



Respiratory and Dermal Symptoms and Raised Serum Concentrations of Biomarkers of Oxidative Stress among Pesticide Retailers

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Abstract

Background: Recently concern has been raised regarding possible health effects resulting from exposure of a group of pesticide retailers to chemicals they handle.

Objective: To investigate the prevalence of respiratory and dermal symptoms, as well as biomarkers of oxidative stress, among pesticide retailers and to compare them with those of an unexposed comparison group.

Methods: 70 male pesticide retailers and 64 male construction workers (served as the comparison group) were investigated. Blood samples were taken from all participants to assess the biomarkers of oxidative stress. A data sheet and the European Community Respiratory Health Survey II questionnaire were used to determine the prevalence of dermal and respiratory disorders, respectively.

Results: After adjusting for age, weight, height, education level, job tenure, average daily work, presence of family history of respiratory diseases, marital status, smoking status, and number of cigarettes smoked per day, we found that wheezing (OR 4.07, 95% CI 1.17 to 14.17), cough (OR 3.38, 95% CI 1.15 to 9.98), and mucus hypersecretion (OR 3.66, 95% CI 1.45 to 9.05) were significantly more prevalent among pesticide retailers compared with the comparison group. The prevalence of tingling and dryness of skin exposed individuals was significantly higher than unexposed participants. The mean serum concentrations of glutathione and malondialdehyde in the exposed group were significantly higher than those in the comparison group.

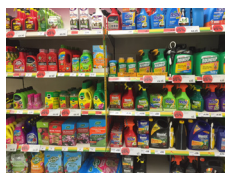
Conclusion: Occupational exposure to low doses of a mixture of pesticides by retailers was associated with increased prevalence of dermal and respiratory symptoms as well as raised concentrations of biomarkers of oxidative stress.

Keywords: Signs and symptoms, respiratory; Dermatitis, contact; Oxidative stress; Pesticides

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Received: Jul 25, 2018
 Accepted: Sep 25, 2018

Cite this article as: Jalilian H, Neghab M, Tatar M, Taheri S. Respiratory and dermal symptoms and raised serum concentrations of biomarkers of oxidative stress among pesticide retailers. *Int J Occup Environ Med* 2018;9:194-204. doi: 10.15171/ijoem.2018.1417

Introduction

Pesticides including herbicides, insecticides, rodenticides, fungicides, and bactericides families are applied to control, kill, or repel certain forms of plant or animal life (pests) including weeds, insects, rodents, fungi, bacteria, or other organisms.¹ The report of the Environmental Protection Agency (EPA) demonstrates that world pesticide usage was about six billion pounds in 2011 of which about 50% was related to herbicides.² Using approximately 45% of the total produced active pesticide ingredients, European countries are the largest global users.³

In 2011, more than 3.5 thousand tons of pesticides, accounting for 0.2% of the total pesticides used worldwide, were used in Iran. Granules and oils (56%) were the most widely used active pesticide ingredients followed by herbicides (34%), fungicides (5%), insecticides (4%), acaricides (0.8%), and others (0.2%).⁴

In Iran, pesticide retail markets are localized in the urban and rural areas and provide these chemical agents for a wide range of applications. In the household usage, people usually purchase insect sprays or powders, rat baits, and disinfectants to use in homes and gardens. Moreover, these products may be used in industry, urban, and rural environments for the same purposes. The largest applicants of pesticides are farmers who apply toxic chemicals to control a wide range of pests in greenhouse and farms.² Therefore, the Iranian retailers are probably exposed to a mixture of pesticide families with various structures in their shops for the whole working day.

A large body of evidence on workers who deal with pesticides has reported different health consequences including dermal⁵ and respiratory problems,⁶⁻⁸ hematological and biochemical impairments,^{9,10} as well as coronary artery disease¹¹ and cancer^{12,13}. Since 2009, a few studies on the

health of pesticide retailers have suggested that exposure to active pesticide ingredients may induce different adverse health effects in this working community.^{9,14-16}

