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# PESTICIDES EXPOSURE AND HYPERTENSION RISK IN INDONESIAN AGRICULTURE WORKERS: A SYSTEMATIC REVIEW AND META-ANALYSIS

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#### Abstract

Introduction: Agriculture workers exposed to pesticides are at high risk for hypertension, which is known as a cause of cardiovascular disease worldwide. Due to agricultural relevance and pesticides exposure, pesticide use and hypertension have garnered attention. This study investigated pesticide exposure and hypertension risk. Discussion: In line with the PRISMA guidelines, we conducted a systematic review and meta-analysis of cross-sectional studies published between 2015 and 2024. A total of 14 studies from Indonesia focusing on agriculture were selected, representing a variety of geographic areas and research methods. The pooled analysis revealed a prevalence ratio (PR) of 1.64 (95% CI: 1.35-1.99), indicating that farmers exposed to pesticides had a far higher risk of hypertension than those who were not. Long-term exposure, higher doses of pesticides containing active ingredients of commonly used pesticides, such as chlorpyrifos and profenofos, frequent spraying, improper use of personal protective equipment (PPE), age, smoking, and work-related stress all increased risk. Pesticides can affect cardiovascular control through oxidative stress, neuroendocrine disruption, and endocrine disruption, according to global reports. Conclusion: This systematic review and meta-analysis underscores the significant environmental health risks posed by pesticides exposure, particularly its contribution to hypertension among Indonesian agriculture workers. Prolonged exposure, inadequate use of PPE, and poor safety practices exacerbate these risks. The findings highlight the urgent need for stricter environmental health regulations, the implementation of integrated pest management, and improved education on pesticide safety. These measures are essential to protect agricultural workers and reduce pesticide-related health risks in communities.

#### INTRODUCTION

Hypertension commonly referred to as high blood pressure, is one of the most significant factors contributing to cardiovascular disease (CVD) globally and a predominant global risk factor for mortality and disability. The diagnosed population suffering from hypertension (systolic blood pressure ≥140 mmHg, diastolic blood pressure ≥90 mmHg, or receiving treatment) increased twofold from 1990 to 2019, doubled from 650 million adults in 1990 to 1.3 billion adults in 2019 between the ages of 30–79 years worldwide, with nearly half of

those individuals unaware of their condition (1). Thirty-five percent of farmers in Esprito Santo, Brazil, had high blood pressure. This was more common in men (36.6%) (2). High blood pressure was found in 42.0-45.5% of California's Latino farmworkers (3). A meta-analysis of Latino migrant seasonal farmworkers in the US indicated that the prevalence of hypertension varied from 3% to 68% in males and from 3% to 54% in females, with males typically exhibiting higher rates (4).

The national prevalence of hypertension in Indonesia has remained consistently high, with estimates exceeding 34.1% among adults, decreasing to 30.8% in

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2023 (5). The 2023 Indonesian Health Survey results indicate that the prevalence of hypertension among farmers/farm laborers, as diagnosed by a doctor, is 8.1%, while the prevalence based on measurement results is 35.7% (5). The condition is a major risk factor for renal failure, stroke, and CVD, thereby aggravating morbidity and mortality (6-8). Among the numerous environmental and occupational risk factors linked to hypertension, pesticide exposure has gained considerable attention due to its potential contribution to cardiovascular dysfunction (9). This systematic review and meta-analysis is investigating the relationship between environmental exposures, particularly pesticides used in agriculture, and hypertension risk.

Farmers often use pesticides to increase crop yields by eradicating pests, weeds, and fungal infections. Long-term health effects to these kinds of chemicals among agriculture workers like farmers and pesticide applicators have raised significantly (10). One of the adverse health effects due to pesticides exposure namely hypertension, has garnered significant attention. In Indonesia, this health problem is being a priority, where about 30% of the workforce is engaged in agriculture. In addition, pesticide safety regulations are enforced inconsistently.

Pesticides are used a lot in farming, and they contain many different chemicals that have been related to bad health effects, like neurotoxicity. endocrine disruption, and cardiovascular complications (10-11). Farmers are especially at risk since they often come into contact with these harmful compounds by eating, touching, or breathing them in (12-14). Many epidemiological studies demonstrated a relation between long-term exposure to pesticides and high blood pressure. This suggests that pesticides may be involved in the development of hypertension (15-18).

Even though these results are promising, there is currently no complete summary of the effects of pesticide-related hypertension, especially in Indonesia, where pesticides are widely used. Indonesia is mostly an agricultural country, hence it relies on pesticides to boost crop production. The widespread usage of pyrethroids, carbamates, and organophosphates by farmers makes people worry about their health (19). Several studies have shown that agricultural workers were more likely to have high blood pressure. This makes it even more important to look into the link between pesticide exposure and high blood pressure in this community right away (16-17, 20). We still do not know much about how pesticide exposure affects farmers' risk of getting high blood pressure because there have not been many systematic reviews of the evidence that is already out there.

Many studies from around the world have shown how exposure to pesticides can affect heart health and the control of high blood pressure. A study of farm workers in the US found a strong link between exposure to organophosphates and high blood pressure (21). In the same way, studies in China and Brazil have found that agricultural workers who are exposed to pesticides have a higher risk of getting high blood pressure. This supports the idea that these chemicals may cause high blood pressure (16-17, 22).

More and more evidence from Indonesia suggests that exposure to pesticides may be a factor in the high rates of high blood pressure among farmers. Even though these results are interesting, there is not a systematic review that brings together national data on the issue, so more research is needed to strengthen the evidence base. Previous studies have looked at the link between pesticide exposure and high blood pressure on their own, but no thorough systematic review has put together Indonesian epidemiological data to explain this link (23-26).

This study aims to fill this gap by doing a thorough review of the existing literature and including data from a variety of geographical regions in order to accomplish the goal of establishing a more robust knowledge of the issue. These data also reveal a systematic review of the link between pesticide-induced hypertension and the burden of disease in the population. This information could help lawmakers, rules for occupational and environmental health, and ways to keep farm workers safe.

