local wheat flour mill in Shiraz, southern Iran. Thirty-five male workers exposed to flour dust and 32 healthy male non-exposed employees were investigated. The prevalence of respiratory symptoms among them was evaluated and parameters of their pulmonary function were measured. Moreover, to assess the extent to which subjects were exposed to flour dust, airborne concentrations of its inhalable and respirable fractions were measured. **Results.** Airborne concentrations of dust exceeded current permissible level. The prevalence of regular cough, productive cough, wheezing, phlegm and dyspnea was significantly higher in exposed subjects than in non-exposed employees. Similarly, both acute and chronic significant ($p < .05$) decrements in most parameters of pulmonary function were noted. **Conclusions.** Our findings provide corroborative evidence to further support the notion that exposure to flour dust is associated with a significant increase in the prevalence of respiratory symptoms as well as ventilator disorders of the lungs.

flour dust occupational exposure respiratory symptoms functional impairments of the lungs

1. INTRODUCTION

Exposure to flour dust and its related allergens is one of the most prevalent causes of occupational airway disease and occupational asthma in Western Europe [1, 2, 3, 4]. Sensitization to wheat allergens and fungal enzyme, α -amylase, and preva-

lence of occupational airway disease and occupational asthma, has been shown to be high among workers exposed to flour dust [1, 3, 5, 6]. Flour dust is a heterogeneous substance with respiratory sensitizing properties and long-term exposure may cause acute or chronic respiratory disease [7, 8]. Bakers and mill workers are highly exposed to

Funding through Shiraz University of Medical Sciences, vice chancellor for research affairs, contract 83-2250, partially supported this investigation. The authors wish to sincerely thank Miss M. Kazemi, Miss N. Salahshoor and Mr. R. Naziaghdam for their invaluable technical assistance in air sampling and completion of questionnaires.

Correspondence and requests for offprints should be sent to Hamzeh Alipour, Research Center for Health Sciences, Shiraz Univ. Med. Sci., P.O. Box: 71645-111, Shiraz, I.R. Iran. E-mail: H_alipour@yahoo.com.

flour allergens. The workers that are occupationally exposed to flour dust have a higher than normal prevalence of respiratory symptoms, asthma and chronic airway obstruction [9, 10, 11]. They also have a higher degree of nonspecific bronchial responsiveness than control workers [9, 10] and exhibit greater variability of lung function during the work week [9]. Studies of occupational exposure to flour dust with pulmonary function tests have shown significant decreases in lung function parameters such as forced vital capacity (FVC), forced expiratory volume in the first second (FEV₁), peak expiratory flow (PEF) and maximum voluntary ventilation [12, 13, 14, 15, 16, 17]. Currently, more than 14 million tonnes of wheat are produced and used, annually, in Iran [18]. This is mostly ground to flour. A comprehensive literature review revealed that no information exists as to the extent to which millers in Shiraz city are exposed to flour dust. Additionally, the prevalence of respiratory symptoms and/or functional impairments of the lungs, if any, is not known among them. The present study was, therefore, undertaken to address these issues.

2. MATERIALS AND METHODS

2.1. Subjects

This cross-sectional study was carried out at a local wheat flour mill in Shiraz, southern Iran. All 35 male subjects of a local flour mill with a history of past and present exposure to flour dust were investigated. Simultaneously, 32 healthy males, from a cola producing company in the vicinity of the plant, with almost identical demographic characteristics were selected by simple random sampling technique and served as the referent group.

Both groups were volunteer subjects. The study was conducted in accordance with the Declaration of Helsinki [19].

2.2. Measurements of Investigated Variables

2.2.1. Respiratory illness

Subjects were interviewed and respiratory symptom questionnaire, as suggested by the American

Thoracic Society [20], with a few modifications, was administered to all of them. This standardized questionnaire included questions on respiratory symptoms (presence or absence of regular dry and/or productive cough, wheezing, dyspnea, etc.); nasal and eye symptoms; smoking habits; and medical and family history of each subject. Additionally, it contained detailed occupational history and specific questions concerning all jobs held before employment at the plant under study, particularly those associated with the risk of respiratory morbidity. These were then used to obtain symptom prevalence data among exposed and non-exposed groups.

