Cumulative Exposure Characteristics of Vegetable Farmers Exposed to Chlorpyrifos in Central Java – Indonesia; A Cross-sectional Study

Jen Fuk Liem (jenfuk.dr@gmail.com)
Krida Wacana Christian University
Muchtaruddin Mansyur
University of Indonesia

Research Article

Keywords: Pesticide cumulative exposure, exposure assessment, exposure reduction, work practices, occupational characteristics

DOI: https://doi.org/10.21203/rs.3.rs-296524/v1

Abstract

Background

Agriculture is a major economic sector in Indonesia. Chemical pesticides are widely being used in agriculture for the control of the pest. There is a growing concern that pesticide exposure, particularly chlorpyrifos (CPF) exposure combined with other occupational characteristics that determine the level of exposure, can lead to further health impacts for farmers. Our objective was to evaluate the cumulative exposure characteristics among farmers exposed to CPF using a validated algorithm.

Methods

We conducted a cross-sectional study of 152 vegetable farmers aged 18-65 who actively used CPF for at least one year in Central Java, Indonesia. Subject characteristics were obtained using a structured interviewer-administered questionnaire addressed for sociodemographic and work-related characteristics. The cumulative exposure level (CEL) was measured as a function of the intensity level of pesticide exposure (IL), lifetime years of pesticide use and the number of days spraying per years. CEL then classified into two groups, high and low exposure group. The difference in characteristics of the study population was measured using Chi-square, independent-t or Mann-Whitney test. Association between CEL and its characteristics variables were performed by multiple linear regression.

Results

Seventy-one subjects (46.7%) were classified as the high exposure group. The use of multiple pesticide mixtures was common among our study population, with 94% of them using 2 or more pesticides. 73% reported direct contact with pesticides, and over 80% reported being splashed or spilt during preparation or spraying activity. However, we found that the proportion of proper personal protective equipment (PPE) use in our subjects was low. Higher volume of mixture applied ($p < 0.001$) and broader acres of land ($p = 0.001$) were associated with higher cumulative exposure level, while using the long sleeve and long trousers ($p < 0.05$) during pesticide spraying were associated with lower cumulative exposure after adjusted for age and gender.

Conclusions

These findings indicate a lack of knowledge and understanding of the proper use of pesticides. Thus, we recommend comprehensive training on pesticide use and encourage proper PPE to reduce the exposure level.

Background

Agriculture is a major economic sector in Indonesia. Chemical pesticides are widely being used in agriculture for the control of the pest. Organophosphate (OP) is one of the most widely used pesticides today for that purpose. In 2015, more than half of the pesticides used worldwide were organophosphate

(OP) insecticides, with 40% of which were chlorpyrifos (CPF).(1) Indonesia has the same experience of pesticide extensively use (2), and the number of pesticide registered has been grown from 2605 in 2010 to 3207 in 2016.

Workers in the agricultural sector, especially pesticide applicators, will be exposed to certain amounts of OP and develop certain risks to experience health problems. Generally, exposure to CPF and other pesticides occurs through skin contact, inhalation, or ingestion. Occupational pesticide exposure in the agricultural sector was obtained from several activities, including preparing, mixing, loading, spraying pesticide, and cleaning used equipment. Farmers can also be exposed through re-entering the sprayed area, manipulating crops or harvesting the crops that may still be contaminated with pesticides.(3) This condition is followed by the fact that there is limited awareness about the health impacts from pesticide exposure, knowledge of safe work practices, and proper personal protective equipment (PPE) among the farmers.(2, 4) Therefore, there is a growing concern that inappropriate and unsafe use of pesticides may lead to farmers' health impacts.(5, 6) In particular, CPF exposed farmers are vulnerable to several deleterious effects, including neurological symptoms, reproductive hormone alteration, metabolic disruption, and endocrine disruption.(7-10).

Several conditions such as the type of pesticide, the concentration of the pesticide, the length of exposure, the path of exposure and the proper use of PPE are important factors that determine the severity of the exposure.(11-13) The large-scale experiment in an ideal setting to directly assess the dose-response relationship of pesticides exposure to associated health problems have particular difficulties.(12) Suppose particular pesticides exposure will lead to specific health problem. In that case, we could expect a linear dose-response relationship between external dose (i.e. occupational and or environmental exposure) and internal dose (i.e. concentration of a chemical or its toxic metabolite in the human body).(13) However, accurate exposure assessment in epidemiological studies is still difficult to obtain, and real values of exposure to pesticides are not easy to predict. (3) Therefore, indirect measurement of exposure dose from the worker’s specific task to obtain closer to the actual condition may bridge this gap.