This study also looks at other things that could alter the link between high blood pressure and pesticide exposure, like lifestyle, heredity, and socioeconomic position. The major purpose of this systematic review is to look at national epidemiology data to examine if farm laborers who are exposed to pesticides are more likely to have high blood pressure. The goals of this project are to help individuals understand pesticide-related hypertension better and to help make focused interventions to safeguard the health and well-being of Indonesian farmworkers.

#### DISCUSSION

# Search strategy

This systematic review was undertaken according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) (27). A literature search was performed across five electronic databases: PubMed, ScienceDirect, Scopus, ProQuest, and Google Scholar, covering all publications from 1 January 2015 to 31 December 2024. The search terms used included (pesticide AND hypertension OR high blood pressure)

AND (farmer OR farmworker OR agriculture workers OR pesticide applicator) AND Indonesia. References from the retrieved full-text articles and pertinent reviews were examined to identify further eligible publications. All identified publications were imported into EndNote, and duplicate entries were eliminated.

# Study selection and eligibility criteria

The studies were selected according to specific inclusion criteria: (1) Original articles using a crosssectional study design; (2) Studies investigating various agricultural pesticides and their impact on hypertension; (3) Studies with well-defined pesticide exposure; (4) Studies concentrating on pesticide exposure among farmers, farmworkers, agricultural labourers, and individuals engaged in pesticide formulation or application; and (5) Articles published in peer-reviewed journals from 1 January 2015 to 31 December 2024, with no language restrictions. Exclusion criteria for studies included: (1) Qualitative studies or review articles; (2) Brief reports or conference abstracts; and (3) Studies lacking full text and data availability. Three authors carried out independent assessments of the titles and abstracts. Full texts of potentially suitable articles were subsequently downloaded and screened prior to inclusion in our analysis.

## Quality check and data extraction

Data extraction was done separately by three authors utilizing standardized abstraction forms. The characteristics obtained for each eligible study comprised the authors' names, publication year, country of the study, study population, mean age of participants, types of pesticides used, study design, sample size, study outcomes, p-value, and prevalence ratio (PR), if applicable. Differences in evaluating the quality of the studies were resolved through consensus. The quality of the publications was evaluated by examining the methodological rigour, specifically for observational studies, which includes 8 items specifically for assessing cross-sectional study designs established by the Joanna Briggs Institute (28). Answer each question as "yes", "no", or "unclear". In rare cases, the option "NA" (not applicable) may be appropriate. These eight critical appraisal items from the JBI instrument collectively assess four fundamental domains in an analytical crosssectional study: 1) Clarity of Sampling and Context (Items 1-2); 2) Measurement Validity and Reliability (Items 3-4, 7); 3) Confounding Control (Items 5-6); 4) Statistical Soundness (Item 8) (28).

#### Statistical analysis

A fixed-effects meta-analysis was performed based on the assumption that all included studies estimate a single true underlying effect and share one common effect size (29-30). The published PRs and the 95% confidence intervals (CIs) around were used to estimate the pooled PR. In this meta-analysis study, the PRs of a variable were selected, reported, and classified as pesticide exposure to calculate the pooled PRs.

# Systematic Review for Hypertension Risk Geographic Distribution and Participant Characteristics

A total of 2,254 records were obtained from database searches, consisting of PubMed (n=1), ScienceDirect (n=8), Scopus (n=1), ProQuest (n=64), and Google Scholar (n=2,180). Following the elimination of 17 duplicate entries, a total of 2,237 records were retained for title and abstract screening, and after the screening, 2,201 records were excluded. A total of 36 full-text articles were evaluated for eligibility. In these findings, 22 articles were excluded based on unsuitable study designs, including 11 descriptive studies and 8 qualitative studies, as well as one article with unclear outcomes and two with ambiguous pesticide exposure. In total, 14 pieces of research met the inclusion criteria and were continued for data extraction (Figure 1).

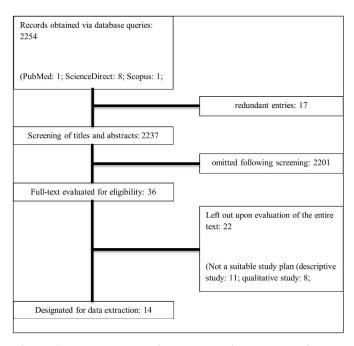


Figure 1. Flowchart showing the selection process of study evaluating the effects of pesticide exposure on hypertension risk in Indonesia

This study reviewed 14 analytical cross-sectional studies conducted across various regions in Indonesia to examine the relationship between pesticide exposure and hypertension among farmers. The selected studies spanned a range of agricultural settings, crop types, and geographic contexts, with studies conducted primarily in Java, Sumatra, and Sulawesi. Overall, the evidence consistently shows a significant association between pesticide exposure and an increased risk of hypertension, with various occupational and behavioral risk factors contributing to this relationship. Table 1 shows the data acquired from these 14 studies, 9 were conducted on Java Island (31-39), 3 on Sumatra Island (26, 40-41),

and 2 on Sulawesi Island (25, 42).

Most studies were conducted on Java Island, with Central Java accounting for the majority, while East Java, West Java, Sumatra (Aceh, Jambi, and Bengkulu), and Sulawesi (Central and Southeast) were also represented. Sample sizes varied widely, ranging from 43 to 354 participants. The majority of study populations consisted of male farmers actively engaged in pesticide application, especially in rice, shallot, vegetable, flower, and coffee farming. Subsequently, age distributions were frequently skewed toward older adult farmers, particularly those aged 45 years and above, who are more likely to have long-term exposure and higher cumulative risk.