2.2.1. Airborne Dust

To assess the extent to which workers had been exposed to flour dust, personal monitoring for airborne inhalable (particle sizes $\geq 5 \mu\text{m}$, materials that are hazardous when deposited anywhere in the respiratory tract) and respirable dust fractions (particle sizes $< 5 \mu\text{m}$, materials that are hazardous when deposited anywhere in the gas-exchange region) was carried out. To estimate the airborne dust concentration, a personal dust sampler (Casella, UK), calibrated with a digital automatic calibrator connected to a filter holder equipped with a 25-mm membrane filter (Whatman glass microfibre filter, GF/A; Krackeler Scientific, USA) through which the air was aspirated by a battery-powered motor at a constant flow rate of 2 L/min was used [21]. Based on a few preliminary tests, the optimum sampling time, to avoid overloading of the filters, was evaluated to be 4 h.

Dust concentration (expressed in milligrammes per cubic metre) was evaluated gravimetrically as the changes of the weight of dried filter (for respirable fraction) or cyclone collector (for inhalable fraction) measured before and after sampling, divided by the volume of the sampled air.

2.2.2. Pulmonary Function Tests

Pulmonary function tests, including mean percentage predicted vital capacity (VC), FVC, FEV₁ and PEF followed guidelines of the American Thoracic Society [22] and were measured with a portable calibrated Vitalograph (UK)

spirometer on site. For evaluation of cross shift changes, pulmonary function tests were measured twice (Saturday morning, following two days' rest, before commencement of work, and Saturday afternoon, after 8 h of exposure). The spirometer was calibrated twice a day with a 1-L syringe in accordance with the standard protocol for the instrument used. The mean percentage predicted value was based on the subject's age, weight, standing height, gender and ethnic background as calculated and adjusted with a spirometer. The subjects were requested not to take shower or smoke for at least 2 h prior to the test. Additionally, they were trained to become familiar with the maneuvers. The standing height and weight of each subject were measured in his normal working clothes. Before the test, they rested in a sitting position for ~5 min. They were then asked to stand in front of the spirometer, as comfortably as possible, and a nose clip was put on. At least three acceptable maneuvers were performed. If the subject showed great variability among the various FVC volumes, up to 5 maneuvers were obtained. The largest volumes (as percentage predicted lung function) were selected for the analysis. The percentage predicted lung values were observed capacities as measured with a spirometer divided by predicted or expected capacities multiplied by 100:

$$\text{predicted lung value (\%)} = \frac{\text{observed capacities}}{\text{expected capacities}} \times 100.$$

2.3. Data Analysis and Statistical Procedures

Normality of parameter distribution was evaluated with Kolmogorov–Smirnov test. The data were

statistically analysed with Student's *t* and χ^2 or Fisher's exact test, where applicable. Equality of variances was examined with Levene's test. Repeated measures of pulmonary functions of exposed subjects were compared with a paired *t* test. The relationships were treated as statistically significant at $p < .05$. Additionally, using multiple linear or logistic regression analysis, the simultaneous effects of confounding variables such as smoking status, lifetime use of cigarette, age and body mass index (BMI), on the prevalence of respiratory symptoms and changes in the parameters of pulmonary function were evaluated. In this study, to control the confounding effects of lifetime use of cigarette, two terms of covariate, i.e., dichotomous, recording zero versus nonzero and the actual pack year were included [23, 24]. Statistical tests, using a two-sided *p* value, were conducted with SPSS version 16.

3. RESULTS

Experimental results are presented as arithmetic mean \pm standard deviation. None of the exposed subjects had past medical or family history of respiratory illnesses or any other chest operations or injuries. Similarly, none of the referent subjects had been exposed to flour or other chemicals known to cause respiratory symptoms or ventilatory disorders during their employment with the plant or prior to it.

