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Volume 17
Issue 1 *February*

Article 5

2-28-2022

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Aditya Pawitra
Department of Environmental Health, Faculty of Public Health, Universitas Airlangga, Surabaya, Indonesia, aditya.pawitra@fkm.unair.ac.id

Khuliyah Candraning Diyanah
Department of Environmental Health, Faculty of Public Health, Universitas Airlangga, Surabaya, Indonesia, k.c.diyanah@fkm.unair.ac.id

Mohd Talib Latif
1) Department of Environmental Health, Faculty of Public Health, Universitas Airlangga, Surabaya, Indonesia 2) Faculty of Science and Technology, Universiti Kebangsaan Malaysia, Selangor, Malaysia, talib@ukm.edu.my

Beni Hari Susanto
Department of Environmental Health, Faculty of Public Health, Universitas Airlangga, Surabaya, Indonesia, beni.hari.susanto-2017@fkm.unair.ac.id

Muhammad F D Lusno
Department of Environmental Health, Faculty of Public Health, Universitas Airlangga, Surabaya, Indonesia, faridlusno@fkm.unair.ac.id

Recommended Citation

Pawitra A , Diyanah KC , Latif MT , et al. Increased Thyroid Hormone Levels in Pesticide Sprayer at Agricultural Area. *Kesmas*. 2022; 17(1): 10-16
DOI: 10.21109/kesmas.v17i1.5487
Available at: https://scholarhub.ui.ac.id/kesmas/vol17/iss1/5

Pawitra, *et al. Kesmas: Jurnal Kesehatan Masyarakat Nasional (National Public Health Journal)*. 2022; 17 (1): 10-16
DOI: 10.21109/kesmas.v17i1.5487

Kesmas: Jurnal Kesehatan Masyarakat Nasional (National Public Health Journal)

Increased Thyroid Hormone Levels in Pesticide Sprayer at Agricultural Area

Aditya Sukma Pawitra[1*], Khuliyah Candraning Diyanah[1], Mohd Talib Latif[1,2], Beni Hari Susanto[1], Muhammad F D Lusno[1]

[1]Department of Environmental Health, Faculty of Public Health, Universitas Airlangga, Surabaya, Indonesia, [2]Faculty of Science and Technology, Universiti Kebangsaan Malaysia, Selangor, Malaysia

Abstract

Pesticides used massively in the agricultural sector would cause many poisoning and serious health problems. Organophosphate pesticides have been identified as endocrine-disrupting chemicals. This study aimed to compare thyroid hormone levels between the sprayers chronically exposed to pesticides and the control respondents who had never been exposed to pesticides. This study was an analytical observational with a cross-sectional design. The total number of respondents was 150, 50 as sprayers and 100 as control respondents. The venous blood samples were examined using the Enzyme-Linked Immunosorbent Assay (ELISA). The findings significantly showed that the sprayer had a higher level of thyroid-stimulating hormone (TSH) (4.776 ± 1.1166), lower triiodothyronine (T_3) (108.822 ± 18.810), and lower thyroxine (T_4) (7.808 ± 1.067). Determinant factors among sprayers that significantly correlated to TSH levels was age (p-value = 0.006); work duration (p-value = 0.000); personal protection equipment (PPE) (p-value = 0.045); body position (p-value = 0.014); type of pesticides (p-value = 0.004), correlated with T_3 levels was age (p-value = 0.037); body position (p-value = 0.045), correlated with T_4 levels was age (p-value = 0.000); PPE (p-value = 0.045). It could be concluded that chronic organophosphate exposure would increase TSH and decrease T_3 and T_4.