Table 1. Flowchart Showing the Selection Process of Study Evaluating the Effects of Pesticide Exposure on Hypertension

Risk in Indonesia		·					
No	Author/ year	Study Design/ Article's quality	Sample	Types of pesticides used	Mean Age of Participants	A significant p-value/ RP/ OR	Study Conclusion
1	Ulfa EF, Darundiati YH, Setiani O, Dewanti NAY /2024(31)	Analytical observational study with a cross-sectional design/ Overall Quality Rating: Moderate Final Score: 6 out of 8	97 Paddy Farmers in Prajegan Village, Sukorejo Sub District, Ponorogo Regency, East Java.	The study examined the use of pesticides but did not specify the exact types	Not explicitly mentioned	<ul> <li>Education level: p = 0.047 (OR = 2.675 (95% CI: 1.105-6.475))</li> <li>Working period: p = 0.023 (OR = 4.164 (95% CI: 1.316-13.178))</li> <li>Pesticide dose: p = 0.002 (OR = 4.200 (95% CI: 1.769-9.972))</li> <li>PPE usage: p = 0.023 (OR = 2.876 (95% CI: 1.238-6.679))</li> </ul>	The study found a significant relationship between hypertension and education level, working period, pesticide dose, and PPE usage.
2	Liem JF, Lumanauw AGE, Sutanti YS, Hudyono J./2023(38)	Analytical observational study with a cross-sectional design/ Overall Quality Rating: Good Final Score: 8 out of 8	90 Pesticide Applicators in Cibodas Village, West Bandung Regency, West Java.	Various pesticides used in agricultural activities but did not specify the exact types	Not explicitly mentioned	<ul> <li>Age &gt; 44 years: p-value = 0.002 (OR = 4.31 (95% CI: 1.68 - 11.04))</li> <li>High daily exposure intensity: p-value = 0.041 (OR = 2.60 (95% CI: 1.04 - 6.52))</li> </ul>	Older age and high daily pesticide exposure intensity are significantly associated with increased hypertension risk.
3	Hidayat CNA, Setiani O, Dewanti NAY, Darundiati YH./ 2023(32)	Analytical observational study with a cross-sectional design/ Overall Quality Rating: Moderate Final Score: 5.5 out of 8	101 Male Shallot Farmers in Wanasari and Jagalempeni villages, Wanasari Sub District , Brebes Regency, Central Java.	Organophosphates (Dursban 200 EC), Carbamates (Tamabas 500 EC, Metindo 40 SP, Larvin 75 WP, Marshal 200 SC), as well as various other insecticides and fungicides	46.16 years (age range: 25–64 years)	<ul> <li>Years of work: p-value = 0.003 (PR = 4.048 (95% CI: 1.650–9.928))</li> <li>Pesticide dosage: p-value = 0.006 (PR = 4.219 (95% CI: 1.578–11.281))</li> <li>Spraying frequency: p-value = 0.007 (PR = 3.581 (95% CI: 1.491–8.602))</li> <li>Use of PPE: p-value = 0.001 (PR = 7.212 (95% CI: 2.516–20.678))</li> </ul>	The study found that 61.4% of respondents experienced hypertension. Significant risk factors included years of work, pesticide dosage, spraying frequency, and the use of personal protective equipment (PPE).

No	Author/ year	Study Design/ Article's quality	Sample	Types of pesticides used	Mean Age of Participants	A significant p-value/ RP/ OR	Study Conclusion
4	Nikmah SS and Pawenang ET./2020(33)	Analytical observational study with a cross-sectional design/ Overall Quality Rating: Moderate Final Score: 6 out of 8	77 Flower Spraying Farmers in Kenteng village, Bandungan Sub-district, Semarang Regency, Central Java.	Not explicitly listed, but categorized as factors influencing hypertension	Not specified in the document	• Knowledge (OR = 7.380 (95% CI: 1.474–36.953)) • Years of service (OR = 3.600 (95% CI: 1.248–10.383)) • Spraying time (OR = 7.347 (95% CI: 2.547–21.189)) • PPE completeness (OR = 2.667 (95% CI: 1.055–6.740))	Farmers' knowledge, length of employment as pesticide sprayers, spraying time, and completeness of personal protective equipment (PPE) are significantly associated with the incidence of hypertension among flower-spraying farmers in Kenteng Village, Bandungan Subdistrict, Semarang Regency.
5	Arifah AS and Wijayanti Y./2023(34)	Analytical observational study with a cross-sectional design/ Overall Quality Rating: Moderate Final Score: 6 out of 8	77 Male Farmers in Campursari Village, Bulu Sub District, Temanggung Regency, Central Java.	Multiple types, including:  Organophosphates Carbamates Dithiocarbamates Neonicotinoids Avermectins Pyrethroids Triazoles Pyrroles Strobilurins Nereistoxins Farmers typically used 1 to 3 mixed pesticides during application.	Not directly stated, but:  • 75.3% (58 out of 77) were aged ≥46 years  • 24.7% were <46 years	<ul> <li>Spraying Time: p-value = 0.010 (PR = 3.913 (95% CI: 1.340– 11.428))</li> <li>Spraying Direction: p-value = 0.004 (PR = 4.063 (95% CI: 1.552–10.632))</li> <li>Use of Personal Protective Equipment (PPE): p-value = 0.009 (PR = 3.675 (95% CI: 1.357–9.952))</li> <li>Pesticide Storage: p-value = 0.030 (PR = 3.200 (95% CI: 1.089–9.404))</li> </ul>	Significant associations were found between hypertension and: • Spraying Time • Spraying Direction • Use of PPE • Pesticide Storage
6	Buana C, Sutriyanti Y, Mulyadi M, Almaini A./2022(26)	Analytical observational study with a cross-sectional design/ Overall Quality Rating: Good Final Score: 7 out of 8	52 Vegetable Farmers in the Sambirejo Public Health Center area, Rejang Lebong Regency, Bengkulu.	The specific chemical types of pesticides are not listed; however, the study discusses combinations of more than two types of pesticides as a variable of interest.	Not specifically stated in the paper.	<ul> <li>Length of time as a farmer (&gt;10 years): p-value = 0.019 (OR = 2.098 (95% CI: 1.04–6.88))</li> <li>Pesticide combination (&gt;2 types): p-value = 0.032 (OR = 2.090 (95% CI: 1.01–5.81))</li> </ul>	The study concludes that there are statistically significant relationships between the length of time working as a farmer (>10 years), pesticide combination (>2 types) and the incidence of hypertension among vegetable farmers in the Sambirejo Health Center area.
7	Nurlaely HS/2023(40)	Analytical observational study with a cross-sectional design/ Overall Quality Rating: Poor Final Score: 3 out of 8	61 Coffee Farmers living in Pante Raya Village, Wih Pesam Sub District, Bener Meriah Regency, Aceh.	Not specified by type (e.g., insecticides, herbicides). The study refers generally to "pesticides," though it mentions that insecticides are commonly used in developing countries like Indonesia.	Not explicitly stated in the article.	• Pesticide use: p-value = 0.000 (OR was not reported in this article)	The study found a strong association between pesticide use and hypertension incidence.