Table 1 shows demographic characteristics, smoking habits and airborne concentrations of flour dust. Although no significant differences were noted between exposed and non-exposed subjects as far as variables such as length of

TABLE 1. Demographic Characteristics and Smoking Status of Subjects

Parameter	Exposed (<i>n</i> = 35)	Non-Exposed (<i>n</i> = 32)	<i>p</i>
Age (<i>M</i> \pm <i>SD</i> ; years)	47.40 \pm 9.26*	42.31 \pm 10.70	.046 ^a
BMI (<i>M</i> \pm <i>SD</i> ; kg/m ²)	23.87 \pm 3.31	24.99 \pm 3.85	.180 ^a
Exposure/employment (<i>M</i> \pm <i>SD</i> ; years)	18.19 \pm 10.50	17.79 \pm 11.80	.225 ^a
Married individuals <i>N</i> (%)	31 (88.57)	29 (90.63)	.397 ^b
Smokers <i>N</i> (%)	13 (37.10)*	3 (9.40)	.008 ^b
Pack year (<i>M</i> \pm <i>SD</i>)	8.27 \pm 18.58*	2.19 \pm 9.07	.040 ^c

Notes. BMI = body mass index (kilograms per square meters); * = significantly different from its corresponding value for the non-exposed group ($p < .05$); a = independent sample *t* test, b = χ^2 Fisher's exact test, c = *t* test.

TABLE 2. Frequency of Respiratory Symptoms Among Exposed and Non-Exposed Subjects (%)

Symptoms	Exposed (n = 35)	Non-Exposed (n = 32)	OR	95% CI	p ^a
Cough	15 (42.86)	1 (3.12)	23.25	[2.84, 190.10]	<.001*
Phlegm	21 (60.00)	2 (6.25)	22.50	[4.60, 109.57]	<.001*
Productive cough	10 (28.52)	1 (3.12)	13.48	[1.61, 112.88]	.004*
Wheezing	12 (34.29)	1 (3.12)	17.71	[2.14, 146.68]	.001*
Dyspnea	28 (80.00)	19 (59.38)	5.90	[1.70, 20.39]	.003*

Notes. *p < .05; a = χ^2 Fisher's exact test.

TABLE 3. Predicted Percentages of Lung Function Among Exposed and Non-Exposed Subjects

Parameters	Exposed (n = 35)		Non-Exposed (n = 32)	p ^a	p ^b
	Saturday Morning	Saturday Afternoon			
VC	74.63 ± 11.20	69.54 ± 11.90	86.75 ± 9.00	<.001*	<.001 [†]
FVC	70.14 ± 13.34	68.29 ± 13.10	88.44 ± 7.40	.311	<.001 [†]
FEV ₁	61.63 ± 14.47	58.49 ± 13.57	88.59 ± 10.20	.035*	<.001 [†]
FEV ₁ /FVC	87.93 ± 10.51	85.81 ± 11.05	100.11 ± 7.23	.051	<.001 [†]
PEF	57.65 ± 15.71	51.13 ± 15.82	68.95 ± 15.80	.003*	.017 [†]

Notes. *p < .05 (paired t test), [†]p < .05 (independent t test); VC = vital capacity, FVC = forced vital capacity, FEV₁ = forced expiratory volume in the first second, PEF = peak expiratory flow; a = Saturday morning versus Saturday afternoon, b = Saturday morning versus non-exposed.

employment, BMI and marital status were concerned, exposed individuals were significantly older than their non-exposed counterparts. Additionally, the proportion of smokers and lifetime users of cigarettes (pack year) were significantly higher in exposed individuals than among referent subjects.

Inhalable and respirable dust concentrations were estimated to be 11.68 and 32.45 mg/m³, respectively.

Table 2 illustrates the distribution of respiratory symptoms. As shown, symptoms such as cough, phlegm, productive cough, wheezing and dyspnea were significantly more prevalent among exposed subjects.