Keywords: endocrine-disrupting chemicals, health risks, thyroid-stimulating hormone, T_3, T_4

Introduction

Chemical pesticides used massively in the agricultural sector are increasingly undeniable and unstoppable, especially in developing countries. The Food and Agriculture Organization (FAO) of the United Nations showed data from 1990 until 2017, the worldwide use of pesticides was increased by 2.01 million tons.[1] Pesticide kill pests and unwanted plants that potentially damage the agricultural product applied throughout the planting season.[2] The high demand for fruits and vegetables with perfect physical condition causes farmers to have no choice other than to use pesticides all over time. Furthermore, worldwide chemical pesticides usage in large quantities for lasting decades impacted human health and the environment.[3-6]

Organophosphate pesticides have been reported as endocrine disruptors chemicals affecting many organ systems.[7,8] A comparison study in conventional and organic farmers in Thailand showed that conventional farmers have thyroid-stimulating hormone (TSH) levels of 1.6 times higher than organic farmers. Some herbicides have a significant relationship between the doses and increased thyroid hormone.[9] Another study in pregnant women who lived in a floricultural area of Mexico showed their TSH was affected when those husbands had an occupation involving contact with pesticides.[10] In a cross-sectional study in Brazil, cumulative exposure to pesticides can affect thyroid function and cause hypothyroidism, especially in men.[11]

Batu City is in a mountainous area with fertile land, good quality water, fresh air, and the right temperature made it suitable for agriculture activities and has long been known as one of the best fruits and vegetable producing regions in Indonesia. The planting period from June to September causes the use of increasing pesticides. Indonesia's fruit and vegetable plant area is 11,697,807 Ha, East Java 1,121,448 Ha, and Batu City is 15,258.09 Ha.[12,13] The physical characteristics of horticultural products, primarily fruits and vegetables that are easily damaged and take place, require visual quality-based requirements such as size, color, smell, and freshness. They tend to overuse pesticides to secure their products.

Factually, most farm sprayers do not use adequate personal protective equipment (PPE) to protect their

***Correspondence*:** Aditya Sukma Pawitra, Department of Environmental Health, Faculty of Public Health, Universitas Airlangga, Surabaya 60115, Indonesia, E-mail: aditya.pawitra@fkm.unair.ac.id, Phone: +62 812-3233-4894*

Received : November 22, 2021
Accepted : January 14, 2022
Published: February 25, 2022

bodies from chemical pesticides exposure. Sometimes they also use pesticide doses that are not according to the rules and do not use the correct spraying method to kill pests fastly. This condition is hazardous to cause acute and chronic poisoning among sprayers. Moreover, some of the pesticides used are identified as systemic poisons that can interfere with hormone production in the body, and they do not realize there are side effects from it. This study aimed to analyze a comparison in thyroid hormone levels, including TSH, T_3, and T_4, between the sprayer pesticides that were chronically exposed to pesticides and the respondents that had never been exposed to pesticides. Thus the local government can take preventive action so that the level of pesticide poisoning can be minimized.

Method

This study was an observational analytic with a cross-sectional design. Data were collected simultaneously and conducted on agricultural areas during planting season from September 2018 to February 2019. Male respondents were chosen using simple random sampling with a proportion of 1:2 between two groups of respondents. The total number of respondents was 150 and originated from two different populations. Fifty male active pesticides sprayers participated as exposed respondents from fruit plantations. Simultaneously, 100 male workers were nonexposed respondents from the same area with similar sociodemographic status. It was ensured that nonexposed respondents never contacted pesticides in agriculture. Respondents who had never received high doses of iodine capsules in the last five years were particular inclusion criteria.[14] While the exclusion criteria for respondents who suffered from chronic diseases and complications.[15]

Data collection was done through interviews, observations, and laboratory examinations. Serum of TSH, T_3, T_4, and age variables were taken from both types of respondents. Simultaneously, the additional data taken from exposed respondents were work duration, the use of PPE, body position when spraying, and the type of pesticides used in the last three months. The laboratory would test serum of TSH, T_3, and T_4. Data of age, work period, and length of work were taken using a questionnaire. While PPE, body position, and type of pesticides have been taken using the observational form. Variable of body mass index (BMI), alcohol intake, smoking, stress level were excluded from this study because from preliminary study showed no variants between respondents.

