

## Effect of Pesticide Exposure on the Incidence of Spontaneous Abortion in Female Farmers

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### Abstract

The continuous use of pesticides impacts short-term health with numerous harmful chronic effects. The harmful effects of pesticides could affect reproduction in women of childbearing age and female farmers, including infertility, low birth weight, preeclampsia, eclampsia, and abortion. This study is observational analytical research with a case-control approach with 38 cases and 38 controls. Data were analyzed using the Chi-square test for bivariate analysis and multiple logistic regression test for multivariate analysis. There were significant associations between the incidence of spontaneous abortion and the following: the intensity of exposure ( $p = 0.001$ ; odds ratio (OR) 12.60), mixing of pesticides ( $p = 0.004$ ; OR 3.69), use of personal protective equipment ( $p = 0.001$ ; OR 7.25), parity ( $p = 0.001$ ; OR 2.763), and time intervals between births ( $p = 0.002$ ; OR 4.12). The results of the multivariate test using multiple logistic regression to determine the risk factor model showed a significant relationship between the incidence of spontaneous abortion with the intensity of exposure, pesticide mixing, personal protective equipment, parity, and birth distance for the exposure intensity variable were OR at 57.78, 3.73, 20.06; 28.48 and 3.98, respectively. In conclusion, female farmers should avoid working directly with pesticides during pregnancy and must use personal protective equipment if they have to participate in agricultural activities.

**Keywords:** Spontaneous abortion; Pesticide exposure; Reproduction; Infertility; Personal protective equipment

### 1. Introduction

In August 2018, the informal sector still dominates labor conditions in Indonesia with a contribution of around 61.80%. One of the informal sectors includes farmers (Statistik and Kulit, 2019). Data from the Central Bureau of Statistics from the 2018 Inter-Census Agricultural Survey stated that the number of female farmers in Indonesia was approximately 8 million. It means that almost 24% of the 25.4 million farmers are women. In Central Java Province in Kutabawa Village, Karangreja District, Purbalingga Regency, more than 20 pesticides are used yearly, including organophosphates and carbamates, such as diazinon, curacron, dursban, lannate, tamacron.

These can cause dangerous short-term health effects and various chronic effects. The harmful effects of pesticides could impair reproduction in women of childbearing age and female farmers, including subfertility, infertility, low birthweight (LBW), pre-eclampsia, eclampsia, and even abortion, malformation, miscarriage, and stillbirth. There is growing evidence that environmental risk factors harm female reproductive systems (Petrelli and Mantovani, 2002). Several pesticides are known to affect endocrine homeostasis in experimental studies in vivo through receptor-mediated estrogenic

or antiandrogenic activity and enzyme inhibition e.g., aromatase (Mantovani, 2002). Chemicals like chlorinated compounds are of particular concern because they persist in the environment and can accumulate biologically (Turusov, Rakitsky, and Tomatis 2002).

Several studies have also proven that organochlorine compounds act as pregnancy antagonists and can cause spontaneous abortion, premature birth, or stillbirth (Tyagi *et al.*, 2015; Bretveld *et al.*, 2006). Pesticides enter the body through the skin, mouth, digestive, and respiratory tracts, and in pregnant women, enter the mother's blood circulation, placenta, and fetal umbilical cord. A study conducted in Ontario, Canada, among female farmers revealed that the risk of spontaneous abortion increased, especially with the use of certain active ingredients such as the herbicides phenoxy-acetic acid, thiocarbamate, and triazine (Arbuckle *et al.*, 2001). Chemical exposure is also known to be associated with fetal death. N-methyl-2-pyrrolidone included in petroleum refining and pesticide formulations has been reported to cause acute toxicity and fetotoxicity (Ooka *et al.* 2021). Other cohort studies have also investigated the association between maternal chemical exposure during pregnancy and the incidence of fetal death (Xu *et al.*, 1998). Studies in the United States and Canada revealed a significant association between pesticide exposure and stillbirth (JB, Collot, and MT 2015).