This study's objective was to evaluate the cumulative exposure characteristics among vegetable farmers exposed to chlorpyrifos in Indonesia using a validated algorithm. We hope our results will provide supporting data that can be applied to reduce the exposure level for farmers.

Methods

Study area and population

We conducted a cross-sectional study of 152 vegetable farmers from 2 villages, Pancot village & Adipuro village, known as the largest garlic production areas in Central Java, Indonesia, from July to October 2020. The sample size was meet minimum requirement of 97 subjects, calculated using a single sample formula to estimate proportions. We introduced the study's objective, goals, and data confidentiality during the recruitment process, and we also provide education to raise awareness about pesticide use and safety precautions to potential participants. Participants enrolled criteria were vegetable farmers aged 18-65 who actively use CPF for at least 1 year. Those who met the criteria and gave written consent to participate in the study then completed a structured interviewer-administered questionnaire and underwent the anthropometric measurement. Subject characteristics were obtained using a structured interviewer-administered questionnaire addressed for sociodemographic and occupational characteristics. Question regarding sociodemographic characteristics consists of several questions such as age, gender, smoking habit and educational background. The interview for agricultural work-related (occupational) characteristics consisted of several specific questions on those related to pesticide exposure, work practice, and the use of personal protective equipment (PPE). We randomly asked several important questions to determine answer's consistency to limit the possibility of misclassification of exposure. All methods were performed in accordance with the relevant guidelines and regulations. The study protocol was approved by the Ethical Committee of the Faculty of Medicine Universitas Indonesia on March 23, 2020 (No. KET-339/UN2.F1/ETIK/PPM.00.02/2020).

Cumulative Exposure Level

The intensity level of pesticide exposure was calculated using the validated method from Dosemeci. The overall exposure intensity level is then combined with information on lifetime years of pesticide use and the number of days spraying per years to produce the cumulative exposure level as shown in the following algorithm:(14)

IL = (Mix + Appl + Repair + Wash) x PPE x Repl x Hyg x Spill

IL = Intensity Level of pesticide exposure

Mix = Pesticide mixing

Appl = Application methods

Repair = Repairing equipment

Wash = Washing equipment after spraying

PPE = Personal Protective Equipment utilisation

Repl = Replacing old gloves

Hyg = Personal hygiene practices

Spill = Spill treatment (changing clothes after a spill)

CEL = IL x Duration x Frequency

CEL = Cumulative Exposure Level

IL = Intensity Level of pesticide exposure

Duration = Lifetime years of pesticide use

Frequency = Number of days spraying per year

There are several similar conditions among study participants in terms of exposure during crop insecticides application. The activities of preparing, mixing, loading, and spraying pesticide using the backpack tank are carried out personally by each study participants in the open area.

Because the CEL was not normally distributed, CEL was classified into two groups, high and low exposure group, with the median as the cut-off point.

Statistical analysis

All analysis was performed using SPSS 20 for Windows.

The study population characteristics were summarised with frequency distribution and percentages for categorical variables, while continuous variables were described using mean ± SD or median (minimum-maximum). Chi-square test, independent t-test or Mann-Whitney test were used to measure the difference in the characteristics of the study population according to the cumulative exposure level group. All p values are two-sided, with significance was considered at $p < 0.05$ for these tests.

Association between CEL and its characteristics variables were performed by multilinear regression analysis. Variables associated with CEL at a significance level of $p \leq 0.20$ in the simple regression analysis were included in the multivariate model. The variables were retained in the final model when they were associated with the CEL at a significance level of 0.05 according to the stepwise procedure.

Results

Our study population was 152 farmers with the mean age of 49,91 ± 9,42 years, consisting of 90.1% male, 92.8% as members of farmers' society, and 86.8% in low educational level. As shown in Table 1, seventy-one farmers (47%) out of 152 were classified as having a high cumulative exposure level according to the Dosemeci algorithm as described previously. The proportion of smoker was 48% and significantly higher in the high CEL group. Ten out of 132 subjects in low educational level had never attended formal education.