The parameters of pulmonary function were also measured for both groups. Table 3 presents predicted percentages of VC, FVC, FEV₁, FEV₁/FVC ratio and PEF. As shown, all parameters of pulmonary function were significantly lower for exposed subjects compared to their non-exposed counterparts (p < .05). The results also showed significant cross shift changes (decrements) in VC, FEV₁ and PEF (Saturday afternoon versus Saturday morning).

Association between exposure to flour dust and changes in the parameters of pulmonary function

is shown in Table 4. A multiple linear regression analysis showed that after adjustment for age, BMI and smoking status, there was a statistically significant association between exposure to flour dust with VC, FVC, FEV₁, and FEV₁/FVC ratio.

Similarly, the association between exposure to flour dust and the prevalence of respiratory symptoms is displayed in Table 5. Logistic linear regression analysis showed that after adjusting for important confounders, there was statistically significant association between exposure to flour dust with the prevalence of wheezing, productive cough, cough, phlegm, and dyspnea (p < .05).

TABLE 4. Association Between Exposure to Flour Dust and Changes in the Parameters of Pulmonary Function Test

Parameter	β	95% CI ^a	SE	p ^b
VC	11.94	[6.14, 17.74]	2.89	<.001
FVC	17.31	[11.37, 23.26]	2.97	<.001
FEV ₁	23.31	[16.81, 29.80]	3.25	<.001
FEV ₁ /FVC	6.87	[4.28, 13.32]	2.30	<.001
PEF	8.41	[-1.45, 18.27]	4.89	.092

Notes. a = value 1 for referent group and value 0 for exposed group; b = multiple linear regression model.

TABLE 5. Association Between Exposure to Flour Dust and Prevalence of Respiratory Symptoms

Outcome	β	SE	OR ^a	95% CI	p ^b
Wheezing	2.69	1.10	14.79	[1.71, 127.80]	.014
Productive cough	2.68	0.85	14.41	[2.73, 76.22]	.002
Cough	2.83	1.32	17.00	[1.27, 126.61]	.032
Phlegm	2.79	1.29	16.26	[1.31, 102.20]	.003
Dyspnea	1.52	0.69	4.55	[1.17, 17.75]	.029

Notes. a = value 0 for referent group and value 1 for exposed group; b = binary logistic regression.

4. DISCUSSION

Our data showed that both groups were similar as far as most demographic variables were concerned. However, exposed subjects were, to some extent, older than their non-exposed counterparts and the proportion of smokers was significantly higher among them.

None of the subjects had past medical or family history of respiratory illnesses or any other chest operations or injuries. Additionally, subjects were exposed to flour dust at a concentration which was far beyond its current threshold limit value (TLV) of 0.5 mg/m³ [25]. Given the above, and the fact that all important confounders were controlled and accounted for in this study, an increased prevalence of respiratory symptoms (cough, phlegm, productive cough, wheezing and dyspnea) as well as significant decrements in the parameters of pulmonary function (VC, FVC, FEV₁, FEV₁/FVC and PEF) may well be explained by exposure to flour dust.

Consistent with other studies [3, 26, 27, 28], respiratory symptoms were found to be significantly more prevalent among exposed subjects (Table 2). Similarly, occupational exposure to flour dust has been reported to lead to reduction of ventilatory capacities [12, 13, 14, 15, 16, 17]. In accordance with these findings, we have shown that exposure to flour dust resulted in significant reductions in some parameters of pulmonary function such as VC, FVC, FEV₁, FEV₁/FVC ratio and PEF.

Fluctuation in lung functional capacities from Saturday morning to Saturday afternoon was an important finding of this study. Exposed subjects performed significantly better in their pulmonary function tests on Saturday morning, after being away from the workplace for the weekend

(Table 3). It is noteworthy that even despite this partial recovery, the differences between exposed and referent subjects remained statistically significant (Table 3). These observations demonstrate that exposure to flour dust induces acute reversible and chronic irreversible functional impairments of the lungs (reduction of the lung functional capacities). The allergen nature of flour dust as well as the exposure scenario (length and severity) described in this study, provide plausible physiological bases and explanations for these observations.