Kesavachandran, *et al*, report respiratory, neurological, gastrointestinal, and cardiovascular disorders among Indian pesticide retailers.¹⁴ Hotton, *et al*, found different levels of α -hexachlorocyclohexane (HCH), β -HCH, γ -HCH, δ -HCH, chlordane, and heptachlor in the blood of agrochemicals retailers.¹⁵ In another study, they found dichloro-diphenyl-trichloro-ethane (DDT) and its derivatives, and Aldrin in the blood samples.¹⁵ In a recent investigation, using hematological and biochemical tests, Rojas-Garcia, *et al*, reported health impairments among retailers but they did not examine the respiratory symptoms.¹⁶

Literature review indicates a paucity of studies related to the health of pesticide retailers, in general, and the issue of respiratory health, skin disorders and the status of biomarkers of oxidative stress among this occupational group, in particular. Therefore, the current study was undertaken to investigate the prevalence of respiratory and dermal symptoms as well as biomarkers of oxidative stress among pesticide retailers and to compare them with those of a group of unexposed comparison group.

Materials and Methods

Study Design and Participants

The Pesticide Retailers Union of Shiraz was asked for the list of all registered retailers and pesticides they sell in Fars province. Assuming an estimated prevalence of respiratory problems of 30% among workers exposed to pesticide,¹⁷ we decided to study 75 of 103 active shops in Shiraz. They were selected at random from the list and served as the exposed group. Two investigators attended the shops to describe the

objectives and methodology of the study for and invite those who were working there for at least 6 hours/day and had at least one year of experience in a pesticide store to participate in the study. Selected participants had no history of pre-existing respiratory or dermal disorders when they commenced working as a pesticide retailer; nor had they history of past exposure to other toxic chemicals.

Eligible cases (93% of the visited retailer shops, n=70) completed a demographic questionnaire, a questionnaire on use of personal protective equipment (PPE), a questionnaire on respiratory symptoms, and a data collection sheet on skin disorders. Additionally, a stock valuation of pesticides was carried out in all shops and all items were categorized in the major groups, where applicable.

The contact information of participants was recorded to coordinate for taking fasting blood samples for measuring the serum levels of biomarkers of oxidative stress.

Serving as the unexposed comparison group, 64 men, without history of exposure to pesticides, were randomly selected from the construction workers of the city council contractors; they satisfied the same eligibility criteria as the exposed group.

The Ethics Committee of Shiraz University of Medical Sciences (SUMS) approved the protocol of the current study. The participants answered the questionnaires anonymously and were able to withdraw from the investigation at any time. Moreover, the retailers and the comparison group completed an informed written consent form before participating in the study.

Respiratory and Dermal Symptoms

The European Community Respiratory Health Survey questionnaire II (ECRHS II) was used to examine respiratory symptoms.¹⁸ This questionnaire has been widely used to assess the prevalence of respiratory problems among people who are oc-

cupationally or environmentally exposed to pesticides or other toxicants.¹⁹⁻²² Those who had smoked at least one cigarette per day since at least 30 days prior to the study, were considered “current smoker;” those who used to be smoker but had quit smoking at least one year before the study were considered “ex-smoker;” and, those who had had exposure to environmental tobacco smoke (at home or workplace) during the last year were considered “passive smoker.”

A self-structured data collection sheet was used to investigate dermal symptoms including dryness, irritation, flaking, redness, itching, hypopigmentation and hyperpigmentation, and dermatitis. Each symptom had a short description, indicating a clear and simple definition. The participants were asked to indicate whether they experience these symptoms “never or rarely” or “often” during the last two weeks in the face and neck, arms and elbows, hands, legs, and waist and abdomen.

Sampling

Fasting blood samples (5 mL) were taken from all participants between 7:30 and 9:30 am with sterile vacutainers containing no additives to obtain the serum for analysis of oxidative stress indicators. The samples were coded, kept in a cold box, and transferred to the laboratory within two hours of sample collection. The serum was separated by centrifugation at the laboratory and then stored at -20°C until analysis.

Biochemical Assays

Serum malondialdehyde (MDA) level, as an end-product of lipid peroxidation, was measured by Beuge and Aust method.²³ To measure the activity of catalase serum glutathione (GSH) level was spectrophotometrically measured at 412 nm using DTNB (Ellman's reagent).²⁴ Serum was diluted by 66.7 mM potassium phosphate

Table 1: Personal characteristics of the retailers and the comparison group. Values are either mean (SD) or n (%).

