Original Article

Risk and Hematological Effects of Pesticides on Occupationally Exposed Workers in Iran's Pesticide Production Industry in 2018

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Abstract

Aim: In developing countries, pesticide poisoning, regardless of occupational exposure or deliberate actions, is one of the major public health problems. To determine the impact of occupational exposure to pesticides on workers' health status, this study evaluated the consequences of pesticide exposure and its effects on hematological indices. **Materials and Methods:** Eighty workers of pesticide production factories were studied in two experimental and control groups during 2018–2020. Data were collected using demographic, occupational, health questionnaires, and blood analysis. The collected data were analyzed using SPSS software (ver. 23), Chi-square, and U Mann–Whitney test considering a significance level of 0.05. **Results:** The age range of subjects was 23–56 years (mean = 36.21 ± 6.744). A significant difference was observed between studied groups in terms of marital status, education level, and work shift. In addition, levels of erythrocyte sedimentation rate (ESR) ($P = 0.036$), white blood cell (WBC) ($P = 0.009$), uric acid ($P = 0.033$), and alkaline phosphates ($P < 0.001$) were significantly different between the two studied groups. The results showed a significant difference between the hematology Index level of toxin production workers and workers in administrative and service units. **Conclusion:** As expected given the type of their job, a significant difference was observed between studied groups in terms of marital status, education level, and work shift, use of safety equipment, as well as residency. Furthermore, levels of ESR, WBC, uric acid, and alkaline phosphates were significantly different. It seems that pesticide toxins exposure in the poison-production industry causes hematological changes, which may be dangerous in a long time.

Keywords: Hematology index, occupational exposure, pesticide production, toxins effect

Introduction

Human is exposed to a variety of pesticides at work environments such as agricultural environments, structural control of pests, general pesticide programs, pesticides factories, and transportation of pesticides.[1,2]

Pesticide poisoning is one of the major public health problems in developing countries, in most of which workers mainly expose to organophosphate pesticides.[2]

The widespread use and exposure to pesticides lead to long-term and acute health problems for the community.[3]

Pesticide-related occupational diseases are common in temperate and humid areas due to impractical or improper use of safety equipment.[4]

The proper function of the immune system is very important for the body. The immune system is responsible for protecting the body against diseases through combating germs and bacteria invading the body. The human immune system consists of acquired and innate parts. Innate immunity has three parts, including physicochemical barriers, humoral, and cellular components.[1]

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The immune response plays a significant role in the pathophysiology of many diseases such as asthma and pulmonary diseases, autoimmune diseases, malignancies, and cancer. The application of immunotoxicity biomarkers in human epidemiological studies and clinical trials may improve our understanding of the underlying mechanisms associated with environmental exposure and the occurrence of immune diseases.[5]

The main toxic effect of organophosphates includes neurotoxicity caused by acetylcholinesterase inhibition. Organophosphates affect a variety of immune responses, including antibody production level, interleukin-2 (IL-2) production, T-cell proliferation, and inhibition of natural killer cells, lymphokine-activated killer cells, and the activity of cytotoxic T-lymphocytes.[6]

Workers of the pesticide production line, in particular, powder pesticides, often show changes in their hematology index. These changes may lead to the high prevalence of diseases such as chronic bronchitis among this group of workers. High peripheral blood leukocyte count indicates occupational exposure to these substances. Increased leukocyte counts have been reported in workers working in the production of lindane, organophosphorus, or pyrethroids, carbamates, and nitrophenol pesticides.[7]

This increase in leukocyte count can be due to the direct effect of the pesticide on bone marrow or the result of disorders such as chronic bronchitis and the presence of inflammation. Pesticide exposure is one of the main causes of the high prevalence of chronic lung disease in farmers. Moreover, chemical factories workers working in the pesticide production line are often affected by the harmful effects of these compounds, and diseases such as chronic bronchitis. Most pathological changes are observed in workers working with powders pesticides.[7-10]