Venous blood samples were taken as much as 5 mL by laboratory medical analyst staff, both exposed and nonexposed respondents. Blood samples that have been taken immediately poured into a vacutainer tube for prevented blood clotting before centrifugation. Each tube would be labeled with specific information from the respondent and transferred into the laboratory. Blood samples were centrifuged at the temperature room at 4,000 rpm/10 minutes to take the serum. Before proceeding with the assay, all reagents, serum reference calibrators, and controls were let at room temperature (20-27°C). The microplate wells for each serum calibrator, control, and patient specimen were assayed in duplo. Any unused microwell strips were replaced back into the aluminum bag, sealed, and stored at 2-8°C. Then, pipette 0.025 mL (25 μL) of the appropriate serum specimen into the assigned well for fT_4 (pipette 0.050 mL (50 μL) for fT_3, and pipette 0.025 mL (25 μL) for TSH). Next, 0.050 mL (50 μL of Enzyme Reagent fT_4 or fT_3 was added to the appropriate wells (for TSH, add 0.100 mL (100 μL) of TSH Enzyme Reagent). The microplate was swirled gently for 20-30 seconds to mix and cover and added 0.050 mL (50 μL) of biotinylated x-fT_4 or (x-fT_3) reagent to the appropriate wells (for TSH, this step could be skipped). The microplate was swirled gently for 20-30 seconds to mix and cover, then incubated for 60 minutes at room temperature. The contents of the microplate were discarded by decantation or aspiration. If decanting, blot the plate dry with absorbent paper, and add 0.350 mL (350 μL) of wash buffer. Repeat two (2) additional times for a total of three (3) washes using an automatic or manual plate washer, and follow the manufacturer's instruction for proper usage. If a squeeze bottle is occupied, fill each well by pressing the container (avoiding air bubbles) to dispose of the wash. Decant the wash and repeat two (2) additional times. Lastly, 0.100 mL (100 μL) of substrate solution was added to all wells. It is important to always add reagents in the same order to minimize reaction time differences between wells. The examination of serum concentration levels from TSH, T_3, and T_4 used the ELISA technique.[16]

Data were analyzed using the IBM SPSS Statistics 23. Respondent data with a ratio scale were first be tested for normality using Kolmogorov-Smirnov, such as TSH, T_3, and T_4. The data showed was not normally distributed, then it would be followed by Mann-Whitney analysis to find out the differences between two groups of respondents. A linear regression analysis test with dummy variables were performed to determine the factors influencing the variation of hormones in exposed respondents.

Results

The serum TSH levels, T_3, and T_4, in the two groups of respondents were statistically tested whether it could be seen that there were significant differences, as shown in Table 1. Differences in serum levels between exposed and nonexposed respondents showed significant statistical test results with p-values (0.000) < 0.05. The serum TSH levels of the exposed respondent had significantly higher means, whereas serum T_3 and T_4 had lower means levels.

The Table 2 of risk factors in the exposed respondents: 24 respondents age was more than 50 years old, 24 respondents had worked for 5-10 years, 25 respondents used simple PPE that did not meet the requirements, 32 respondents did not adjust the positioning body with the wind direction when spraying pesticides, and 25 respondents use organophosphate pesticides. The statistically tested factors significantly influenced increasing TSH levels and decreasing T_3 and T_4 in respondents exposed to pesticides shown in Table 3.

Analytic statistical test of risk factors for serum TSH, T_3, and T_4 levels in the exposed group showed in Tables 3, age had a significant effect on all serum levels, work duration had a significant impact on serum TSH levels, the use of inappropriate PPE affected the serum TSH levels, and T_4 the body's adjustment to the wind direction affects the levels of TSH and T_3, and the type of pesticide used affects the serum TSH level.