Variable	Retailers (n=70)	Comparison group (n=64)	p Value
Age (yr)	40.1 (9.1)	40.0 (7.8)	0.81
Weight (kg)	79.42 (10.71)	78.78 (20.77)	0.82
Height (m)	1.74 (0.05)	1.73 (0.01)	0.57
Average daily work (hr/day)	8.8 (1.9)	8.9 (1.6)	0.92
Length of employment (yrs)			
<5	20 (28%)	12 (19%)	0.20
5–10	28 (41%)	36 (56%)	
>10	22 (31%)	16 (25%)	
Education			
Diploma or lower	27 (39%)	20 (31%)	0.64
Associate degree	28 (41%)	28 (44%)	
Bachelor or higher	14 (20%)	16 (24%)	
Smoking status			
Never smoker	51 (73%)	51 (80%)	0.02
Current smoker	15 (21%)	5 (8%)	
Ex-smoker	4 (5%)	8 (13%)	
Passive smoker	20 (29%)	4 (6%)	
Length of smoking (years)			
<10	50 (71%)	51 (80%)	0.07
>10	20 (29%)	13 (20%)	
Cigarettes per day amongst current smokers			
<5 (light smoker)	35 (50%)	13 (20%)	0.03
≥5 (regular smoker)	35 (50%)	51 (80%)	
Marital status			
Single	15 (22%)	8 (13%)	0.08
Married	53 (75%)	56 (87%)	
Other	2 (3%)	0 (0%)	

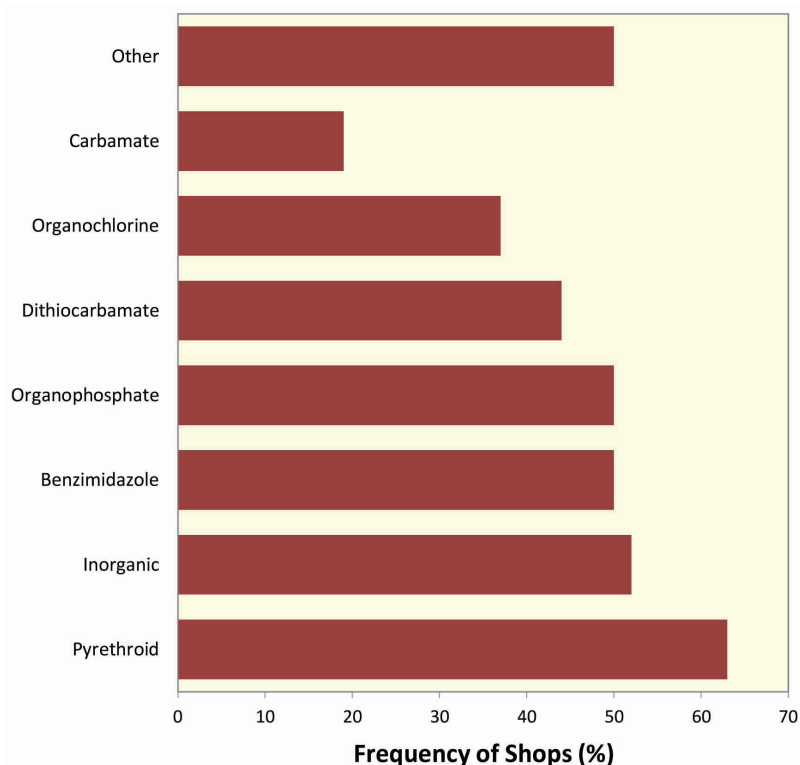


Figure 1: Distribution of pesticides sold in the shops

buffer (pH=7.0) and then the decomposition of H_2O_2 (by catalase) was monitored at 240 nm for 3 min at 25 °C according

to the method described by Aebi, *et al.*²⁵ The results were expressed as U/g serum protein. Finally, serum protein was determined by Bradford assay using crystalline BSA as the standard.²⁶

Data Analysis

Comparison of mean values and frequency-based data was made by *Student's t* test for independent samples between the exposed and comparison groups. χ^2 test was used to compare categorical data. Association between exposure to pesticides and the prevalence of respiratory symptoms was investigated by logistic regression model, adjusted for age, weight, height, education level, work experience, average daily work, family history of respiratory diseases, marital status, smoking status, and number of cigarettes smoked per day. A p value <0.05 was considered statistically significant. Bonferroni correction was used for multiple comparisons.