Epidemiological evidence from the western countries suggests an increasing trend in the prevalence of immune-related diseases such as asthma, autoimmune diseases, and cancer. This increase is not attributed solely to the development of diagnostic approaches. There are concerns that this increasing trend is partly due to changing patterns of exposure to chemicals like insecticides.[1] Insecticides exert multiple effects on human health, depending on environmental and occupational exposure. Current knowledge indicates that exposure to insecticides may have adverse effects on the reproductive system, nervous function, and various chronic disorders due to their slow and long-term evolutionary breakdown rate. Current information confirmed the relationship between exposure to insecticides and adverse effects on the immune system. However, the specific effects on various immune system compounds such as cytokines and other immune factors require further verification. Studies have revealed that exposure to insecticides affects immune function, and related disorders development depends on dose and duration of exposure.[2]

Given the aforementioned information, the increasing production, the use of chemical pesticides, and their impact on the body and especially the immune system as a body defense against various diseases, the present study was conducted to determine the effect of occupational exposure to pesticides on the function of hematology index.

Materials and Methods

Populations and sampling

This study was a fundamental cross-sectional, cohort, and prospective experiment performed in Isfahan city. The study population included all workers in the plant pesticide production line as case/intervention population and personnel of their administrative units as control population during 2018–2020. Administrative personnel were not involved with the production line, and they had no contact with the produced toxins. Workers at the production line produced toxins such as paraquat, glyphosate, diazinon, permethrin, chlorpyrifos, cypermethrin, and acetamiprid. A cluster sampling method was employed to determine the sample size. To this end, the country was first divided into four quadrants, and a quarter of the southeast was selected as the research environment. Then, two factories were selected by cluster sampling, and sampling was performed equally in each factory. Based on the statistics of previous studies,[11] the sample included 80 individuals randomly divided into control and intervention groups using 4-block randomized blocks. Thus, for the experimental group, 40 production line workers, and for the control group, 40 administrative and service personnel were randomly selected. Inclusion criteria included male gender, age of 20–58 years, no activities related to pesticides such as farming, livestock, conscious tendency to participate in the study, no comorbidities affecting the immune system (such as kidney, liver, and cardiovascular diseases or cancer). Exclusion criteria were no tendency to continue the study and no sample approval by the internal medicine specialist. The study data were collected in four sections, including demographic, occupational, health questionnaire, and clinical laboratory examination test results. The content validity index and face validity of the questionnaires were 0.68. The patterns of routine blood tests are depicted in Table 1.

Data analysis

The data were analyzed using SPSS version 21 (IBM SPSS, New York, USA), and Chi-Square and U Mann–Whitney tests were considered a significant result where the confidence interval was 95% and $P < 0.05$.

Results

In the present study, 80 subjects with the age range of 23–56 years (mean = 36.21 ± 6.744) were evaluated in two control and intervention groups without significant mean age difference by U Mann–Whitney test analysis ($P = 0.988$). The average work experience of the studied population was 9 years, with a range of 1–18 years. However, the difference between groups based on work experience didnot statistically significant (P = 0.478). The demographic characteristics of both populations are presented in Table 2.

According to the Chi-square test results, a significant difference was observed between studied groups in terms of marital status, education level, and work shift, use of safety equipment and residency, expected given the type of the job. Table 3 presents the levels of blood indicators in control and case groups.

According to the results, levels of erythrocyte sedimentation rate (ESR) (P = 0.036), white blood cell (WBC) (P = 0.009), uric acid (P = 0.033), and alkaline phosphates (P < 0.001) were significantly different between the two studied groups. Other hematological indices had no statistically significant difference between the two populations.

Discussion

The present study was designed to evaluate the role of occupational exposure to pesticides on the hematology index among 80 pesticide production line workers and administrative and service personnel. The results of demographic data

Table 1: Laboratory tests performed in the study

Index	Normal range	Unit	Index	Normal range	Unit
FBS	70-115	mg/dl	HB	14-18	Gr %
BUN	5-24	mg/dl	HCT	41-54	%
Creatinine	0.4-1.4	mg/dl	RBC	4-6 × 106	/Cu mm
Uric acid	3.6-8.2	mg/dl	WBC	4000-10000	/Cu mm
TG	60-200	mg/dl	Neutrophil	%	
Cholesterol	<200	mg/dl	Lymphocyte	%	
Bilirubin total	Up to 1.2	mg/dl	Monocyte	%	
Bilirubin direct	Up to 0.30	mg/dl	MCV	80-96	Fl
Total protein	6.6-8.8	g/dl	MCH	25-33	Pg
Albumin	3.5-5.5	g/dl	MCHC	28-40	%
Globulin	3.5-5.2	g/dl	Platelete	150,000-450,000	/mm^3
HDL cholesterol	30-60	mg %	ESR	0-10	Mm/1 h
LDL cholesterol	<130	mg %	SGOT/AST	<37	IU/L
Alkaline phosphatase	80-306	IU/L	SGPT/ALT	<41	IU/L