Discussion

Pesticides play an essential role and are extensively used in modern agricultural systems worldwide. By 2020, global pesticide usage is estimated at approximately 3.5

Table 1. Descriptive and Analytical Statistics of Thyroid-Stimulating Hormone, T_3, and T_4 Levels from Exposed and Nonexposed Respondent

Group	Category	TSH (µIU/mL)	T_3 (ng/dL)	T_4 (µg/dL)
Exposed respondent (n = 50)	Mean	4.776±1.1166	108.822±18.810	7.808±1.067
	Maximum	6.8	146.2	9.6
	Minimum	2.3	82.5	5.5
Nonexposed respondent (n = 100)	Mean	3.504±0.971	146.302±18.635	9.955±1.136
	Maximum	5.2	182.5	11.9
	Minimum	1.5	109.4	8.2
p-value		0.000*	0.000*	0.000*

Notes: *) Significant level (p-value<0.05), TSH = Thyroid-Stimulating Hormone, T_3 = Triiodothyronine, T_4 = Thyroxine

Table 2. Distribution Frequency of Risk Factor on Active Pesticide Sprayers

Risk Factor	Category	n	%
Age (years old)	<30	8	16
	31-50	18	36
	>50	24	48
Work duration (years)	<5	5	10
	5–10	24	48
	>10	21	42
Personal protective equipment (PPE)	Full coverage body	6	12
	Simple and meet the requirement	19	38
	Simple and did not meet the requirement	25	50
Body position	Adjusted with wind direction	18	36
	Not adjusted with wind direction	32	64
Type of pesticides	Non-Organophosphate	25	50
	Organophosphate	25	50

Table 3. A Linier Regression Test for Determinant Factor with Level Thyroid-Stimulating Hormone, T_3, and T_4 on Active Pesticide Sprayers

Determinant Factor	Category	TSH (µIU/mL)	T_3 (ng/dL)	T_4 (µg/dL)
Age	p-value	0.006*	0.037*	0.000*
	Standardized coefficient	0.216	-0.289	-0.526
Work duration	p-value	0.000*	0.692	0.399
	Standardized coefficient	0.429	-0.066	-0.130
Personal protective equipment (PPE)	p-value	0.045*	0.990	0.045*
	Standardized coefficient	0.127	-0.002	-0.277
Body position	p-value	0.014*	0.045*	0.646
	Standardized coefficient	0.211	-0.307	-0.462
Type of pesticides	p-value	0.004*	0.206	0.386
	Standardized coefficient	0.224	-0.169	-0.107

Notes: *) Significant level (p-value<0.005), TSH = Thyroid-Stimulating Hormone, T_3 = Triiodothyronine, T_4 = Thyroxine million tons, where China is the top, followed by the USA and Argentina. Farmers use pesticides to prevent planthopper pests and improve the quality of agricultural products. Many pesticides cause acute, chronic poisoning, and death in developing countries as toxic chemicals.[17-19] Poisoning of pesticides mainly occurs during preparation and application, such as mixing, loading, spraying, and cleaning the equipment. Hence, the agricultural workers mostly got chronic poisoning because they were repeatedly exposed to adverse health effects and death.[20,21] The study in Batu City in 2019 showed that some sprayers had decreased their hemoglobin levels.[22] Also, some pesticides are classified as Endocrine Disruptor Pesticides, which would disrupt all the human body's hormonal system and genome activity; in specific periods, it damages organs and tissues that play major carcinogenesis for an extended period.[23-25]

Globally, an estimated 1.8–2.2 billion people are at risk of exposure to pesticides from the agricultural sector. The highest potential for pesticide poisoning is formulators and sprayers because they are at increased risk since they handle pesticides, toxic chemicals, toxic solvents, and inert carriers.[21,26] Some studies to predict pesticide exposure using the Agricultural Operator Exposure Model (AOEM) on formulators and sprayers has been shown that more than 50% of respondents have exceeded the Acceptable Operator Exposure Level (AOEL) for daily exposure, this caused increased health risks due to accumulation of active ingredients of pesticides, especially organophosphate pesticides.[27,28]