Exposed subjects were significantly older than referent subjects and a significantly higher proportion of them were smokers (Table 1). To control the simultaneous effects of these confounders, multiple linear regression analysis was performed. This model showed that exposure to flour dust was the major determinant and cause of reduced ventilatory capacities.

Furthermore, the adjusted association between the prevalence of respiratory symptoms and exposure to flour dust was evaluated with binary logistic regression analysis. The result showed that after adjusting for potential confounders, there was a significant association between exposure and the prevalence of wheezing and productive cough.

A comparison between the adjusted (Table 5) and crude (Table 2) odd ratios showed that these figures were generally smaller in multivariate than in univariate analysis. The reason for this apparent difference may well be explained by the fact that exposed subjects were significantly older than their unexposed counterparts. Similarly, the proportion of smokers and the severity of smoking in the exposed group were significantly higher than those of referent subjects. Therefore, the observed differences are very likely to be

related to a positive confounding effect of age along with smoking.

5. CONCLUSION

The collected data showed that occupational exposure to high concentrations of flour dust is associated with respiratory symptoms and functional impairments (acute reversible and chronic irreversible effects).

Therefore, engineering measures such as local exhaust ventilation and the use of proper protective respirators are justified to eliminate or reduce exposure to this compound to protect current workers from the development of severe respiratory diseases and the newly employed employees from contracting such disorders.

REFERENCES

1. Meijster T, Tielemans E, de Pater N, Heederik D. Modeling exposure in flour processing sectors in the Netherlands: a baseline measurement in the context of an intervention program. *Ann Occup Hyg.* 2007;51(3):293–304. Retrieved October 18, 2012, from: <http://annhyg.oxfordjournals.org/content/51/3/293.long>
2. Latza U, Baur X. Occupational obstructive airway diseases in Germany: frequency and causes in an international comparison. *Am J Ind Med.* 2005;48(2):144–52.
3. Harris-Roberts J, Robinson E, Waterhouse JC, Billings CG, Proctor AR, Stocks-Greaves M, et al. Sensitization to wheat flour and enzymes and associated respiratory symptoms in British bakers. *Am J Ind Med.* 2009;52(2):133–40.
4. Hur GY, Koh DH, Kim HA, Park HJ, Ye YM, Kim KS, et al. Prevalence of work-related symptoms and serum specific antibodies to wheat flour in exposed workers in the bakery industry. *Respir Med.* 2008;102(4):548–55.
5. Brisman J, Järholm B, Lillienberg L. Exposure-response relations for self-reported asthma and rhinitis in bakers. *Occup Environ Med.* 2000;57(5):335–40. Retrieved October 18, 2012, from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1739948/>
6. Heederik D, Houba R. An exploratory quantitative risk assessment for high molecular weight sensitizers: wheat flour. *Ann Occup Hyg.* 2001;45:175–85.
7. Meo SA. Dose response of years of exposure on lung functions in flour mill workers. *J Occup Health.* 2004;46(3):187–91.
8. Ijadunola KT, Erhabor GE, Onayade AA, Ijadunola MY, Fatusi AO, Asuzu MC. Pulmonary functions of wheat flour mill workers and controls in Ibadan, Nigeria. *Am J Ind Med.* 2005;48(4):308–17.
9. Choudat D, Bensefa L, Causse-Sounillac E, Conso F. Methacholine bronchial responsiveness and variations in lung function among workers exposed to flour. *Scand J Work Environ Health.* 2005;31(1):59–64.
10. Joly N, Martin-Silva B, Choudat D, Vicrey C, Rossignol C, Conso F. Symptômes et fonction respiratoires des artisans boulangers de la région Poitou-Charentes [Respiratory symptoms and lung function among bakers in Poitou-Charente district]. *Arch Mal Prof.* 1997;58:641–7.
11. Cullinan P, Cook A, Nieuwenhuijsen MJ, Sandiford C, Tee RD, Venables KM, et al. Allergen and dust exposure as determinants of work-related symptoms and sensitization in a cohort of flour-exposed workers; a case-control analysis. *Ann Occup Hyg.* 2001;45(2):97–103. Retrieved October 18, 2012, from: <http://annhyg.oxfordjournals.org/content/45/2/97.long>
12. Wagh ND, Pachpande BG, Patel VS, Attarde SB, Ingle ST. The influence of workplace environment on lung function of flour mill workers in Jalgaon urban center. *J Occup Health.* 2006;48(5):396–401.
13. Letran A, Palacin A, Barranco P, Salcedo G, Pascual C, Quirce S. Rye flour allergens: an emerging role in baker's asthma. *Am J Ind Med.* 2008;51(3):324–8.
14. Salvatori N, Reccardini F, Convento M, Purinan A, Colle R, De Carli S, et al. Asthma induced by inhalation of flour in adults with food allergy to wheat. *Clin Exp Allergy.* 2008;38(8):1349–56.