Results

No significant difference was observed between the retailers and the comparison group in terms of all personal characteristics, but smoking status (p=0.02) and the number of cigarettes smoked per day among the current smokers (p=0.03) (Table 1).

The studied pesticide retailers rarely used overall working cloth (8.6%), a respiratory mask (1.4%), gloves (13%), or Wellington boots (4%) during their work.

The most abundant toxic substances were pyrethroid; 63% of shops had at least one pyrethroid pesticide in stock. This followed by inorganic and organophosphate pesticides (Fig 1).

In univariate analysis, the prevalence of wheezing, chest tightness, cough, chronic cough, and mucus hypersecretion in studied retailers were significantly higher than the comparison group. After adjusting for

TAKE-HOME MESSAGE

- A large body of evidence indicates a wide range of health problems among workers occupationally exposed to pesticides.
- Pesticide retailers may be exposed to a mixture of pesticides families with different structures in their shops for the whole working day.
- This study showed that almost all pesticide retailers did not use personal protective equipment.
- This occupational group suffered more often from respiratory and dermal problems.
- Findings demonstrated a raised serum concentrations of oxidative stress biomarkers among pesticide retailers.

age, weight, height, education level, work experience, average daily work, family record of respiratory diseases, marital status, smoking status, and number of cigarettes smoked per day amongst current smokers, wheezing, cough, and mucus hypersecretion remained statistically significant (Table 2).

The most common dermal symptom was tingling, appeared in the face and neck, hands, and legs of the studied retailers. It was followed by dryness of the skin, appeared in their arms, elbows, and hands. No significant differences were found for flaking and hyperpigmentation between the exposed and unexposed comparison groups (Table 3).

The GSH and MDA levels in the pesticide retailers were significantly ($p < 0.001$) higher than the comparison group (Fig 2). The catalase activity did not significantly differ between the two groups.

Discussion

After adjusting for potential confounders, wheezing, cough, and mucus hypersecretion were found to be significantly more prevalent among the exposed pesticide retailers compared with the unexposed construction workers. The prevalence of tingling in facial skin, neck, hands, and legs, as well as skin dryness in the arms, elbows, and hands were also significantly higher in the exposed group. The mean GSH and MDA activities were significantly higher in the pesticide retailers too.

Only few studies have investigated the respiratory and skin problems among pesticide retailers. Moreover, these investigations have mainly focused on other pesticide-exposed occupations such as farmers and pesticide spray applicators.^{7,8} A report on US pesticide retailers shows that the most common upper respiratory symptoms include pain and irritation (38%), shortness of breath (18%), and cough (10%).²⁷

Table 2: Prevalence of respiratory symptoms among pesticide retailers. Crude and adjusted ORs were calculated by binary logistic regression analysis. The model was adjusted for age, weight, height, education level, work experience, average daily work, family history of respiratory diseases, marital status, smoking status, and number of cigarettes smoked per day.

Symptom	OR (95% CI)	
	Crude	Adjusted
Wheezing	4.43 (1.66 to 11.81)	4.07 (1.17 to 14.17)
Chest tightness	3.00 (1.22 to 7.34)	2.77 (0.99 to 7.80)
Cough	4.32 (1.85 to 10.11)	3.38 (1.15 to 9.98)
Chronic cough	2.86 (1.04 to 7.85)	2.86 (0.86 to 9.52)
Mucus hypersecretion	3.57 (1.68 to 7.60)	3.66 (1.48 to 9.05)
Chronic bronchitis	2.16 (0.92 to 5.06)	1.96 (0.68 to 5.66)
Shortness of breath	2.05 (0.97 to 4.35)	2.22 (0.6 to 5.78)
Asthma	1.88 (0.86 to 4.14)	2.48 (0.64 to 9.57)