Table 1
Sociodemographic characteristics, lifestyle factors and physical condition of CPF exposed farmers grouped according to the cumulative exposure level

Variable	**Cumulative Exposure Level**		**p-value**
	High (n = 71)	**Low (n = 81)**	
Age (years) (mean ± SD)	51,49 ± 8,6	48,52 ± 9,92	0.052^{tt}
Member of farmer's society (n %)	66 (93)	75 (92,6)	0.931^{cs}
Male (n %)	65 (91,5)	72 (88,9)	0.583^{cs}
Low educational level (n %)	65 (91.5)	67 (82.7)	0.108^{cs}
Smoker (n %)	41 (57,7)	32 (39,5)	0.025^{cs}
Obese (n %)	16 (22,5)	14 (17,3)	0.417^{cs}
tt = independent t-test; cs = chi-square			

Significantly few farmers reported using pesticides according to the user instructions (2.0%), and all of them were in the low CEL group.

As shown in Table 2, the high exposed group was characterised with a broader arable land area, longer daily working time, longer duration of spraying pesticide, and more volume of mixture applied than the low exposure group. The three CEL (i.e.IL, duration and frequency) functions were also significantly higher in the high exposure group. On the other side, the proportion of farmers who used more than three pesticides in the mixture was higher in the low exposure group. The number of days spraying per year was considered high, with > 100 days per year on average.

Table 2
Agricultural work-related characteristics of CPF exposed farmers grouped according to the cumulative exposure level

Variable	Cumulative Exposure Level		p-value
	High (n = 71)	Low (n = 81)	
Arable land area (acres)*	0.25 (0.03–0.70)	0.15 (0.01–0.50)	0.001
Number of arable lands*	4 (1–13)	3 (1–9)	0.026
Daily work duration (hours)*	7 (3–10)	6 (3–10)	0.003
Duration of spraying pesticide (hours/day)*	0.57 (0.14–2.00)	0.30 (0.04–2.25)	< 0.001
Volume of the mixture applied (litre/day)*	27.2 (7.0–81.6)	14.6 (2.3–85.0)	< 0.001
Number of days spraying per year*	104 (52–364)	73 (37–364)	< 0.001
Lifetime years of pesticide use*	30 (7–45)	25 (1–40)	< 0.001
Intensity level of pesticide exposure*	13.5 (7.1–20.7)	9.8 (1.0–21.9)	< 0.001
Spraying in the morning time (n %)	48 (67,6)	44 (54.3)	0.095[cs]
Used more than 3 pesticides in mixture (n %)	15 (21.1)	30 (37.0)	0.032[cs]
Using a manual pesticide sprayer (n %)	13 (18.3)	23 (28.4)	0.145[cs]
Not using any PPE for spraying (n %)	25 (35.2)	12 (14.8)	0.003[cs]

*Median (minimum-maximum) with p-value by Mann-Whitney test; cs = Chi-square

There are numbers of similar conditions among study participants in terms of exposure during crop insecticides application.

Preparing, mixing, loading, and spraying pesticide using the backpack tank are carried out personally by each study participants in the open area.

None of the subjects wore a respirator, coverall, or disposable outer work clothes. The proportion of apron, goggles, and chemical gloves user in our study population was also tiny (Table 3). However, most of them are frequently use long sleeve clothes or long trousers during farm works. Four subjects who used chemical gloves in pesticide exposed activity reported that gloves were only replaced if they were damaged and that they often continued to use the damaged gloves.

Table 3
Distribution of PPE usage, work clothes and work practices of the study population

Variable	Frequency - n (%)	
	Rare / never	Frequent
Personal Protective Equipment		
Apron	150 (98.7)	2 (1.3)
Face mask	79 (52.0)	73 (48.0)
Goggles	151 (99.3)	1 (0.7)
Chemical gloves	148 (97.4)	4 (2.6)
Boots*	64 (42.1)	88 (57.9)
Work clothes		
Long sleeve clothes	15 (9.9)	137 (90.1)
Long trousers	14 (9.2)	138 (90.8)
Work practices		
Wiping sweat with work clothes	123 (80.9)	29 (19.1)
Re-enter the field after spraying	119 (78.3)	33 (21.7)
Spraying against the wind	151 (99.3)	1 (0.7)
Splashed or spilled during spraying	19 (12.5)	133 (87.5)
Splashed or spilled while loading the pesticide	28 (18.4)	124 (81.6)
Eat in the middle of the work-time	147 (96.7)	5 (3.3)
Direct contact with pesticides	41 (27.0)	111 (73.0)
Proper shower after spraying	12 (7.9)	140 (92.1)
Changing clothes after spraying	7 (4.6)	145 (95.4)