FBS: Fast blood sugar, BUN: Blood urea nitrogen, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, Hb: Hemoglobin, HCT: Hematocrit, RBC: Red blood cell, WBC: White blood cell, MCV: Mean cell volume, MCH: Mean cell hemoglobin, MCHC: Mean cell hemoglobin concentration, ESR: Erythrocyte sedimentation rate, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, TG: Triglyceride, SGOT: Serum glutamic-oxaloacetic transaminase, SGPT: Serum glutamic pyruvic transaminase

Table 2: Frequency distribution of personal and occupational characteristics of both control and intervention groups

Variable	Group intervention, frequency (%)	Control, frequency (%)	Total, frequency (%)
Married	37 (92.5)	29 (72.5)	82.5
Single	3 (7.5)	11 (27.5)	17.5
Chi-square test results			
Elementary	19 (45.5)	0 (0)	19 (23.8)
Middle school	9 (22.5)	0 (0)	9 (11.3)
High school	10 (25)	7 (17.5)	17 (21.3)
Associate degree	2 (5)	1 (2.5)	3 (3.8)
Bachelor	0 (0)	25 (62.5)	25 (31.3)
Masters and higher	0 (0)	7 (17.5)	7 (8.8)
Chi-square test results			
City	6 (15)	40 (100)	46 (57.5)
Village	34 (85)	0 (0)	34 (42.5)
Chi-square test results			
Shift work			
Morning	3 (7.5)	40 (100)	43 (53.8)
Rotational	37 (92.5)	0 (0)	37 (46.3)
Chi-square test results			
Use of safety equipment			
Yes	34 (85)	0 (0)	34 (42.5)
No	6 (15)	40 (100)	46 (57.5)
Chi-square test results			

Table 3: Central dispersion indices and probability value distribution of blood indices data in two groups

Mean	SE	Minimum	Maximum	Skewness	P	P value
ESR	4.80	0.336	1	18	1.706	0.001
HB	14.59	0.114	10.30	16.60	−1.247	0.001
HCT	44.41	0.344	29.30	50.10	−1.998	0.001
RBC	5.257	0.057	4.160	6.980	1.363	0.001
WBC	7830	179.542	4800	12100	0.586	0.045
MCV	85.297	0.741	59.54	97.82	−1.560	0.001
MCH	28.747	0.312	18.48	35.87	−1.093	0.001
MCHC	32.909	0.107	30.29	34.79	−0.555	0.038
Platelet	221612.5	5070.219	105000	321000	−0.044	0.664
FBS	84.15	2.006	65	220	5.766	0.001
BUN	13.68	0.226	11	20	1.075	0.001
Creatinine	0.905	0.179	0.60	1.40	0.436	0.085
Uric acid	5.343	0.124	3.50	8.30	0.385	0.144
TG	152.13	8.127	56	338	0.948	0.001
Cholestrol	173.61	3.114	121	263	0.663	0.063
Bilirubin total	1.024	0.045	0.57	2.34	1.510	0.001
Bilirubin direct	0.212	0.012	0.10	0.58	1.227	0.001
Protein total	7.626	0.033	7	8.3	−0.073	0.083
Albumin	4.494	0.315	3.90	5.20	0.163	0.326
Globulin	3.076	0.030	2.30	3.70	−0.137	0.109
A/G ratio	1.468	0.021	1.08	2.13	0.583	0.185
SGOT	25.96	1.046	11	81	3.117	0.001
SGPT	23.14	1.465	10	73	1.691	0.001
Alkaline phosphatase	204.26	6.311	118	375	0.635	0.009
HDL cholesterol	38.59	0.810	21	51	−0.228	0.041
LDL cholestrol	109.68	2.645	67	193	0.902	0.001