Exposure to pesticides in women of childbearing age can cause hormonal dysfunction, one of which is thyroid hormone that can cause hypothyroidism (Rathore *et al.*, 2002). One of the effects of hypothyroidism on women's reproductive health is spontaneous abortion (Krassas, Poppe, and Glinooer 2010), which is incident loss of fetus (miscarriage) at gestational age < 20 weeks or fetal weight < 500 g. Thus, pesticide exposure in pregnant women can cause thyroid dysfunction, leading to hypothyroidism and spontaneous abortion. The risk of stillbirth and spontaneous abortion increases among female workers exposed to pesticides (Caporossi and Papaleo, 2011). Spontaneous abortion is 12 - 15% per year (Garcia-Enguidanos *et al.*, 2002), and stillbirth occurs in 1.8% of all recognized pregnancies each year, indicating that approximately 2.6

million stillbirths annually occur worldwide (Lawn *et al.*, 2016).

In 2021, Purbalingga Regency was one of 20 districts with the highest infant and maternal death rates in Central Java Province, with 3.91% of cases. Karangreja sub-district had six cases of infant mortality and three of maternal deaths. Many factors influence infant and maternal mortality rates, one of which is a modern lifestyle in the health sector (Purba, 2010). The risk of spontaneous abortion has been studied in several groups of workers who use pesticides. In a study on family farmers in Ontario, Canada, researchers found an enhanced risk of spontaneous abortion in pregnancy age (< 12 weeks) caused by exposure to phenoxy acetic acid herbicides with an OR = 1.5; during gestation (12 - 19 weeks) to glyphosate exposure with OR = 1.7; and exposure to various other pesticides with OR = 1.5.

## 2. Materials and Methods

### 2.1 Study design

The type of research used a retrospective case-control study design to determine the relationship between the case and the control group based on their exposure status. This approach was chosen because it can provide information about past exposures (pesticides) before the outcome (spontaneous abortion). The research was conducted in the agricultural area of Kutabawa Village, Karangreja District, Puralingga Regency, from April to October 2022.

### 2.2 Sample size and sampling technique

The samples included 38 female farmers with a history of spontaneous abortion and 38 female farmers with no history of spontaneous abortion to act as controls. Data collection was conducted with interviews using a questionnaire and observation using a checklist. The inclusion criteria for the case group were pregnant women in 2020 who had experienced spontaneous abortions and were willing to become informants. The control inclusion criteria were pregnant women in 2019 with no history of spontaneous abortion.

### *2.3 Data analyses*

To analyzed the association of spontaneous abortion incidence with exposure levels, mixing of pesticides, storage, use of personal protective equipment (PPE), smoking history, parity, age, and birth distance in female farmers in the Karangreja Health Center Work Area using the chi-square test and odds ratio (OR). Multivariate analysis was used in logistic regression to analyze the results of the bivariate analysis that had statistical ( $p < 0.25$ ) and biological significance. For the effect of the variables studied on the influencing variable,  $p < 0.05$  at  $= 5\%$  was considered significant. Furthermore, the OR was calculated to estimate the magnitude of the risk of the independent variable on the dependent variable.

### *2.4 Ethical standards disclosure.*

The research proposal was approved by the Health Ethics Commission of the Faculty of Public Health, Diponegoro University with the registration number: 397/EA/KEPK-FKM/2021. Informed consent from each respondent was obtained before interviewing and data were deidentified.

## **3. Results and Discussion**

### *3.1 Results*

Environmental factors can influence human reproduction through direct tissue toxicity or endocrine-mediated mechanisms (Hoyer, 2001). As shown in Table 1, 80% of female farmers in the agricultural area of the Karangreja Health Center Work Area, Karangreja District, Purbalingga Regency exposed to a high level of pesticide exposure intensity experienced abortions. In comparison, 19.2% of female farmers did not undergo miscarriage. The results of the analysis revealed a significant association between the intensity of pesticide use and the incidence of abortion with a p-value of 0.001. This is because the impact of pesticides does not necessarily result in direct complaints.

The effects of pesticides are generally in the form of chronic poisoning that is not perceived immediately. However, in the long term, it may cause health problems. Although very rare, pesticides can also cause acute poisoning, for example, when consumers consume agricultural products that contain large amounts of residue (Djojsumarto, 2008). The longer the working period in agriculture, the greater the risk of being exposed to the harmful effects of pesticides (Purba, 2010).