No	Author/ year	Study Design/ Article's quality	Sample	Types of pesticides used	Mean Age of Participants	A significant p-value/ RP/ OR	Study Conclusion
8	Mawaddah RAE, Sugiarto, Kurniawati E./2022(41)	Analytical observational study with a cross-sectional design/ Overall Quality Rating: Moderate Final Score: 5.5 out of 8	61 Vegetable Farmers who conduct pesticide spraying in the working area of Paal Merah II Community Health Center, Jambi City.	Organophosphate group, Insecticides, Fungicides. Many farmers mixed more than two types of pesticides.	The exact mean age is not mentioned.	<ul> <li>Working duration (years of service): p value = 0.046</li> <li>Use of PPE: p value = 0.020</li> <li>Not explicitly stated in terms of OR or prevalence rate.</li> </ul>	Significant associations were found between hypertension and:  • Working duration • Use of PPE
9	Nurkhayati S, Nurjazuli, Joko T./2018(35)	Analytical observational study with a cross-sectional design/ Overall Quality Rating: Moderate Final Score: 6 out of 8	60 Horticulture Farmers in Kapuhan Village, Sawangan Sub District, Magelang Regency, Central Java	Primarily organophosphate insecticides. Brand names: Curacron 500 EC and Dursban 200 EC	• 41 years (range: 20–60 years)	<ul> <li>Years of farming experience:         p-value = &lt;0.0001</li> <li>Pesticide dosage:         p-value = 0.005</li> <li>Pesticide storage practices: p-value = 0.015</li> <li>OR was not reported in this article</li> </ul>	The study found that diastolic blood pressure among horticulture farmers in Kapuhan Village was significantly associated with years of farming experience, pesticide dosage, and pesticide storage practices.
10	Agustina F, Suhartono, Dharminto. /2018(36)	Analytical observational study with a cross-sectional design/ Overall Quality Rating: Moderate Final Score: 6 out of 8	Horticultural Farmers in Gerlang Village, Blado Sub District, Batang Regency, Central Java	Synthetic insecticides, particularly those containing organophosphates and carbamates	Not explicitly stated; inclusion criteria specify age range 41–60 years	<ul> <li>Pesticide Usage Level: p-value</li> <li>= 0.032 (PR =</li> <li>2.222 (95% CI:</li> <li>1.129-4.375))</li> <li>Type of Pesticide: p-value = 0.021 (PR = 2.955 (95% CI: 1.134-7.699))</li> </ul>	Organophosphates and carbamates inhibit cholinesterase enzyme, leading to the accumulation of acetylcholine, which can disrupt blood pressure regulation and potentially cause hypertension.
11	Zulfania KD, Setiani O, Dangiran HL./2017(37)	Analytical observational study with a cross-sectional design/ Overall Quality Rating: Good Final Score: 7.5 out of 8	43 Farmers who work as pesticide sprayers in Sumberejo Village, Ngablak Sub District, Magelang Regency, Central Java	The study doesn't mention specific pesticide names, but general exposure through activities such as mixing, spraying, handling equipment, and post-harvest contact is documented.	40.49 years (range: 24–62 years)	Pesticide exposure (systolic blood pressure): p-value = 0.001 (PR = 4.333 (95% CI: 2.443–7.686)) Pesticide exposure (diastolic blood pressure): p-value = 0.050 (PR = 2.053 (95% CI: 1.488–2.832)) Cholinesterase levels (systolic blood pressure): p-value = 0.041 (PR = 2.925 (95% CI: 1.343–6.370))	Significant associations were observed between:  Pesticide exposure and both systolic and diastolic blood pressures Cholinesterase levels and systolic blood pressure
12	Yuyun W, Irma, Handayani L./2024(42)	Analytical observational study with a cross-sectional design/ Overall Quality Rating: Moderate Final Score: 5.5 out of 8	104 Farmers in Wakoko Village, Pasarwajo Sub District, Buton Regency, Southeast Sulawesi	The study doesn't mention specific pesticide names.	Not explicitly stated, but majority are aged ≥35 years	<ul> <li>Age ≥ 35 years: p-value = 0.000</li> <li>Stress: p-value = 0.006</li> <li>Heavy coffee drinking: p-value = 0.004</li> <li>Smoking: p-value = 0.000</li> <li>High pesticide exposure: p-value = 0.000</li> <li>OR or PR were not explicitly reported in this study.</li> </ul>	This study found statistically significant associations between hypertension and several risk factors among farmers, especially:  • Advanced age • Occupational stress • High frequency of coffee consumption • Smoking habits Exposure to pesticides