FBS: Fast blood sugar, BUN: Blood urea nitrogen, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, HB: Hemoglobin, HCT: Hematocrit, RBC: Red blood cell, WBC: White blood cell, MCV: Mean cell volume, MCH: Mean cell hemoglobin, MCHC: Mean cell hemoglobin concentration, ESR: Erythrocyte sedimentation rate, TG: Triglyceride, SGOT: Serum glutamic-oxaloacetic transaminase, SGPT: Serum glutamic pyruvic transaminase

analysis outlined that the mean age of participants was 36.21 ± 6.744 years, ranging from 23 to 53 years. The majority of participants (32.5%) had 5–8 years of job experience. Among 80 participants, 66 (82.5%) were married and 14 (17.5%) were single. According to their level of education, 25 (31.3%) had BA, seven (8.8%) had MA, 3 (3.8%) associate degree, 17 (21.3%) diploma, nine (11.3%) had middle school degree, and 19 (23.8%) had elementary school degree or were illiterate. Forty-six were from urban (57.5%) and 34 (42.5%) were from rural areas. The majority of them were in the morning shift (53.7%) and 37 rotational shifts (46.3%). The results showed a statistically significant difference between the two groups in terms of ESR level, leukocyte count, uric acid, and alkaline phosphatase. Their difference regarding other hematological indices was not significant. The results of the WBC count analysis showed a significant difference between case and control groups. Findings from previous studies have indicated contradictory results. Osely and some other researcher demonstrated that total blood cell count and lymphocyte phenotype markers were not different between case and control groups.[9,10] In contrast, Galloway and Handy (2003) reported mild leukopenia in the pesticide-exposed group.[12] Kłuciński *et al*. (2001) and Ramírez-Santana *et al*. revealed a significant reduction in WBC count of workers exposed to pesticides,[13,14] as reported by Osely *et al*. (2010). These results were in line with our study. M.C. Fiore observed a significant enhancement in the T8 cells of women exposed to aldicarb-contaminated groundwater.[15] According to the results, the level of blood IL-2 between the studied groups was not significantly different. McClure *et al*. (2001) compared the immune system function of farmers' family who had been exposed to organophosphate pesticides with the control group. They evaluated the IL-2 level and did not observe any significant difference between groups in terms of IL-2 level.[11] This result is similar to our study, whereas Li observed a reduction in IL-2 level in workers of pesticide production line factories and the control group.[16]

According to several studies, pesticides exposure causes immunotoxicity, immunoglobulins and C 3 component of complement changes and alteration in plasma esterases which can be as biomarkers.[16-21] There was a significant difference between the two groups in terms of demographic variables such as education ($P < 0.05$) and the use of safety equipment ($P < 0.05$). Both groups were not demographically matched, and therefore, demographic characteristics could not be used as an index for comparing safety levels. More relevantly, most of the hematological indices such as ESR, hemoglobin (HB), hematocrit (HCT), red blood cell (RBC), WBC, mean cell volume (MCV), mean cell hemoglobin (MCH), mean cell hemoglobin concentration (MCHC), fast blood sugar (FBS), blood urea nitrogen (BUN) triglyceride, bilirubin total, and bilirubin direct.

Protein total, serum glutamic-oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT), alkaline phosphatase, high-density lipoprotein (HDL), and low-density lipoprotein (LDL) had significantly changed in the population exposed to pesticides compared to the control population ($P < 0.05$).

Due to ethical limitations and occupational safety standards, it was not possible to use the same control group, and therefore, administrative personnel of the factory were used as a control group. Due to the cost of the tests, it was not possible to repeat the tests and ensure the accuracy of the results. These limitations may affect the generalizability of our findings, and thus, more in-depth disclosures will be warranted.

Conclusion

According to our findings, the demographic data such as education level and use of safety equipment was significantly different between the toxin-exposed population and the control group. In addition, pesticide exposure during a mean of 5–8 years was associated with significant changes in majority of the blood/hematology indices, such as levels of leukocytes, alkaline phosphatase, ESR, HB, HCT, RBC, WBC, MCV, MCH, MCHC, FBS, BUN triglyceride, total bilirubin, bilirubin direct, SGOT, SGPT, HDL, and LDL. The alterations in pivotal hematological factors among workers exposed to pesticides will predispose them to various diseases. Therefore, proper prevention and control strategies for mitigating the toxins exposure among workers seem necessary.

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Conflicts of interest

There are no conflicts of interest.