The percentages of female farmers in the agricultural area of the Karangreja Health Center, Karangreja District, Purbalingga Regency who mixed pesticides incorrectly and who did and did not experience spontaneous abortion were 71.1% and 28.9%, respectively ( $p = 0.004$ ). Thus, there was a strong association between pesticide mixing and the incidence of abortion.

The percentages of female farmers in the agricultural area of the Karangreja Health Center, Karangreja District, Purbalingga Regency who stored pesticides in the house and who did and did not experience spontaneous abortion were 54.4% and 45.5%, respectively ( $p = 1.000$ ). Thus, there was no association between pesticide storage and the incidence of abortion in female farmers in the agricultural area of the Karangreja Community Health Center Karangreja District, Purbalingga Regency.

In Table 1, the percentages of female farmers in the agricultural area of the Karangreja Health Center, Karangreja District, Purbalingga Regency who practiced incomplete use of personal protective equipment (PPE) and who did and did not experience spontaneous abortion were 75.5% and 24.5%, respectively ( $p = 0.001$ ). Thus, there was an association between personal protective equipment (PPE) and the incidence of spontaneous abortion.

In this study, the variable related to the incidence of abortion was the parity status in pregnant women with a p-value = 0.001. In contrast, the unrelated variables were smoking, age, and birth distance ( $p = 1.0, 0.317, \text{ and } 0.002$ , respectively).

**Table 1.** Association of spontaneous abortion incidence with exposure levels, mixing of pesticides, storage, use of PPE, smoking, parity, age, and pregnancy delivery distance among female farmers in the Karangreja health center work area

Variable	Abortion Incidence				OR (95% CI)	P- Value
	Abortion		No Abortion			
	n	%	n	%		
<b>Intensity Level</b>						
High	42	80.8	10	19.2	12.600 (4.873 - 32.579)	0.001
Low	12	25	36	75		
<b>Mixing of pesticides</b>						
Incorrectly	32	71.1	13	28.9	3.692 (1.593 - 8.558)	0.004
Correctly	22	40.0	33	60.0		
<b>Pesticide Storage</b>						
Inside the house	24	54.4	20	45.5	1.040 (0.471 - 2.297)	1,000
Outside the house	30	53.6	26	46.4		
<b>Use of PPE</b>						
Incomplete	40	75.5	13	24.5	7.253 (2.995 - 17.564)	0.001
Complete	14	29.8	33	70.2		
<b>Smoking</b>						
Yes	1	100	0	0	1.868 (1.555 - 2.244)	1.000
No	53	53.5	46	46.5		
<b>Parity</b>						
At risk	35	87.5	4	12.5	2.763 (1,871 - 4.080)	0.001
No Risk	19	31.7	41	68.3		
<b>Age (y)</b>						
17–25	24	61.5	15	38.5	1.289 (0.784 - 2.120)	0.317
26– 34	17	48.5	18	51.4		
>35	13	50	13	50		
<b>Birth Distance</b>						
At risk	32	72.2	12	27.3	4.1219 (1.756 - 9.672)	0.002
No Risk	22	39.3	34	60.7		

**Table 2.** Model of association between pesticide exposure and spontaneous abortion incidence in female farmers in the Karangreja health center work area

Variable	Coef	p	OR	95% CI
Exposure Intensity	5.552	0.000	57.78	18.83 - 85.52
Mixing of pesticides	2.999	0.002	3.73	1.609 - 8.651
Personal protective equipment	1.317	≤ 0.001	20.068	3.111 - 129.461
Parity Status	3.350	≤ 0.001	28.48	23.263 - 248.7
Birth Distance	1.380	≤ 0.001	3.976	0.589 - 26.843

The final model was obtained, which was meaningful with regard to the incidence of spontaneous abortion, namely exposure intensity, pesticide mixing, personal protective equipment, parity, and birth spacing. The results of this multivariate test used a multiple logistic regression test with a risk factor model. exposure intensity, pesticide mixing, PPE use, parity status, and birth spacing, the OR were 57.78 (95% CI: 18.83 - 85.52), 3.73 (95% CI: 1.609 - 8.651), 20.068 (95% CI: 3.111 - 129,461), 28.48 (95% CI: 23,263 - 248.7), and 3.976 (95% CI 0.589 - 26.843), respectively. This meant that female farmers in the Karangreja Health Center work area were at 57, 3, 20, 28, and 3 times the risk for spontaneous abortion after controlling for the other variables, respectively.