*p = 0.001 by chi-square, indicates lower proportion of frequent users in high cumulative exposure group

Table 4
The proportion of the type of pesticide used besides chlorpyrifos among the study population

Active ingredient	Chemical class	Utilisation	Frequency (n %)
Mancozeb	Carbamate	Fungicide	87 (57.2)
Abamectin	Avermectin	Insecticide	57 (37.5)*
Difenoconazole	Triazoles	Fungicide	49 (32.2)
Emamectin	Avermectin	Insecticide	17 (11.2)
Lambdacyhalothrin	Pyretroid	Insecticide	14 (9.2)
Chlorfenapyr	Pyrrole	Insecticide	12 (7.9)
Beta-cyfluthrin	Pyrethroid	Insecticide	10 (6.6)
Lufenuron#	Benzamida	Insecticide	9 (5.9)
Methomyl	Carbamate	Insecticide	9 (5.9)
Fipronil	Phenylpyrazole	Insecticide	7 (4.6)
Dimethoate	Organophosphate	Insecticide	6 (3.9)
Imidacloprid	Neonicotinoid	Insecticide	6 (3.9)
Propineb	Carbamate	Fungicide	6 (3.9)
Deltamethrin	Pyrethroid	Insecticide	4 (2.6)
Profenofos	Organophosphate	Insecticide	4 (2.6)
Cypermethrin	Pyretroid	Insecticide	4 (2.6)
Chlorantraniliprole	Diamide	Insecticide	3 (2.0)
Acephate	Organophosphate	Insecticide	2 (1.3)
Dimehypo	Thiosultap	Insecticide	1 (0.7)
Chlorothalonil	Chloronitriles	Fungicide	1 (0.7)
Mefenoxam	Phenylamides	Fungicide	1 (0.7)
Pyraclostrobin	Carbamate	Fungicide	1 (0.7)
Phoxim	Organophosphate	Insecticide	1 (0.7)

*p = 0.01 by chi-square, indicates lower proportion of users in high cumulative exposure group

Product contains a mixture of Lufenuron + Emamectin

$ Product contains a mixture of Methoxyfenozide + Spinetoram

Active ingredient	Chemical class	Utilisation	Frequency (n %)
Methoxyfenozide$	Benzohydrazide	Insecticide	1 (0.7)
Spinetoram$	Spinosyn	Insecticide	1 (0.7)
*p = 0.01 by chi-square, indicates lower proportion of users in high cumulative exposure group			
# Product contains a mixture of Lufenuron + Emamectin			
$ Product contains a mixture of Methoxyfenozide + Spinetoram			

All of the CPF used were in liquid form, with the majority using a concentration of 200 EC (98.7%). Ethylene-bis-dithiocarbamate (EBDC) mancozeb and abamectin was the fungicide and insecticide most frequently used as an addition to CPF in our subjects, as shown in Table 4. Nearly 2 out of 3 additional pesticides used were in liquid form.

As shown in Fig. 1, the use of multiple pesticides is common in our study population. Only 5.9% of the farmers used a single pesticide (CPF) while the other 27%, 38.2%, and 28.9% were used 2, 3, and more than 3 pesticide mixtures.

Using long sleeve and long trousers while spraying, pesticides were associated with lower cumulative exposure while the higher volume of mixture applied and broader acres of land were associated with higher cumulative exposure level after adjusted for age and gender (Table 5).

Table 5
Multiple linear regression analysis of cumulative exposure

Variable	B	SE (B)	Beta	95% CI (Lower; Upper)	p
Age (years)	0.791	0.165	0.319	0.47 ; 1.18	< 0.001
Arable land area (acres)	52.633	15,437	0.289	22.12 ; 83.14	0.001
Volume of the mixture applied (L/day)	0.329	0.107	0.259	0.19 ; 0.54	0.002
Long trousers (work clothes)	-5,691	2.478	-0,160	-10.59 ; -0.79	0.023
Long sleeve (work clothes)	-4,834	2,111	-0,160	-9.01 ; -0.66	0.023
B = Parameter estimate; SE (B) = Standard error for B Coding for the use of work clothes are as follows: 0 = never, 1 = rarely, 2 = often, 3 = always R^2 = 0.361; Adjusted R^2 = 0.339					

Discussion

In general, farmers in our study have lived most of their lives in this profession. For them, farming methods and work practices have been taught and implemented over many years. The high number of spraying days per year and the use of multiple pesticide mixtures, but on the other hand, not using proper PPE in their agricultural activities is a common practice among them.