No	Author/ year	Study Design/ Article's quality	Sample	Types of pesticides used	Mean Age of Participants	A significant p-value/ RP/ OR	Study Conclusion
13	Salikunna NA, Kurniawan A, Fitriana Y, Ramadhan MZ. (25)	Analytical observational study with a cross-sectional design/ Overall Quality Rating: Moderate Final Score: 5.5 out of 8	80 Paddy farmers in Dolago Padang Village, Central Sulawesi	The exact pesticide names are not specified, but participants used >3 types of pesticides, which include substances known to inhibit cholinesterase (such as organophosphates and carbamates, based on discussion).	The mean is not explicitly stated, but majority are aged 50–60 years	<ul> <li>Length of work &gt;5 years: p-value = 0.001 (OR = 2.275)</li> <li>Use of &gt;3 types of pesticides: p-value = 0.008 (OR = 4.389)</li> <li>Spraying in the morning: p-value = 0.001 (OR = 4.588)</li> </ul>	The study found a strong relationship between hypertension and pesticide exposure, particularly:  • Longer duration of farming (>5 years)  • Higher variety of pesticides used (>3 types)  • Spraying pesticides in the morning
14	Prihartono NA, Fitria L, Ramdhan DH, Fitriyani F, Fauzia S, Woskie S./2022(39)	Analytical observational study with a cross-sectional design/ Overall Quality Rating: Good Final Score: 8 out of 8	354 Male rice farmers from Karawang (186 participants) and Bogor (168 participants) Regencies, West Java	Primarily insecticides (herbicides and fungicides were rare in this population)	The mean is not explicitly stated, but majority are aged ≥45 years	<ul> <li>Heat Stress (High WBGT – Karawang): p-value = 0.037 (PR = 1.41 (95% CI: 1.02–1.95))</li> <li>Pesticide Sprayer (vs. non-sprayer): p-value = 0.078 (PR = 1.90 (95% CI: 0.93–3.87)) (borderline significant)</li> </ul>	In West Java, Indonesia, 46.6% of male rice growers had hypertension. Occupational risks, such as pesticide spraying and high- heat conditions (Karawang), contributed to hypertension, while lifestyle factors like smoking, drinking, and nutrition had no significant effect.

# **Exposure Assessment and Pesticide Use**

The types of pesticides used across studies included combination of organophosphates, carbamates, pyrethroids, neonicotinoids, avermectins, triazoles, and strobilurins. However, not all studies reported the specific names or chemical classes. Several studies simply referenced "mixed pesticides" or "various insecticides and fungicides" without further classification. In many cases, exposure intensity was inferred based on working duration, spraying frequency, number of pesticide types used, or lack of protective equipment use. Only a few studies incorporated biomonitoring, such as blood cholinesterase levels, to objectively quantify internal exposure.

#### **Occupational Risk Factors**

Several occupational factors were identified as significant predictors of hypertension, and length of employment or working duration in agriculture was a commonly cited variable. For instance, a working period longer than 10 years significantly increased the risk of hypertension (OR = 4.164) (25), and similar trend (OR = 2.098) (26). Similarly showed that farmers with a longer exposure history had a fourfold risk increase (PR = 4.048) (32). These findings suggest that cumulative exposure plays a critical role in hypertension pathogenesis among farmers.

Spraying frequency and pesticide dosage were also consistently associated with elevated blood pressure. Some studies found statistically significant associations between frequent pesticide application and increased hypertension prevalence (32,35). Further, researcher also reported that morning spraying was particularly associated with higher blood pressure (OR = 4.588), possibly due to increased dermal absorption linked to dew and higher humidity (25).

# Personal Protective Equipment (PPE) and Safe Practices

The use or lack of PPE was reported as another strong risk factor. Multiple studies showed that inadequate or incomplete use of protective gear significantly increased hypertension risk. Some studies found that PPE use had a protective effect and also reported a significant association (33-34). Furthermore, poor pesticide storage and spraying direction, particularly spraying against the wind, were associated with increased exposure and subsequent hypertension (34).

#### Sociodemographic and Behavioral Risk Factors

Age was consistently associated with hypertension. Older age groups (typically over 44 or 45 years) showed a significantly higher prevalence of hypertension (38,42). According to the study conducted

in West Java, the majority of hypertensive farmers were aged  $\geq$ 45 years (39). Behavioral factors such as smoking, stress, and coffee consumption were also assessed. Smoking (p = 0.000), occupational stress (p = 0.006), and high coffee intake (p = 0.004) were all significantly associated with hypertension among pesticide-exposed farmers (42).

## **Biomarker and Physiological Measures**

Some of the more methodologically rigorous studies included objective measurements of pesticide exposure through biomonitoring. A significant association reported between blood cholinesterase levels and both systolic and diastolic blood pressure (37). This study is among the few that directly link internal exposure metrics to hypertension outcomes, providing strong support for the hypothesis that pesticides may disrupt cardiovascular regulation, potentially through cholinergic and neuroendocrine pathways.

## **Statistical Analysis and Strength of Associations**

The majority of the studies used bivariate analyses (e.g., Chi-square tests, Odds Ratios, and PR), and several also applied multivariate regression to control for confounding variables. Some researcher used modified Cox regression to estimate adjusted prevalence ratios (aPRs), identifying high heat stress (aPR = 1.41) and pesticide spraying activities (aPR = 1.90) as idependent predictors of hypertension (39). The use of multivariate models improves the robustness of findings, allowing for better isolation of pesticide exposure effects from lifestyle or environmental variables.

#### **Regional and Agricultural Contexts**

Geographically, the studies provided insights into diverse agricultural contexts, from flower sprayers in greenhouses (Central Java) to open-field rice farmers in Sulawesi. Some regional factors may influence the nature and intensity of exposure. For instance, the Karawang region in West Java had significantly higher heat stress levels (WBGT), which was itself a risk factor for hypertension. Similarly, coffee farming in highland areas such as Aceh may involve different pesticide types and exposure pathways compared to lowland vegetable farming in Java.

# **Hypertension Prevalence**

Hypertension prevalence among farming communities varied from 30% to over 60% in some studies. For example, study in Brebes reported that 61.4% of male shallot farmers experienced hypertension (32), meanwhile, another study also found a prevalence

of 46.6% among male rice farmers in West Java (39). These figures suggest that the prevalence of hypertension in farming populations may exceed national averages (35.7%), especially in groups with prolonged or intense pesticide exposure.

