

# REVIEW ARTICLE

## Health Risk of Pesticides Exposure among Workers: A Review

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### ABSTRACT

Pesticides are intended to control both pests and weeds. Pesticide exposure is inevitable to the workers that use pesticides in their work. Exposure to pesticides is harmful to the workers' health physically and mentally. The exposure to pesticides can be short-term, intermediate repeated, and long-term repeated via eye contact, inhalation, ingestion, dermal, or injection. The human health risk assessment method is endorsed by the US Environmental Protection Agency (USEPA) intended to assess human health from exposures. Various types of pesticide exposure can increase the health risk. Thus, this study aimed to review the possible health risk occurred upon exposure to pesticides either directly or indirectly worldwide. Related works of the literature search were done using Science Direct, Google Scholar, PubMed, and Mendeley to review some articles related to the health risk of pesticides exposure which was published between the years 2002 to 2021. Respiratory cases and cancer have already been linked to pesticides exposure. The practical control measures are proper handling of pesticides and proper usage of personal protective equipment (PPE) to minimize or avoid the contact altogether.

**Keywords:** Pesticides, Health risk, Respiratory, Cancer, Tumour

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### INTRODUCTION

United Nations states that the current human population is at 7.7 billion in 2021 and is estimated to grow to around 8.5 billion in 2030 (1). As a result, the food demand worldwide would also be expected to increase together with the usage of pesticides and their exposure to agricultural workers. Pesticides are intended to control both pests and weeds in various applications (2). The US Environmental Protection Agency (USEPA) stated pesticides are substances used to manage both pests and weeds. (3,4). According to the World Health Organization (WHO), pesticides are chemical

compounds used to kill pests; including rodents, fungi, insects, and unwanted plants (weeds). In public health, pesticides are used to kill vectors of disease, such as mosquitoes, while their use in agriculture is focused to kill crop-damaging pests (5). Extensive use of pesticides has been revealed to raise the risk of cancer, neurological and birth abnormalities (6).

Pesticides are classified according to the organisms they are meant to kill such as herbicides, insecticides (organophosphates (OPs), neonicotinoids, pyrethroid, organochlorines, carbamates, and pyrethroids), fungicides, bug sprays, pediculicides, and rodenticides, for the physical state (vaporous fumigant), and chemical arrangement such as natural, inorganic, engineered, or organic (biopesticides) (7). Organophosphates are classified based on their chemical classifications while acaricides are classified based on their target effect;

or by their biochemical mode of action (MoA) (8). In addition, organophosphates and carbamates act as acetylcholinesterase (AChE) inhibitors, disrupting nerve impulse transmission at the synaptic level. Besides, pyrethroids act on the voltage-gated sodium channels in cell membranes to disrupt the Na<sup>+</sup> ion flux. Moreover, the neonicotinoids are neurotoxic, resulting in paralysis and the death of insects (9).

Dermal, oral, eye, and respiratory pathways (inhalation) are regular pathways for pesticides to enter the human body. There are 3 types of pesticide exposure and their health effects namely; short-term (oral, dermal, inhalation exposure, eye discomfort, skin irritation, skin sensitization, and neurotoxicity), intermediate repeated (oral, dermal, inhalation, nerve system damage over a longer period of 30–90 days), and long-term repeated (prolonged and repeated exposures such as chronic non-cancer and cancer effects) via eye contact, inhalation, ingestion, dermal, or injection (10). The short-term effects of pesticide exposure are shown where the frequency of pesticide application in the previous three days and the previous 4–10 days on health indicators. Short-term health effects included alterations in complete blood count, hepatic and renal functions, and nerve conduction velocities and amplitudes. Long-term pesticide exposure was found to be associated with increased abnormality of nerve conduction, especially in sensory nerves. It also affected a wide spectrum of health indicators based on blood tests and decreased the tibia nerve compound muscle action potential amplitudes.

Dermal exposure is the most common route of exposure due to dermal assimilation and absorption process from exposure of large residue of pesticides from the procedure of spill, sprinkle, spray drift, during mixing, stacking, arranging, and cleaning (2,10). Duration of exposure, temperature, skin moist, types of pesticides, and individual resistance was the cofounding factors that can be affecting the pesticides' physicochemical properties and their abilities to be assimilated through the skin (11,12). Furthermore, exposure through oral ingestion during spraying and transferring to other unlabelled containers or food vessels could cause serious poisoning to the workers (13). Besides, the potential for respiratory introduction is extraordinary due to the presence of unstable constituents in pesticides. Breathing in adequate amounts of pesticides could harm nose, throat, and lung tissues (14,15). Furthermore, eye tissues damage could also happen as a result of exposure. Genuine or even lethal disorder happens when pesticides were captivated by the eyes in sufficient amounts (16). In the case of granular pesticides, their severity to the eyes depends on the mass and weight of individual particles (17). The pellets might skip off vegetation or different surfaces at high speed by application through power equipment enough to cause critical eye harm. Although the scale is comparatively small as compared to spraying huge drops with traditional equipment, nevertheless the

danger of pesticides exposure still exists (18).