15. Droste J, Myny K, Van Sprundel M, Kusters EM, Bulat P, Braeckman L, et al. Allergic sensitization, symptoms, and lung function among bakery workers as compared with a nonexposed work population. *J Occup Environ Med*. 2003; 45(6):648–55.
16. Zodpey Sp, Tiwari RR. Peak expiratory flow rate in flour mill workers. *Indian J Physiol Pharmacol*. 1998;42(4):521–6.
17. Patouchas D, Efremidis G, Karkoulas K, Zoumbos N, Goumas P, Spiropoulos K. Lung function measurements in traditional bakers. *Acta Biomed*. 2008;79(3):197–203. Retrieved October 18, 2012, from: http://www.actabiomedica.it/data/2008/3_2008/patouchas.pdf
18. Safikhan S. Survey of the trend of wheat production over the last decade. *Mahnameh Dam, Kesht va Sanat*. 2007;94:58–9.
19. World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. Adopted by the 18th general assembly, Helsinki, Finland, June 1964. Retrieved October 18, 2012, from: <http://www.wma.net/en/30publications/10policies/b3/17c.pdf>
20. Ferris BG. Epidemiology standardization project. *Am Rev Respir Dis*. 1978; 118 (6 Pt 2):1–120.
21. SKC HSE air sampling guide. Retrieved October 18, 2012, from: <http://www.skinc.com/HSEGuide/method.asp>
22. ATS [American Thoracic Society] statement—Snowbird workshop on standardization of spirometry. *Am Rev Respir Dis*. 1979;119(5):831–8.
23. Robertson C, Boyle P, Hsieh CC, Macfarlane GJ, Maissonneuve P. Some statistical considerations in the analysis of case-control studies when the exposure variables are continuous measurements. *Epidemiology*. 1994;5(2):164–70.
24. Greenland S, Poole C. Interpretation and analysis of differential exposure variability and zero-exposure categories for continuous exposures. *Epidemiology*. 1995; 6(3):326–8.
25. American Conference of Governmental Industrial Hygienists (ACGIH). Threshold limit values for chemical substances and physical agents and biological exposure indices. Cincinnati, OH, USA: ACGIH; 2009.
26. Ijadunola KT, Erhabor GE, Onayade AA, Ijadunola MY, Fatusi AO, Asuzu MC. Prevalence of respiratory symptoms among wheat flour mill workers in Ibadan, Nigeria. *Am J Ind Med*. 2004;45(3):251–9.
27. Droste J, Vermeire P, Van Sprundel M, Bulat P, Braeckman L, Myny K, Vanhoorne M. Occupational exposure among bakery workers: impact on the occurrence of work-related symptoms as compared with allergic characteristics. *J Occup Environ Med*. 2005;47(5):458–65.
28. Hur GY, Koh DH, Kim HA, Park HJ, Ye YM, Kim KS, et al. Prevalence of work-related symptoms and serum-specific antibodies to wheat flour in exposed workers in the bakery industry. *Respir Med*. 2008;102(4):548–55.