### 3.2 Discussion

The study's results revealed that the frequency of high-intensity levels of pesticide exposure with maternal abortion was 80.8%. This study showed an association between the level of exposure to spontaneous abortion incidence among female farmers in the agricultural area of Kutabawa Village Subdistrict Karangreja Purbalingga Regency with a p-value < 0.05, which is 0.001. The study results can be interpreted that female farmers with a history of direct contact with pesticides by virtue of their work as farmers are more at risk of being exposed to pesticides, thus increasing the risk of abortion. Mothers exposed to pesticides have a risk of 12.6 times the incidence of spontaneous abortion.

The length of exposure to pesticides in agricultural areas or at home will increase the risk of poisoning because the longer a woman is exposed, the more pollution by pesticides occurs through inhalation or direct contact through the skin. Thus, it enters the lungs and the mother's blood flow and gets transmitted to the fetus through the placenta resulting in impaired fetal growth. Therefore, there is an increased risk of miscarriage or spontaneous abortion in young pregnant women (Rahayu *et al.*, 2015).

The practice of using pesticides by the farmers in this study comprised mixing pesticides. It is reported that 71.1% of female farmers in the agricultural area Village in

Subdistrict Karangreja Regency Purbalingga, in an unhappy marriage, experienced an abortion. The results indicate that there was an association between the method of mixing pesticides in female farmers in agricultural areas. Subdistrict Karangreja Regency Purbalingga with a variable value of pesticide mixing  $p = 0.004$ . Female farmers who mixed incorrectly had 3.692 times the risk of experiencing abortion.

Another study conducted in the United States showed that women who lived in areas with high use of pesticides had a 1.9 – 2 times higher risk of giving birth to babies with disabilities than women who lived in areas that did not use pesticides (Setiyobudi *et al.*, 2011). The best way to mix pesticides is to do it outside the house with the recommended proportions of mixing, special bucket, a clean water source, and always using personal protective equipment. If it accidentally gets splashed on the body, it is recommended to wash the area immediately with soap.

This study indicated that there was no relationship between storage of pesticides with incidence of spontaneous abortion among the female farmers in agricultural villages in Subdistrict Regency Karangreja Purbalingga ( $p > 0.05$ ).

Exposure to pesticides stored in the house can cause poisoning if food items or ready-to-eat foods are contaminated with pesticides. The storage of pesticides causes the risk of poisoning, one of which has an impact on the fetus in pregnant women (Gesese *et al.*, 2016). Storage of pesticides should be carried out according to the rules, which state that they should be stored in a closed room and protected from sunlight to reduce evaporation. Then the pesticide containers that are not used should be thrown away and should not be traded because the remaining pesticides in the packaging can react with the air and pollute the surrounding environment.

We found out that 75.5% of female farmers in the agricultural village in subdistrict Karangreja Regency Purbalingga who did not use PPE in agricultural activities experienced spontaneous abortion ( $p = 0.001$ ). Farmers who did not use personal protective equipment in activities with pesticides had 7.253 times the risk of experiencing spontaneous abortion in agricultural areas.

The presence and duration of pesticide exposure supported by not using complete PPE will increase the dose of pesticides absorbed by the body. Pesticides entering the body will accumulate in tissues, proteins, and bones. Fat-soluble pesticides are stored in the body for a long period and can interfere with the growth of the fetus (Winnoto *et al.*, 2016). Therefore, it is necessary to carry out government-sponsored agricultural extension and health extension services in the field of agriculture to increase farmers' awareness of using PPE when using pesticides.

#### 4. Conclusion

In conclusion, the risk factor for spontaneous abortion were the intensity of exposure, mixing of pesticides, the use of PPE, parity, and birth spacing. The government is advised to provide counseling to farmers regarding the safe, appropriate, and correct use of pesticides. The government should also control the distribution of pesticides used by farmers. Meanwhile, farmers must be more careful in storing, managing and using pesticides.

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