## MATERIALS AND METHODS

### Search Strategy

The systematic and comprehensive electronic search was conducted using relevant articles that related to the health risk of pesticides exposure among workers in four digital scientific journal databases which are Science Direct, Google Scholar, PubMed, and Mendeley. The literature search term was executed using keywords such as "pesticide" OR "pesticides exposure" OR "pesticides exposure among workers" OR "health risk" AND "pesticides exposure" published from 2002 to 2021. The articles in the English language were eligible to be included in this review. The eligibility of studies was based on the relevance to the health risk of pesticides exposure among workers.

Besides, the eligibility of studies was based on the relevance to health risk factors, the effect of pesticides exposure, and health outcomes affecting workers. In addition, the screening process of the article was based on the content of the full text and removing duplicates. All the study designs were included in this review. The final review and outcomes writing of all the selected articles based on their inclusion criteria as above. Most of the work associated pesticide exposure with adverse effects, except for work from Weichental et al. 2012 (19) and Burns and Juberg 2021 (20). The former work stated that most of the 32 pesticides examined were not strongly associated with cancer due to rate ratios (RR) and odds ratios (OR) were not that precise, while the latter was not discussed in this work due to the conflict of interest.

## RESULTS

### Study Locations

The studies were conducted in seven countries, USA, Vietnam, France, Brazil, Ethiopia, Thailand and China. All these countries were identified as developing countries except the USA and France.

### Health Risk of Pesticide Exposures

In this review, pesticide exposure can cause various health risks depending on the individual. Pesticide exposure poses a health risk depending on the toxicity of the ingredients as well as the extent of exposure. Pesticides have been linked to several detrimental health effects, which vary depending on the degree and duration of exposure. Pesticides had a wide range of health effects, including mild sensitivity, rashes, respiratory difficulties, neurotoxicity, reproductive issues, and even cancer. In this review, the health risk reported worldwide were respiratory disease of many symptoms, tumor or cancer, and others diseases like minor psychiatric disease (MPD), Parkinson's disease,

nervous system problem, and diabetes. Therefore, the related diseases were then focused on in this review with certain classes of pesticides. Summaries of the health effects due to pesticide exposures among workers worldwide were shown in Table 1.

### Pesticide Exposure and Respiratory Diseases

There were four studies reported the symptom of respiratory disease experienced by the agricultural

workers and farmers that exposed to pesticides including chronic bronchitis, asthma, emphysema, tuberculosis, reduced lung function, cough, chronic cough, shortness of breath, nasal allergies, hay fever, chest tightness, and breathlessness. Two studies from Ethiopia and Brazil stated that cough and shortness of breath were common respiratory diseases symptom. Besides, the study from Southwestern France also reported that pesticides exposure resulted in a brain tumor caused by head

**Table 1 Summary of pesticide exposure and health effects worldwide**

Country, Year	Study design	Workplace/ Occupations	Types of Pesticides	Types of Disease	Types of Health Effects
California USA, 2002 (21)	Case study	Agricultural workers	Insecticides, nematicides, and fungicides	Respiratory disease	Chronic effects, delayed. systemic - Fibrosis of lungs - Progressive respiratory insufficiency
Vietnam, 2006 (22)	Cross-sectional study	Farmers	Herbicides 2,4-dichlorophenoxyacetic acid and 2,4,5-trichlorophenoxyacetic acid	Chronic respiratory diseases	Chronic effects, delayed, systemic - Chronic bronchitis, asthma, emphysema, or tuberculosis
Ethiopia, 2017 (23)	Cross-sectional study	Farmers	Organophosphates, organochlorine, and phosphoglycine	Respiratory disease	Chronic effects, delayed, systemic - Reduced lung function, chronic cough, shortness of breath
Brazil, 2018 (24)	Cross-sectional study	Family farmers	Organophosphates, carbamates, pyrethroids, nitriles, diamides, neonicotinoids, avermectins, and benzimidazole	Respiratory disease	Acute effects and immediate - Cough, nasal allergies,  Chronic effects and delayed - hay fever, chest tightness, and breathlessness
Nakhon Sawan, Thailand, 2020 (25)	Case-control study	Farmers and non-farmer	Herbicides, insecticides, and fungicides	Lung cancer	Chronic effects, delayed and systemic - DNA damage, protein damage, mutagenicity, necrosis, and apoptosis
Brazil, 2021 (26)	Case-control study	Pesticide users	Herbicides and fungicides	Head and neck cancer (HNC)	Chronic effects, delayed and systemic - Lip, oral cavity, nasal and oropharynx cancers - Lymphoma cancer
Southwestern France, 2007 (27)	Case-control study	Pesticide workers	Fungicides 80%	Brain tumor	Chronic effects, delayed and systemic - Head trauma - Had gliomas, meningiomas, neurinomas, and lymphomas - Brain injury and memory impairment