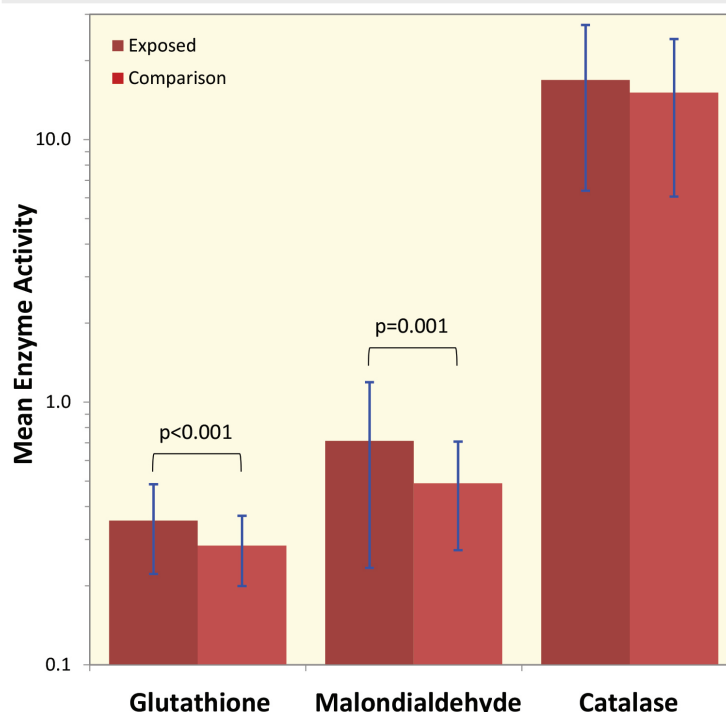


Figure 2: Comparison of oxidative stress indicators between the exposed retailers and the comparison group. Error bars represent SD. The unit of measurements is µM/L for glutathione and malondialdehyde and U/g serum protein for catalase activities. Note that the Y-axis has a logarithmic scale.

Table 3: Distribution of the studied symptoms in pesticide retailers and the comparison group

Symptom	Face and neck			Arms and elbows			Hands			Legs			Waist and abdomen		
	Exposed	Comparison	p value	Exposed	Comparison	p value	Exposed	Comparison	p value	Exposed	Comparison	p value	Exposed	Comparison	p value
Dryness															
Never or rarely	81	92	0.069	77	95	0.003*	64	84	0.008*	91	94	0.61	96	98	0.35
Often	19	8		23	5		36	16		9	6		4	2	
Tingling															
Never or rarely	73	92	0.004*	93	95	0.55	74	92	0.006*	94	98	0.020*	93	94	0.83
Often	27	8		7	5		26	8		6	2		7	6	
Flaking															
Never or rarely	89	94	0.29	94	97	0.47	82	92	0.07	87	91	0.69	97	98	0.61
Often	11	6		6	3		18	8		11	9		3	2	
Redness															
Never or rarely	87	94	0.20	93	98	0.12	83	98	0.002*	91	100	0.016*	100	100	1
Often	13	6		7	2		17	2		9	0		0	0	
Itching															
Never or rarely	73	92	0.004*	90	94	0.43	77	92	0.017*	90	94	0.43	91	98	0.07
Often	27	8		10	6		23	9		10	6		9	2	
Hypopigmentation															
Never or rarely	84	95	0.038*	94	98	0.20	90	98	0.04*	97	100	0.17	96	100	0.09
Often	16	5		6	2		10	2		3	0		4	0	
Hyperpigmentation															
Never or rarely	94	95	0.79	97	100	0.17	94	97	0.47	99	100	0.34	99	100	0.34
Often	6	5		3	0		6	3		1	0		1	0	

Continued
Table 3: Distribution of studied symptoms in pesticide retailers and the comparison group

Symptom	Face and neck			Arms and elbows			Hands			Legs			Waist and abdomen		
	Exposed	Comparison	p value	Exposed	Comparison	p value	Exposed	Comparison	p value	Exposed	Comparison	p value	Exposed	Comparison	p value
Dermatitis															
Never or rarely	88	95	0.15	94	98	0.20	80	95	0.008*	99	100	0.34	100	100	1
Often	12	5		6	2		20	5		1	0		0	0	