Our study showed that the high exposure group's intensity level was significantly higher compared to low exposure group due to the significantly higher scores for PPE utilisation, personal hygiene practices, and spill treatment. Since proper PPE utilisation was significant in the exposure reduction strategy, choosing not to use proper PPE will result in a higher internal dose. Several studies have covered the issue that proper use of PPE was significantly associated with lower dimethyl metabolites (15), lower DAP concentrations (16) and the use of full-body coveralls during pesticides handling and spraying was significantly associated with lower OP metabolites level.(17)

Dermal exposure and inhalation are the main routes of exposure for agricultural pesticides exposure.(11) All of the CPF used in our subjects were in emulsifiable concentrates that are readily absorbed through skin contact. Thus, direct contact should be avoided, and proper dermal protectors such as chemical gloves, coverall, or apron will reduce the exposure dose.(18) Among our subjects, 73% had reported direct contact with pesticides, and over 80% had reported being splashed or spilt during preparation or spraying activity. Contradictory, we found that the most frequently used PPE in our study population were face mask (cloth masks or surgical masks) and boots which did not provide sufficient protection against CPF exposure. However, we also found that appropriate clothing (i.e. long sleeve and long trousers) while spraying pesticides were associated with lower cumulative exposure. These findings are relevant to reduced exposure because long sleeves and trousers provide a partial barrier against direct contact due to splashes or spills.(11, 18) The proportion of proper PPE use in our study population was 2% while the proportion of ‘no PPE used’ was 24%. The similar condition of low frequency of PPE use has been reported by several studies with agricultural workers in different countries.(4, 19–24)

Generally accepted that advising the use of PPE does not always result in adequate protection (25), so work practices come into play. Regarding the hygiene practices and spill treatment, we found that nearly all of our subjects reported having proper showering and changing clothes after spraying, just in agreement with the results from other researchers.(4, 26) All farmers also claim to wash their hands after being exposed to pesticides and before eating. We suggest this represents a more general attitude rather than acceptable practices in exposure reduction as reported in the previous study in Iran and Indonesia that there is no consistency between perception and work practices.(4, 21) Nevertheless, changing clothes was found to be significantly associated with lower exposure levels, so that this practice was as crucial as PPE utilisation, especially to control dermal exposure. (17)

Our study also found that very few farmers reported the use of pesticides according to the user instructions.
A previous study reported that the level of education promoted safety behaviours among farmers.(21, 27, 28) Farmers with higher education, in general, are having a good sense in safety behaviour during

pesticide handling. Higher education will also help farmers to obtain relevant knowledge in work practices and choose the proper PPE.(29) Regarding the use of pesticides, 94% of our subjects reported using two or more pesticides. The high frequency of farmers using multiple pesticides was also found in other countries.(19, 23) Ethylene-bis-dithio-carbamate (EBDC) mancozeb and abamectin were the fungicide and insecticide most frequently used in our subjects, similar to the previous study.(30)

Our findings provide a clearer picture of the farmers' characteristics in the informal agricultural sector in Indonesia and may also represent conditions in other countries condition.

There are some limitations to our study that should be taken into consideration while interpreting our results. All of the information regarding agricultural activities were self-reported by the farmers that may result in exposure misclassification. However, the possibility of misclassification has been limited by randomly asking several important questions to determine the answers' consistency. There are several parameters related to exposure doses that we could not get in the interview. We did not have information regarding the exact quantity of CPF or other pesticides used by the farmers. We also did not have information about the time of proper showering or hand washing after direct exposure to or after pesticides handling.

Conclusions

The CEL in our study population was characterised by a high-intensity level, longer lifetime years of pesticide use, and a high number of days spraying per year. The IL was determined mainly by the low frequency of PPE use, especially proper dermal protectors and work practices (hygiene practices and spill treatment). As an addition to CEL, the occupational characteristics such as a higher volume of mixtures applied, wider arable areas, and long work clothes also determine the exposure dose. These findings indicate a lack of knowledge and understanding of the proper use of pesticides, the potential health impacts, and exposure control. We recommend comprehensive training on pesticide use and mentoring for farmers. We also encourage proper PPE, particularly dermal protector, and proper work clothes during pesticide handling to reduce the exposure level.