CONTINUED

**Table 1 Summary of pesticide exposure and health effects worldwide. (cont.)**

Country, Year	Study design	Workplace/ Occupations	Types of Pesticides	Types of Disease	Types of Health Effects
United States, 2000 (28)	Cross-sectional study	Pesticides applicators	Chlorpyrifos of 80% fungicides	Brain cancer	<p>Acute effects, immediate and local</p> <ul style="list-style-type: none"> <li>- visual and smell changes</li> </ul> <p>Chronic effects, delayed and systemic</p> <ul style="list-style-type: none"> <li>- changes in nerve conduction velocity, arm or hand tremor, vibrotactile sensitivity</li> </ul>
Southern Brazil, 2014 (29)	Cross-sectional study	Tobacco farmer	Flumetralin, clomazone, neonicotinoids, dithiocarbamate, glyphosate, organophosphate, metalaxyl, sulfentrazone, iprodione, pyrethroids, and triazine	Minor psychiatric diseases (MPD)	<p>Acute effects and immediate</p> <ul style="list-style-type: none"> <li>- Headache or dizziness together with nausea or vomiting</li> </ul> <p>Chronic effects and delayed</p> <ul style="list-style-type: none"> <li>- Depression, anxiety and somatic disorders</li> </ul>
French, 2018 (30)	Cohort study	Agricultural farmers	Fungicides, insecticide, and diquat and paraquat herbicides	Parkinson's disease	<p>Chronic effects, delayed and systemic</p> <ul style="list-style-type: none"> <li>- Degeneration of dopaminergic neurons and pesticide poisoning.</li> </ul>
Thailand, 2018 (31)	Case-control study	Agricultural farmers	Insecticides, herbicides, fungicides, rodenticides, and molluscicides	Diabetes	<p>Chronic effects, delayed and systemic</p> <ul style="list-style-type: none"> <li>- Insulin resistance in fat cells</li> <li>- Higher blood glucose</li> </ul>
China, 2015 (32)	Cohort study	Agricultural farmers	Omethoate, pyrethroid, and organophosphates	Nervous system problem	<p>Chronic effects, delayed and systemic</p> <ul style="list-style-type: none"> <li>- Alterations in complete blood count, hepatic and renal function, and nerve conduction such as velocities and amplitude</li> <li>- Increased abnormality nerve conduction in sensory nerves.</li> </ul>

trauma occur among pesticide workers.

In California USA, a study reported that high toxicity of the fungicides, insecticides, and nematicides affected the respiratory systems of high-exposure groups such as structural pest control operators and farm workers (21). A study in Vietnam stated that veterans who applied Agent Orange (the mixture of two equal parts of the herbicides (2,4,5-trichlorophenoxyacetic acid and 2,4-dichlorophenoxyacetic acid) showed a higher frequency of chronic respiratory diseases, such as asthma, emphysema, chronic bronchitis, or tuberculosis (22). Furthermore, organophosphates (chlorpyrifos), organochlorine (dichlorodiphenyltrichloroethane (DDT), and phosphoglycine (glyphosate) were significantly increased the risk of respiratory disease among Ethiopia farmers. The reported respiratory symptoms were reduced lung function, chronic cough, and shortness of breath (23).

In Brazil, the higher pesticides exposure could affect the farmer's respiratory health. They regularly used 49 pesticides from 31 chemical groups includes organophosphates, nitriles, diamides, neonicotinoids, carbamates, pyrethroids, avermectins, and benzimidazole. Their families also experienced respiratory symptoms due to pesticide exposure such as cough, nasal allergies, hay fever, chest tightness, and breathlessness. These symptoms were reported on the peak during crop seasons and rarely seen during off-seasons (24).

### **Pesticides Exposure and Cancer**

There were two studies which were in Thailand, and Brazil that reported pesticides exposures can cause cancer. Lung cancer was reported among farmers and non-farmers in Thailand while head neck cancer (HNC) was reported among pesticide users in Brazil. Lung cancer was positively associated with the lifetime use of herbicides, insecticides, and fungicides. In an experimental study, pesticide elevated the level of reactive oxygen species (ROS) ROS is an oxygen-containing an unpaired electron, such as hydrogen peroxide, superoxide, and hydroxyl radical, which are highly unstable and may cause DNA damage, protein damage, mutagenicity, necrosis, and apoptosis. Besides, pesticides also increase the risk of cancer via other mechanisms including tumor promotion, epigenetic effects, genotoxicity, hormonal action, and immune toxicity (25).