References

1. Corsini E, Liesivuori J, Vergieva T, Van Loveren H, Colosio C. Effects of pesticide exposure on the human immune system. Hum Exp Toxicol 2008;27:671-80.
2. Gangemi S, Gofita E, Costa C, Teodoro M, Briguglio G, Nikitovic D, *et al*. Occupational and environmental exposure to pesticides and cytokine pathways in chronic diseases (Review). Int J Mol Med 2016;38:1012-20.
3. Ranjbar A, Pasalar P, Abdollahi M. Induction of oxidative stress and acetylcholinesterase inhibition in organophosphorous pesticide manufacturing workers. Hum Exp Toxicol 2002;21:179-82.
4. Pearson JN, Patel M. The role of oxidative stress in organophosphate and nerve agent toxicity. Ann N Y Acad Sci 2016;1378:17-24.
5. Yadav J, Singh D, Kumar D. Organophosphates and carbamates as inhibitors of acetylcholinesterase in *Eisenia fetida*. Pollution Res 2017;36:277-81.
6. Mladenović M, Arsić BB, Stanković N, Mihović N, Ragno R, Regan A, *et al*. The targeted pesticides as acetylcholinesterase inhibitors: Comprehensive cross-organism molecular modelling studies performed to anticipate the pharmacology of harmfulness to humans *in vitro*. Molecules 2018;23:2192:1-37.
7. Colović MB, Krstić DZ, Lazarević-Pašti TD, Bondžić AM, Vasić VM. Acetylcholinesterase inhibitors: Pharmacology and toxicology. Curr Neuropharmacol 2013;11:315-35.
8. Mandour RA. Environmental risks of insecticides cholinesterase inhibitors. Toxicol Int 2013;20:30-4.
9. Osely EM. Influence of Some Pesticides on Humoral and Cellular Immunity of Exposed Workers in Pesticides Industries. Ain Shams: Ain Shams University; 2010.
10. Vine MF, Stein L, Weigle K, Schroeder J, Degnan D, Tse CK, *et al*. Effects on the immune system associated with living near a pesticide dump site. Environ Health Perspect 2000;108:1113-24.
11. McClure GY, Helm RM, Stine K, Burks AW, Jones SM, Gandy J. Evaluation of immune parameters in propanil-exposed farm families. Arch Environ Contam Toxicol 2001;41:104-11.
12. Galloway T, Handy R. Immunotoxicity of organophosphorous pesticides. Ecotoxicology 2003;12:345-63.
13. Kłuciński P, Kossmann S, Tustanowski J, Friedek D, Kamińska-Kołodziej B. Humoral and cellular immunity rates in chemical plant workers producing dust pesticides. Med Sci Monit 2001;7:1270-4.
14. Ramírez-Santana M, Zúñiga L, Corral S, Sandoval R, Scheepers PT, Van der Velden K, *et al*. Assessing biomarkers and neuropsychological outcomes in rural populations exposed to organophosphate pesticides in Chile–study design and protocol. BMC Public Health 2015;15:116.
15. Fiore MC, Anderson HA, Hong R, Golubjatnikov R, Seiser JE, Nordstrom D, *et al*. Chronic exposure to aldicarb-contaminated groundwater and human immune function. Environ Res 1986;41:633-45.
16. Li Q. New mechanism of organophosphorus pesticide-induced immunotoxicity. J Nippon Med Sch 2007;74:92-105.
17. Wysocki J, Kalina Z, Owczarzy I. Serum levels of immunoglobulins and C 3 component of complement in persons occupationally exposed to chlorinated pesticides. Med Pr 1985;36:111-7.
18. Sahlander K, Larsson K, Palmberg L. Daily exposure to dust alters innate immunity. PLoS One 2012;7:e31646.
19. Silva V, Mol HGJ, Zomer P, Tienstra M, Ritsema CJ, Geissen V. Pesticide residues in European agricultural soils – A hidden reality unfolded. Sci Total Environ 2019;653:1532-45.
20. Hernández A, Gómez MA, Pena G, Gil F, Rodrigo L, Villanueva E, *et al*. Effect of long-term exposure to pesticides on plasma esterases from plastic greenhouse workers. J Toxicol Environ Health A 2004;67:1095-108.
21. Lionetto MG, Caricato R, Calisi A, Giordano ME, Schettino T. Acetylcholinesterase as a biomarker in environmental and occupational medicine: New insights and future perspectives. Biomed Res Int 2013;2013:321213.