This study found that the exposed pesticides respondent had a mean level of serum TSH significantly higher than the nonexposed respondent. In contrast, the mean level of serum T_3 and T_4 was significantly lower in exposed respondents, as shown in Table 1. Some studies previously documented in pesticides sprayer and farmers that certain herbicides, fungicides, and insecticides are thyroid disruptors, which had different impacts on the rest of the population.[28-30] This study controlled several variables that could affect serum thyroid hormone levels, such as iodine tablet consumption and a history of chronic disease. It could be ascertained that differences in serum levels of thyroid hormone between the two groups are indeed caused by exposure to pesticides. The same results were shown in a study in Iran conducted on 40 sprayers and 20 controls by controlling variable chronic disease, alcohol consumption, and diabetes status.[31] The thyroid hormone production is through a series of peroxidation reactions that require iodide, hydrogen peroxide, thyroid peroxidase enzymes, and iodine acceptor proteins.[32] Thyroid peroxidase enzyme (TPO) was essential key to producing or synthesizing TSH, T_3, and T_4 and major autoantigen in autoimmune thyroid diseases.[33] The TSH measurement was very useful for evaluating thyroid function. Next, measurements such as T_3 and T_4 will complete the diagnosis of thyroid disorders. This study could be classified as the exposed respondent to be hypothyroidism or hyperthyroidism.

The field observations showed that respondents used organophosphate, carbamate, and pyrethroid pesticides. They used pesticides in various active ingredients: mancozeb, heptachlor, aldicarb, chlorpyrifos, cypermethrin, and dichlorvos. Some results of the biomarker study showed that mancozeb is classified as an anti-TPO chemical; thereby, they would consider the changeability of follicular cells that reduce T_3 and T_4 production in humans even at sufficient iodine concentration.[34] The study review results also showed that heptachlor, aldicarb, chlorpyrifos, cypermethrin, and dichlorvos were included in the list of endocrine disruptor pesticides, which might disrupt progesterone, estrogen, and androgen activity.[35] Most sprayers and formulators in this study were not aware of the health hazards of the toxicity of pesticide poisoning. They stated that the pesticide used was the most widely used hereditary and proven effective in driving out planthopper pests and would continue it for the next planting period.

This study also calculated the potential risk of several factors expected to influence thyroid hormone synthesis in the sprayer and formulator body. As shown in Table 3, all the risk factors analyzed with statistical tests correlate significantly with the synthesis of thyroid hormones such as TSH, T_3, and T_4. Positive correlations occurred at serum TSH levels, whereas negative correlations at T_3 and T_4 levels showed in the linear regression test. Increased respondents' age, longer duration of work, use of PPE that did not meet requirements, body positions that did not adjust to wind direction, and organophosphate pesticides would increase TSH levels in the body and cause T_3 and T_4 levels to decrease. This result was in line with research conducted on 122 greenhouse workers in Danish that in the spring or planting season, the mean of TSH levels increased while T_3 and T_4 levels decreased; it was caused plants need more pesticide intake.[36] This case was also shown in Brazil's agricultural population that their thyroid hormone increased in the peak of planting season.[11] This study's sprayers and formulators said they worked almost every day because they had to spray pesticides on several plantations. When it is close to the harvest period, it should be sprayed more frequently to maintain the fruits and vegetable quality. It could be ensured that pesticides are highly exposed to their body almost every day.

Statistical analysis in this study showed that the increase of the exposed respondent's age was significantly correlated and impacted increasing TSH levels by 0.216, decreasing T_3 by 0.289, and T_4 by 0.526. This result was supported with analysis using Agricultural Health Study data at 22,246 male sprayers showed that participants without thyroid disease, those in each thyroid disease category, were more likely to be older with an average age of 45.6±12 years.[37] A similar study also showed that age molecular disease (AMD) was positively associated with thyroid function (OR = 7.9) in sprayer pesticide cases.[38] The respondents in this study said they had consistently worked as a pesticide sprayer since they were young; therefore, it would simultaneously extend their working duration. Statistical analysis showed that the work duration would significantly be increasing TSH levels by 0.429. This work duration indicates that the respondent has been chronically exposed to pesticides.