*After Bonferroni correction

Kesavachandran, *et al*, found that respiratory problems occur eight times (RR 8.64, 95% CI 1.23 to 60.61) more often in pesticide shopkeepers compared with general population; the pesticide shopkeepers had a significant reduction in their spirometry indices too.¹⁴ A large body of evidence indicates an association between exposure to organophosphate pesticides and respiratory symptoms.^{28,29} Peiris-John, *et al*, reported that occupational exposure to low levels of organophosphate pesticides could lead to restrictive lung dysfunction.³⁰ In another study, the prevalence of cough, nasal discharge, nasal irritation, and chest tightness were significantly higher in the agricultural workers exposed to anticholinesterase pesticides compared with controls.³¹ The significant increase observed in the prevalence of respiratory symptoms among studied retailers may thus be explained by their exposure to organophosphorus compounds—the second most abundant pesticides handled by them. Exposure to paraquat, a widely used herbicide, is also known to be associated with increased wheezing and decreased lung functional capacities among agrarian subjects.^{32,33} Ye, *et al*, found a link between occupational exposure to pesticides and chronic bronchitis.³⁴ A study conducted in southern Ghana found a significant exposure-response relationship between exposure to fungicides and both wheezing and phlegm production.³⁵ Additionally, Neghab, *et al*, reported pulmonotoxicity in response to occupational exposure to a mixture of pesticides.³⁶ In line with these findings, in this study, a significant association was found between respiratory symptoms and pesticide exposure. The risks evaluated were very high, probably because the studied pesticide retailers rarely used PPE.

Recent investigations revealed that those pesticide shopkeepers who do not use any PPE on a regular basis, carry a

four-fold risk of developing dermal problems.¹⁴ Burning sensation was also found to be more common among Mexican pesticide retailers than a control group (30% vs 12%).¹⁶ A study on flower farm workers reported a high prevalence of rash on hands (32%) and all other parts of the body (33%).³⁷ Another investigation showed that even in greenhouse workers who have low exposure to pesticides, the prevalence of skin symptoms (redness, itching, burning) is 17%.³⁸ Both organophosphorus and pyrethroid compounds are frequently handled by retailers and are known to cause allergic contact dermatitis and a wide range of skin disorders such as redness, sensation of stinging, burning, itching and tingling.³¹⁻³⁹ Therefore, one might tentatively conclude that unprotected exposure to these compounds may be causally linked with the observed effects among retailers.

We and some other investigators have recently examined possible hepatotoxic, nephrotoxic and hematotoxic effects of exposure to pesticides by retailers.^{9,16} However, the levels of biomarkers of oxidative stress among retailers have rarely been investigated. Formation of free radical, lipid peroxidation, and alteration in the scavenging enzyme system,⁴⁰ as well as a relationship between pesticide exposure and adverse changes in the level of oxidative stress indicators, have been reported.⁴¹⁻⁴³ Colle, *et al*, found that exposure to paraquat and maneb increases the production of reactive oxygen species (ROS).⁴⁴ These radicals attack the cell membranes, resulting in lipid peroxidation and elevation of MDA.⁴⁰ Recent studies in Indian pesticide spray applicators have demonstrated that exposure to organophosphate pesticide significantly increases lipid peroxidation, resulting in an elevated level of MDA and SOD activity.^{41,42} A study on farm workers revealed that chronic exposure to organophosphate, synthetic pyrethroid, and carbamate pesticides might be associated

with increased activities of catalase, SOD, and lipid peroxidation in erythrocytes.⁴⁵ Our results were consistent with the findings of other investigators on oxidative stress indicators and antioxidant status of subjects with chronic exposure to pesticides, where increased MDA and stimulated antioxidant markers among them have been reported.^{41,42,45} The increased content of antioxidant markers, such as GSH, in erythrocytes and the activities of SOD and catalase are probably an initial adaptive response to the increased oxidative stress following exposure to pesticides.⁴³

In conclusion, the current study provided evidence to support the notion that occupational exposure to even low doses of a mixture of pesticides by retailers is associated with adverse dermal and respiratory effects as well as a significant rise in the levels of biomarkers of oxidative stress.

Acknowledgments

The authors would like to thank all the pesticide retailers and construction workers of city Council Contractors for their participation and cooperation in this study.

Conflicts of Interest: None declared.

Financial Support: This study was financially supported by the Vice Chancellor for Research and Technology, Shiraz University of Medical Sciences, Shiraz, Iran (grant No. 10480).

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