In addition, pesticide exposure specifically herbicides and fungicides lead to head and neck cancer (HNC) and was found to have a positive association with larynx cancer. Despite the mechanisms being unknown, the increased risk had been linked to the duration of exposure. Smoking, a potential risk was observed to look at the interaction of pesticide-tobacco consumption among heavy smokers (>36 packs/year). The risk could

be reduced with the use of protective equipment and careful handling while the sprinkling of pesticides (26).

In Southwestern France, 80% percent of pesticides used were mainly on fungicides in the vineyard. Pesticide exposures were found to cause brain tumors either directly through spraying or mixing or indirectly in re-entry tasks while performing tasks. Later, it revealed that pesticides also have a potential role in the occurrence of brain tumors. More cases have been reported as compared to control in terms of occupational handling of chemical products, living near power lines, or having a personal history of radiotherapy but no significant difference was found. In addition, fewer cases were reported on using cellular phones or consuming aspartame, and a comparable proportion of cases and controls reported a history of head trauma as compared to control (27).

Chlorpyrifos was also found to cause brain cancer among pesticides applicators (28). A significant exposure-response pattern was found to have an association with cancer incidence relatives among non-exposed applicators. Other symptoms of exposure to chlorpyrifos include changes in nerve conduction velocity, arm or hand tremor, vibrotactile sensitivity, visual and smell changes, or, in other words, neurobehavioral skills, memory issues, emotional states, weariness, and muscle weakness will affect persons. Furthermore, exposure to chlorpyrifos, diazinon, dieldrin, metolachlor, and pendimethalin also increased lung cancer incidence relative among non-exposed applicators. However, fourteen pesticides were not associated with increased the lung cancer incidence in pesticide applicators such as atrazine, captan, carbaryl, chlorothalonil, cyanazine, dichlorvos, S-Ethyl dipropylthiocarbamate (EPTC), fonofos, glyphosate, imazethapyr, malathion, permethrin, phorate, and trifluralin.

### **Pesticides Exposure and Other Diseases**

Pesticide exposure and poisoning can cause other diseases among agricultural workers whereas minor psychiatric disease (MPD), Parkinson's disease, and diabetes were reported among Brazilian farmers, French farmers, and Thai farmers respectively.

Ninety-nine percent of pesticides namely organophosphate, metalaxyl, sulfentrazone, iprodione, flumetralin, clomazone, neonicotinoids, dithiocarbamate, glyphosate, pyrethroids, and triazine were used in the Southern Brazil farms. The pesticides exposures mainly through direct contact, loading and mixing the sprayer tank, contact with leaves, and contact during transportation. The increased risk of minor psychiatric diseases (MPD) was found to be different due to pesticides exposures such as pesticide application and having contact with soaked clothes full of pesticides (29).

In the French agricultural cohort (AGRICAN) studies reported that pesticide usage in agriculture could risk Parkinson's disease. A strong association was found between pesticide usage and the risk of Parkinson's disease due to degeneration of dopaminergic neurons. In addition, a dose-effect relationship was observed between the lifelong use with the active ingredients such as dithiol carbamate fungicides, rotenone insecticide, and the diquat and paraquat. (30).

An in-vivo study among Thai farmers that involved the tissue-culture procedure revealed that fungicide exposure could lead to higher blood glucose and insulin resistance in fat cells. Three types of insecticides namely organophosphate, carbamate, and organochlorine were found to be associated with diabetes. Endosulfan (an organochlorine) and permethrin (a pyrethroid) insecticides were reported to have significant association with diabetes. Furthermore, eight fungicides such as copper sulfate, mancozeb, maneb, metalaxyl, benzilate, carbendazim, thiophanate-methyl, and zineb were also reported to have been positively associated with the occurrence of diabetes. Less protein in the diet, low educational level, and socioeconomic background were found to be risk factors of diabetes (31).

A cohort study among farmers in China demonstrated that pyrethroid and organophosphates exposure adversely affects blood cells, the liver, and the peripheral nervous system (32). Thirteen percent of farmers had suffered from at least one acute health problem during 2009 to 2011 with a large percentage of them also demonstrated abnormalities in hepatic function, renal function, electrolyte balance, and T clinical total neuropathy score (TNSc). Short-term exposure caused changes in total blood count, hepatic and renal function, and nerve conduction parameters like velocities and amplitude while long-term exposure caused raise nerve conduction abnormalities in sensory nerves.

#### Limitation

This work only covered studies published within 20 years (2002-2021) and limited to the six countries. The authors might have missed out on publications in languages other than English.

#### CONCLUSION

In conclusion, pesticide exposures can cause many diseases affecting the health of agriculture workers. Most synthetic pesticides are harmful to human health. The associated health risks are usually respiratory diseases and cancer. Proper handling of pesticides and the usage of personal protective equipment (PPE) are important to minimise contact.

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