Experience and knowledge are needed to protect the body from these chemicals in applying pesticides. Body adjustment to the wind direction does require experience and awareness of each sprayer. Investigation of the respondents showed that they do not consider wind direction. This study found that it was statistically proven that the proper adjustment of the sprayer's body position while avoiding the drift of pesticides was a protective factor in reducing the dose of pesticides absorbed in the body. This result was in line with the study in Ghana that the majority of sprayer disregards drifts of pesticides towards the body, including their face when wind blowing.[4] The pesticide spraying protocol states that it must avoid sensitive areas of the body from pesticide drifts and stop immediately when the wind is not constant and not assured.[39]

Some respondents said that using complete PPE when spraying would put excessive strain and reduce the movement's effectiveness. They tend to use improvised personal protective equipment. Further investigation showed that in the middle of the spraying process, respondents removed the PPE portion because they felt it was too hot. As is known, there are three main pathways for the entry of pesticides into the human body, including skin contact, ingestion, and inhalation.[20] Previous studies showed a significant correlation between using the appropriate PPE and acute poisoning.[40] Furthermore, wearing four or more PPE had a lower prevalence of acute poisoning.[4,41] One of the last defenses in preventing the entry of toxic chemicals into the body was to use an appropriate PPE that covers the entire toxicant pathway.

Conclusion

The conclusion from this study that the significant difference in the sprayer has a higher level of thyroid-stimulating hormone (TSH) (4.776±1.1166), lower triiodothyronine (T_3) (108.822±18.810), and lower thyroxine (T_4) (7,808±1.067) compare to the respondents that had never been exposed to pesticides. This health risk is faced by pesticide sprayers who work daily in the agricultural area, mainly fruit plantations. The linear regression result test shows that the determinant factors that strongly influence TSH, T_3, and T_4 in pesticides sprayer include age, work duration, personal protective equipment, sprayer body position, and type of pesticide. Based on this study's results, the authors recommend that groups constantly exposed to pesticides use personal protective equipment that meets the requirements and pay attention to all good practices in pesticide application. The authors also suggest farmer groups as community organizations that oversee farmers and sprayers to conduct coaching and share experiences among members routinely.

Abbreviations

FAO: Food and Agriculture Organization; TSH: Thyroid-Stimulating Hormone; T_3: Triiodothyronine; T_4: Thyroxine; Ha: Hectare; mL: milliliter; PPE: Personal Protective Equipment; BMI: Boddy Mass Index; ELISA: Enzyme-linked immunosorbent assay; rpm: Revolutions per Minute; ng/dl: nanograms per deciliter; µIU/mL: micro-international units per milliliter; µg/dL: micrograms per deciliter; USA: The United States of America; AOEM: Agricultural Operator Exposure Model; AOEL: Acceptable Operator Exposure Level; TPO: Thyroid Peroxidase; AMD: Age Molecular Disease; OR: Odds Ratio.

Ethics Approval and Consent to Participate

Respondents received detailed explanations for rights and obligations when participating in this study. Without pressure from the research team, respondents who agreed participated in giving their informed consent before blood specimen collection and interviews. The Ethics Committee granted ethical approval from the Faculty of Public Health, Universitas Airlangga, with number 227/HRECC.FODM/V/2019.

Competing Interest

The author declares that there are no significant competing financial, professional, or personal interests that might have affected the performance or presentation of the work described in this manuscript.

Availability of Data and Materials

The datasets used and analyzed during the current study are available in the authors' internal database. Please contact the corresponding author to get the data.

Authors' Contribution

ASP contributed to analyzing and writing subchapter abstracts and discussion, KCD contributed to data collection, plotting data, and writing subchapter introduction and methods, while MTL contributed to all reviews of this manuscript. BHS and MFDL contributed to preparing instruments collecting data, and writing subchapter results and conclusions.

Acknowledgment

Universitas Airlangga funded this study through The Annual Budget Activity Plan Universitas Airlangga year 2018. The authors want to thank the respondents who have voluntarily participated, the Batu City Government that support this study, and the enumerators who have

collected data.

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