Abbreviations

CEL : Cumulative Exposure Level

CPF : Chlorpyrifos

EBDC : Ethylene-bis-dithio-carbamate

IL : Intensity Level of pesticide exposure

OP : Organophosphate

PPE : Personal Protective Equipment

Declarations

Ethics approval and consent to participate

The study protocol was approved by the Ethical Committee of the Faculty of Medicine Universitas Indonesia on March 23, 2020 (No. KET-339/UN2.F1/ETIK/PPM.00.02/2020). Informed consent was obtained from all subjects

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

Funding

This research was supported by Prodia Group. The funders had no role in the design of the study, in the collection, analysis, and interpretation of data, or in the writing of the manuscript and the decision to publish.

Authors' contributions

LJ: participated in the design of the study, collected and processed the data, was conducted the statistical analysis and wrote the first draft of the manuscript.

MM: participated in the study's design, supervised the statistical analysis and provided valuable insight for revising the manuscript.

All authors have read and approved the manuscript.

Acknowledgements

We are very grateful to all farmers who participated in this research. We also thank the support team for their contribution during preparation phase and assistance during the recruitment.

References

1. Casida JE, Bryant RJ. The ABCs of pesticide toxicology: amounts, biology, and chemistry. Toxicol Res (Camb). 2017;6(6):755-63.
2. Maden Evd, Wulansari M, Koomen I. Occupational Pesticide Exposure in Vegetable Production: A literature and policy review with relevance to Indonesia. Netherlands: vegIMPACT; 2014.
3. Gangemi S, Miozzi E, Teodoro M, Briguglio G, De Luca A, Alibrando C, et al. Occupational exposure to pesticides as a possible risk factor for the development of chronic diseases in humans (Review). Mol Med Rep. 2016;14(5):4475-88.
4. Yuantari MG, Van Gestel CA, Van Straalen NM, Widianarko B, Sunoko HR, Shobib MN. Knowledge, attitude, and practice of Indonesian farmers regarding the use of personal protective equipment against pesticide exposure. Environ Monit Assess. 2015;187(3):142.
5. Dhananjayan V, Ravichandran B. Occupational health risk of farmers exposed to pesticides in agricultural activities. Current Opinion in Environmental Science & Health. 2018;4:31-7.
6. Goldner WS, Sandler DP, Yu F, Hoppin JA, Kamel F, Levan TD. Pesticide use and thyroid disease among women in the Agricultural Health Study. Am J Epidemiol. 2010;171(4):455-64.
7. Khan K, Ismail AA, Abdel Rasoul G, Bonner MR, Lasarev MR, Hendy O, et al. Longitudinal assessment of chlorpyrifos exposure and self-reported neurological symptoms in adolescent pesticide applicators. BMJ Open. 2014;4(3):e004177.
8. Ventura C, Nieto MR, Bourguignon N, Lux-Lantos V, Rodriguez H, Cao G, et al. Pesticide chlorpyrifos acts as an endocrine disruptor in adult rats causing changes in mammary gland and hormonal balance. J Steroid Biochem Mol Biol. 2016;156:1-9.
9. Shrestha S, Parks CG, Goldner WS, Kamel F, Umbach D, Ward M, et al. Pesticide Use and Incident Hypothyroidism in Pesticide Applicators in the Agricultural Health Study. Environ Health Perspect. 2018;126(9):1-12.
10. Li J, Ren F, Li Y, Luo J, Pang G. Chlorpyrifos Induces Metabolic Disruption by Altering Levels of Reproductive Hormones. J Agric Food Chem. 2019;67(38):10553-62.
11. Damalas CA, Koutroubas SD. Farmers' Exposure to Pesticides: Toxicity Types and Ways of Prevention. Toxics. 2016;4(1).
12. Kim KH, Kabir E, Jahan SA. Exposure to pesticides and the associated human health effects. Sci Total Environ. 2017;575:525-35.
13. Machado SC, Martins I. Risk assessment of occupational pesticide exposure: Use of endpoints and surrogates. Regul Toxicol Pharmacol. 2018;98:276-83.
14. Dosemeci M, Alavanja MC, Rowland AS, Mage D, Zahm SH, Rothman N, et al. A quantitative approach for estimating exposure to pesticides in the Agricultural Health Study. Ann Occup Hyg.