# **Summary of Key Associations**

Across the 14 studies reviewed, several consistent and statistically significant associations were reported: Long-term exposure to pesticides (>5 or >10 years), use of multiple pesticide types (e.g., >2 or >3 kinds), inadequate PPE use, spraying against the wind or in high-humidity conditions, morning spraying activities, smoking, stress, and dietary factors such as excessive caffeine intake, and age ≥45 years.

The findings from the reviewed studies collectively offer robust evidence that pesticide exposure constitutes a significant occupational risk factor for hypertension among Indonesian farmers. The association persists across diverse geographic settings, farming practices, and pesticide types. Furthermore, inadequate protective behaviors and certain environmental conditions exacerbate this risk. The use of objective biomarkers in some studies reinforces the causal plausibility of these findings.

#### Meta-analysis for an increased risk of hypertension

In this study, 13 out of 14 selected articles were included in the meta-analysis, and 1 article (41) was excluded from the meta-analysis due to a lack of information regarding the number of participants with hypertension exposed to pesticides or PR. The fixed-effect meta-analysis conducted on 13 cross-sectional studies showed a pooled PR of 1.64 (95% CI: 1.35–1.99), showing that the prevalence of hypertension was significantly higher among pesticide-exposed agricultural workers compared to their non-exposed counterparts (Figure 2). The CI does not cross 1.0, reinforcing the statistical significance of the association. This result suggests a statistically significant association, with a 1.64-fold greater prevalence of hypertension in the exposed group.

The forest plot showed consistency across studies, with no major outliers, and the funnel plot did not show substantial asymmetry, showing minimal evidence of publication bias (Figure 3). The relatively narrow Cl and the symmetry of effect sizes across studies show low between-study heterogeneity, thereby supporting the suitability of the fixed-effect model. Moreover, all studies showed a positive direction of association, further reinforcing the robustness of the pooled effect estimate.

This discussion aims to provide a comprehensive synthesis of findings from 14 Indonesian studies assessing the relationship between pesticide exposure and the prevalence of hypertension. These findings are compared with global studies to assess the consistency of

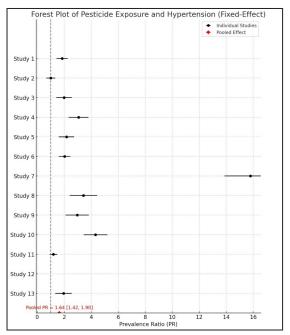


Figure 2. Forest Plot of Pesticide Exposure and Hypertension (Fixed-Effect)

evidence. Additionally, underlying biological mechanisms linking pesticide exposure to elevated blood pressure will be discussed, and potential methodological biases in the studies will be critically examined.

A systematic review of 14 studies conducted in various agricultural regions of Indonesia shows a constant connection between pesticide exposure and hypertension risk among farmers. All included studies used cross-sectional observational designs,

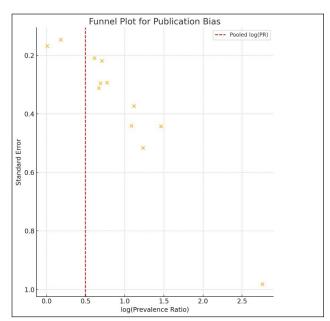


Figure 3. Funnel Plot for Publication Bias

which inherently limit causal inference. However, the consistency of findings across diverse geographical settings, crop types, and populations enhances the strength of the overall evidence. Notably, all 14 studies reported significant associations between various aspects of pesticide exposure and hypertension. Key occupational factors included the duration of pesticide use, type and number of pesticides applied, frequency and method of spraying, and use of PPE.

For instance, some researcher found that hypertension risk increased significantly with longer working periods (OR = 4.16), higher pesticide doses (OR = 4.20), and poor use of PPE (OR = 2.87) (31). Similarly, another study observed that years of work, dosage, and spraying frequency were all significantly associated with hypertension (p-values < 0.01), and PPE usage had a protective effect (PR = 7.21) (32). And, reported that inappropriate spraying direction (PR = 4.06) and storage practices (PR = 3.20) were associated with increased hypertension prevalence (34). This shows that both direct exposure (e.g., from spraying) and indirect exposure (e.g., from storage or equipment cleaning) are relevant.

Several studies reported specific classes of pesticides implicated in hypertension, particularly organophosphates, and carbamates, which are known cholinesterase inhibitors like Dursban 200 EC (organophosphate), Tamabas (carbamate) (32). Furthermore, organophosphate and carbamate exposure correlated with higher blood pressure due to inhibition of cholinesterase and resultant acetylcholine accumulation with elevated systolic blood pressure (p = 0.041) (36-37).

Farmers often used multiple pesticide types simultaneously, a practice associated with compounded health risks. Using of >2 pesticide types significantly increased hypertension odds (OR > 2.0) (25-26). This co-exposure amplifies the toxic burden and complicates the attribution of effects to a single substance. Age and education levels were found to moderate the impact of pesticide exposure. Being older than 44 years significantly increased hypertension risk (OR = 4.31), and high daily exposure intensity had a similar effect (OR = 2.60) (38). Beside that lower education levels were associated with greater risk (OR = 2.67), possibly due to a reduced understanding of safety procedures (31). The role of lifestyle factors, such as stress, smoking, and coffee consumption (42). However, even after accounting for these, high pesticide exposure remained significantly associated with hypertension (p = 0.000), suggesting an independent occupational risk Pathway.

The studies include diverse agricultural zones

across Central Java, West Java, Aceh, Jambi, Bengkulu, Sulawesi, and Southeast Sulawesi, reflecting a broad demographic and environmental spectrum. They also vary in crop type from paddy fields (25,31) to shallots (32), vegetables (26,41), flowers (33), and coffee (40). Despite these variations, the core association between pesticide exposure and hypertension remained consistent, underscoring the robustness of the findings.