2002;46(2):245-60.

15. Seesen M, Lucchini RG, Siriruttanapruk S, Sapbamrer R, Hongsibsong S, Woskie S, et al. Association between Organophosphate Pesticide Exposure and Insulin Resistance in Pesticide Sprayers and Nonfarmworkers. Int J Environ Res Public Health. 2020;17(21).
16. Aguilar-Garduno C, Blanco-Munoz J, Roxana Antonio K, Escamilla-Nunez C, Juarez-Perez CA, Schilmann A, et al. Occupational predictors of urinary dialkyl phosphate concentrations in Mexican flower growers. Int J Occup Environ Health. 2017;23(2):151-9.
17. Koureas M, Tsakalof A, Tzatzarakis M, Vakonaki E, Tsatsakis A, Hadjichristodoulou C. Biomonitoring of organophosphate exposure of pesticide sprayers and comparison of exposure levels with other population groups in Thessaly (Greece). Occup Environ Med. 2014;71(2):126-33.
18. Macfarlane E, Carey R, Keegel T, El-Zaemay S, Fritschi L. Dermal exposure associated with occupational end use of pesticides and the role of protective measures. Saf Health Work. 2013;4(3):136-41.
19. Barron Cuenca J, Tirado N, Vikstrom M, Lindh CH, Stenius U, Leander K, et al. Pesticide exposure among Bolivian farmers: associations between worker protection and exposure biomarkers. J Expo Sci Environ Epidemiol. 2020;30(4):730-42.
20. Lu JL. Ergonomic and health assessment of farmers' multi-pesticide exposure. Ergonomics SA. 2017;29(1).
21. Sharifzadeh MS, Abdollahzadeh G, Damalas CA, Rezaei R, Ahmadyousefi M. Determinants of pesticide safety behavior among Iranian rice farmers. Sci Total Environ. 2019;651(Pt 2):2953-60.
22. Okonya JS, Kroschel J. A Cross-Sectional Study of Pesticide Use and Knowledge of Smallholder Potato Farmers in Uganda. Biomed Res Int. 2015;2015:759049.
23. Kapeleka JA, Sauli E, Sadik O, Ndakidemi PA. Biomonitoring of Acetylcholinesterase (AChE) Activity among Smallholder Horticultural Farmers Occupationally Exposed to Mixtures of Pesticides in Tanzania. J Environ Public Health. 2019;2019:3084501.
24. Lermen J, Bernieri T, Rodrigues IS, Suyenaga ES, Ardenghi PG. Pesticide exposure and health conditions among orange growers in Southern Brazil. J Environ Sci Health B. 2018;53(4):215-21.
25. Garrigou A, Laurent C, Berthet A, Colosio C, Jas N, al. e. Critical review of the role of PPE in the prevention of risks related to agricultural pesticide use. Safety Science, Elsevier. 2020;123 pp.104527.
26. Callahan CL, Hamad LA, Olson JR, Ismail AA, Abdel-Rasoul G, Hendy O, et al. Longitudinal assessment of occupational determinants of chlorpyrifos exposure in adolescent pesticide workers in Egypt. Int J Hyg Environ Health. 2017;220(8):1356-62.
27. Damalas CA, Koutroubas SD. Farmers' behaviour in pesticide use: A key concept for improving environmental safety. Current Opinion in Environmental Science & Health. 2018;4:27-30.
28. Geleta DH, Alemayehu M, Asrade G, Mekonnen TH. Low levels of knowledge and practice of occupational hazards among flower farm workers in southwest Shewa zone, Ethiopia: a cross-sectional analysis. BMC Public Health. 2021;21(1):232.

29. Li J, Dong L, Tian D, Zhao Y, Yang H, Zhi X, et al. Association between pesticide exposure intensity and self-rated health among greenhouse vegetable farmers in Ningxia, China. PLoS One. 2018;13(12):e0209566.
30. Schilmann A, Lacasana M, Blanco-Munoz J, Aguilar-Garduno C, Salinas-Rodriguez A, Flores-Aldana M, et al. Identifying pesticide use patterns among flower growers to assess occupational exposure to mixtures. Occup Environ Med. 2010;67(5):323-9.