Some studies went beyond reporting associations and attempted to establish biological plausibility. The inhibition of cholinesterase enzymes, showing that this leads to an accumulation of acetylcholine in the nervous system, thereby affecting heart rate and vascular tone (36-37). This neurophysiological disruption provides a mechanistic explanation for pesticide-induced changes in blood pressure regulation.

The quantitative results of the meta-analysis reinforce the findings of the systematic review, which qualitatively linked pesticide exposure to elevated blood pressure. The meta-analysis now provides a clear and quantifiable estimate of risk, strengthening the case for the harmful cardiovascular effects of occupational pesticide exposure (31-32). The findings from Indonesia align strongly with international studies examining the relationship between pesticide exposure and hypertension, further affirming a biologically plausible and statistically supported association. In China, a casecontrol study involving 2730 participants reported that chronic exposure to organophosphate pesticides was significantly associated with hypertension risk (22). This parallels the Indonesian results where similar pesticide classes (e.g., Dursban 200 EC, Curacron 500 EC) were linked to hypertension.

Similarly, India has documented strong correlations between pesticide exposure and elevated blood pressure. A study in India investigated the immediate health impacts of organophosphate pesticide exposure among farmers in Kashmir, showing that such exposure correlates with numerous neurological and health symptoms, although cardiovascular effects are comparatively less significant (43). According to reports, occupational and environmental exposure, especially prolonged or unprotected contact, may disrupt cardiovascular regulation, contributing significantly to elevated blood pressure. Factors such as the non-use of PPE, longer duration of exposure, and unsafe storage practices were reported as significant (31,34)

According to the study carried out by Thai vegetable farmers found that those who use pesticides are more likely to experience hematological diseases, as well as possible dysfunctions of the liver and kidneys, which can lead to hypertension and other complications (44). A

study from Ghana similarly supports the Indonesian data investigated the knowledge, perceptions, and practices of pesticide application among cocoa farmers in Ghana. They found that even while the farmers understood enough, they still stored and used pesticides in a way that was dangerous and didn't use personal protective equipment (PPE), which increased the risk of exposure and health concerns, including a possible risk of high blood pressure. (45).

Study in southern Brazil looked examined the health concerns that farmers endure from being around chemicals (46). They talked about how to wear PPE and how to spot symptoms that last a short time or a long time. The study indicated that 35.91% of farmers had high blood pressure, which is a long-term health concern that may be linked to being around chemicals for a long period. A lot of the people in the research (38.02%) also suffered depression, which is another long-term impact of using pesticides. Notably, the study emphasized the usage of many pesticides kinds, with many farmers being exposed to more than two, which increases the risk of both acute symptoms like headaches and eye irritation, as well as chronic diseases like hypertension. The ineffective use of PPE, with only 17.6% of farmers using all necessary protective gear, exacerbates the health hazards linked with chemical exposure.

While pesticide regulations are stricter in high-income nations, exposure still exists. Using data from the NHANES study, identified a positive association between urinary biomarkers of non-persistent pesticides and hypertension, confirming that confirming that in the United States, people exposed to pesticides tend to have high blood pressure (23). According to global findings collectively reinforce the Indonesian data: pesticide exposure, particularly organophosphates, and carbamates, is consistently linked to blood pressure elevation across diverse countries, climates, and agricultural practices.

The development of hypertension due to pesticide exposure can be explained by several interlinked biological pathways: 1) Cholinesterase Inhibition and Autonomic Dysregulation: Many pesticides used in the reviewed studies (e.g., organophosphates such as Dursban and Curacron) act as cholinesterase inhibitors. This leads to an accumulation of acetylcholine at neural synapses, over-activating the parasympathetic system (47). Paradoxically, chronic overstimulation can lead to autonomic dysregulation, resulting in increased sympathetic tone and vasoconstriction, hence elevating blood pressure. Reduced cholinesterase levels to systolic hypertension, providing empirical support for this mechanism; 2) Oxidative Stress and Endothelial

Dysfunction: Pesticides generate reactive oxygen species (ROS), which damage endothelial cells lining the blood vessels (48-50). This impairs nitric oxide (NO) production, a critical vasodilator, leading to increased vascular resistance. Studies in India and Indonesia report similar mechanisms, where long-term exposure to mixed pesticides led to endothelial impairment and sustained high blood pressure (36); 3) Endocrine Disruption: Certain pesticides act as endocrine disruptors, interfering with cortisol, aldosterone, and catecholamine pathways that regulate fluid balance and vascular tone (11, 51).

Disruption of the renin-angiotensin-aldosterone system (RAAS) by pesticide exposure may result in sodium retention, volume overload, and hypertension; 4) Chronic Inflammation: Pesticide-induced cellular stress activates inflammatory pathways, including cytokines like TNF-α and IL-6, which have been associated with vascular stiffening and blood pressure increases (52-54). 5) Epigenetic Modifications: Recent studies suggest that chronic pesticide exposure can alter DNA methylation patterns in genes related to vascular function and BP regulation (55, 56). Though not directly explored in Indonesian studies, it provides a novel mechanism potentially underlying long-term cardiovascular effects.

Studies incorporating biomonitoring to measure pesticide exposure have become increasingly important in understanding the health impacts of agricultural chemicals, particularly their effect on cholinesterase levels and cardiovascular health. Studies found significant associations between blood cholinesterase levels and both systolic and diastolic blood pressure, suggesting that pesticide exposure disrupts cardiovascular regulation, likely via cholinergic and neuroendocrine pathways. This supports the growing body of evidence linking pesticide exposure to hypertension, with research indicating that organophosphates and carbamates, commonly used in agriculture, inhibit acetylcholinesterase and affect neurotransmitter regulation, which can lead to hypertension (57, 58). Environmental factors such as topography, proximity to water bodies, and agricultural practices have been identified as key influences on exposure levels, with low topography areas showing higher risks of cholinesterase inhibition and associated health outcomes (59). Moreover, the long-term effects of pesticide exposure are compounded by insufficient use of personal protective equipment (PPE), exacerbating the environmental health risks in agricultural settings (60). These findings highlight the critical role of environmental management practices and regulations in mitigating the harmful health impacts of pesticides, particularly for vulnerable populations such as farm workers.

While the consistency of findings strengthens

causal inference, several potential biases may affect the interpretation of the reviewed studies: 1) Cross-sectional Design Limitations. All 14 studies used cross-sectional designs, which cannot establish causality. These studies can identify associations, but temporality, i.e., whether pesticide exposure preceded hypertension, remains unclear; 2) Recall and Reporting Bias. Several studies relied on self-reported exposure frequency, PPE use, and health history. Farmers may underreport or overestimate their pesticide use or misremember past symptoms. introducing recall bias; 3) Exposure Misclassification. Many studies did not quantify actual pesticide exposure levels (e.g., via blood tests or environmental sampling) and only documented usage patterns. This could lead to misclassification bias, where actual high-exposure individuals are grouped with lower exposure categories: 4) Confounding Variables. While some studies adjusted for age, smoking, and coffee consumption, others did not rigorously control for other lifestyle factors like diet, stress, obesity, or genetics, all of which could confound the relationship between pesticide use and hypertension; 5) Small Sample Sizes; and 6) Publication Bias. Considering the growing concern about pesticide safety, there may be a tendency to publish only positive findings, possibly inflating perceived associations.

To address regarding the potential biases in these studies, it is important to consider several key factors that might influence the observed relationship between hypertension and pesticide exposure, particularly for farmers with a history of hypertension and lifestyle factors such as smoking and high salt consumption. Farmers who have had high blood pressure in the past may be more likely to get it again because of their genes, their past lifestyle choices, or their current health problems. These people may also be more sensitive to how pesticides affect their heart health, especially if they are exposed to them for a long time. This pre-existing condition can make things unfair because these people may already be at a higher risk for high blood pressure, no matter how much they are exposed to pesticides. Male shallot farmers who were exposed to pesticides had a much higher risk of developing high blood pressure. They also said that smoking and age were important factors in this risk.

The study made it clear that pesticide exposure was still a major risk factor, but lifestyle factors could also be a cause. (32). It is well known that lifestyle choices like smoking and eating a lot of salt can raise the risk of hypertension. Several studies have shown that smoking raises the risk of getting high blood pressure because it harms the health of blood vessels. High salt intake also raises blood pressure by making the heart work harder

and holding onto more fluid. In this case, the farmers in the study may have a higher risk of high blood pressure because they smoke or eat a lot of salt. (38). Being around pesticides and making certain choices, like smoking or consuming a lot of salt, could raise a blood pressure. Smoking and eating badly could make chemicals' impact on blood pressure much worse. For instance, persons who smoke and already have severe vascular health may be more influenced by the neurophysiological effects of being among chemicals. Too much salt can make the heart work harder and make people more likely to have high blood pressure when they are around pesticides.

To know how to utilize conventional PPE and make it better for farmers, it needs to look at how PPE works with pesticide exposure and the major routes that pesticides get into the body. PPE is gear that keeps a body safe, like gloves, masks, goggles, and other items. It is vitally necessary to observe particular safety regulations so that people do not breathe in, absorb through their skin, or swallow pesticides. The best way to utilize PPE is to wear the proper sort for the pesticide based on the work being done. Pesticides can get into the body in a number of ways, including through the mouth, skin, or lungs. To minimize these dangers, PPE needs to be altered depending on how someone gets in, which means that the proper gear needs to be used for each way of getting in. For instance, farmers should wear gloves, long-sleeved shirts, and boots when they put insecticides on their skin. They should also wear masks when they mix or spray insecticides to keep their lungs safe. Not utilizing PPE appropriately or at all is closely associated to being exposed to more pesticides, which can cause high blood pressure and other health concerns. (25, 32, 38).

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#### **CONCLUSION**

The research we looked at reveal that Indonesian farm workers exposed to pesticides are far more likely to have high blood pressure. Data from Java, Sumatra, and Sulawesi show that being around pesticides is a substantial environmental health risk factor for high blood pressure. Studies have found that farmers who stay around pesticides for a long period, do not wear personal PPE properly, or spray pesticides a lot tend to have higher blood pressure. The data demonstrate that how long a person is exposed to pesticides, how often they are applied, and what kinds of pesticides are

utilized all have an effect on the development of high blood pressure. Moreover, environmental factors such as inadequate safety practices in pesticide handling and the lack of PPE usage exacerbate the health risks, emphasizing the need for stricter environmental health regulations in agricultural practices.

From the aspect of environmental health, the findings emphasize the importance of implementing integrated pest management (IPM) techniques, educating farmers about proper pesticide usage, and ensuring the availability and use of protective equipment. These steps are very important for lowering the health risks of pesticides, especially high blood pressure, in farming communities.

The report also recommends for better health monitoring systems and the addition of environmental health laws that deal with the direct and indirect impacts of pesticide exposure. In conclusion, this systematic review and meta-analysis shows that pesticides exposure poses serious risks to the health of the environment, especially for Indonesian agricultural workers who are more likely to develop high blood pressure.

These risks get worse when people are exposed to them for a long time, do not use PPE properly, or do not follow safety rules. The results show that we need stricter rules for environmental health, better pest control, and more information about how to use pesticides safely right away. These steps are necessary to keep farm workers safe and lower the health risks of pesticides in communities.

#### **AUTHORS' CONTRIBUTION**

All authors participated actively in this study and article writing and are partially responsible for the material, including concepts, designs, analysis, and revision. All authors played the roles of SS: Conceptualization, Methodology, Software, Data curation, Validation, Writing- Original draft preparation, and Supervision. KA: Resources, Data curation, Validation, Writing, Reviewing, and Editing. MAR: Resources, Data curation, Validation, Visualization.

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