



Associação entre o uso de agrotóxicos e as malformações congênitas em Marialva-PR: estudo ecológico

Association Between Pesticide Use and Congenital Malformations in Marialva, Paraná, Brazil: An Ecological Study

Asociación entre el uso de plaguicidas y las malformaciones congénitas en Marialva-PR: estudio ecológico

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RESUMO

Os agrotóxicos são amplamente utilizados em áreas rurais e urbanas e podem representar riscos à saúde humana devido ao seu potencial tóxico. Este estudo teve como objetivo investigar a associação ecológica entre o uso de agrotóxicos e a ocorrência de malformações congênitas no município de Marialva, Paraná. Trata-se de estudo quantitativo ecológico com dados secundários de 2015 a 2020. Informações sobre nascidos vivos, óbitos fetais, óbitos infantis e malformações congênitas foram obtidas no SINASC, SIM e DATASUS; os dados sobre utilização de agrotóxicos foram obtidos no SIAGRO/ADAPAR. Foram ajustados modelos de regressão exponencial para explorar a associação entre os desfechos e o uso total e por classe de agrotóxicos. No período, registraram-se 3.127 nascidos vivos e 37 óbitos infantis, dos quais 17 foram atribuídos a malformações congênitas. O modelo para o uso total de agrotóxicos não foi estatisticamente significativo ($p > 0,05$; $R^2 = 0,39$). O modelo para herbicidas foi significativo ($p < 0,05$; $R^2 = 0,80$). Fungicidas apresentaram o maior coeficiente de determinação ($R^2 = 0,93$), enquanto inseticidas apresentaram o menor ($R^2 = 0,17$). Os valores de R^2 expressam a proporção da variância observada explicada por cada modelo e, isoladamente, não comprovam significância estatística nem causalidade. Os resultados indicam associações ecológicas exploratórias e devem ser interpretados com cautela devido ao pequeno número de observações anuais, ao uso de dados agregados e à possibilidade de confundimento e falácia ecológica.

Palavras-chave: Monocultura; Agrotóxicos; Mortalidade infantil.

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ABSTRACT

Pesticides are widely used in rural and urban areas and may pose risks to human health because of their toxic potential. This study aimed to investigate the ecological association between pesticide use and congenital malformations in Marialva, Paraná, Brazil. This quantitative ecological study used secondary data from 2015 to 2020. Information on live births, fetal deaths, infant deaths, and congenital malformations was obtained from SINASC, SIM, and DATASUS, whereas pesticide-use data were obtained from SIAGRO/ADAPAR. Exponential regression models were fitted to explore associations between the outcomes and total pesticide use and pesticide classes. During the study period, 3,127 live births and 37 infant deaths were recorded; 17 infant deaths were attributed to congenital malformations. The total-pesticide model was not statistically significant ($p > 0.05$; $R^2 = 0.39$). The herbicide model was significant ($p < 0.05$; $R^2 = 0.80$). Fungicides had the highest coefficient of determination ($R^2 = 0.93$), whereas insecticides had the lowest ($R^2 = 0.17$). R^2 represents the proportion of observed variance explained by each fitted model and, by itself, does not establish statistical significance or causality. These findings indicate exploratory ecological associations and should be interpreted cautiously because of the small number of annual observations, aggregate data, potential confounding, and the risk of ecological fallacy.

Keywords: Monoculture; Pesticides; Infant mortality.

RESUMEN

Los plaguicidas son ampliamente utilizados en áreas rurales y urbanas y pueden representar riesgos para la salud humana debido a su potencial tóxico. Este estudio tuvo como objetivo investigar la asociación ecológica entre el uso de plaguicidas y la ocurrencia de malformaciones congénitas en el municipio de Marialva, Paraná, Brasil. Se trata de un estudio cuantitativo ecológico con datos secundarios correspondientes al período de 2015 a 2020. La información sobre nacidos vivos, muertes fetales, muertes infantiles y malformaciones congénitas se obtuvo del SINASC, SIM y DATASUS; los datos sobre el uso de plaguicidas se obtuvieron del SIAGRO/ADAPAR. Se ajustaron modelos de regresión exponencial para explorar la asociación entre los desenlaces y el uso total y por clase de plaguicidas. Durante el período, se registraron 3.127 nacidos vivos y 37 muertes infantiles, de las cuales 17 fueron atribuidas a malformaciones congénitas. El modelo para el uso total de plaguicidas no fue estadísticamente significativo ($p > 0,05$; $R^2 = 0,39$). El modelo para los herbicidas fue significativo ($p < 0,05$; $R^2 = 0,80$). Los fungicidas presentaron el mayor coeficiente de determinación ($R^2 = 0,93$), mientras que los insecticidas presentaron el menor ($R^2 = 0,17$). Los valores de R^2 expresan la proporción de la varianza observada explicada por cada modelo y, de forma aislada, no demuestran significancia estadística ni causalidad. Los resultados indican asociaciones ecológicas exploratorias y deben interpretarse con cautela debido al pequeño número de observaciones anuales, al uso de datos agregados y a la posibilidad de confusión y falacia ecológica.

Palabras clave: Monocultivo; Plaguicidas; Mortalidad infantil.

1. INTRODUCTION

Proportional mortality due to congenital malformations has been progressively increasing and is among the leading causes of fetal mortality, representing a global problem; approximately 8 million children worldwide have some type of serious congenital defect¹.

The definition of Congenital Malformation (CM), according to the Pan American Health Organization (PAHO), encompasses any defect in the constitution of an organ or set of organs that determines a structural or functional morphological anomaly, present at birth or not, caused by genetic,



environmental, or mixed factors. They can be classified as isolated or associated, physical or mental, simple or multiple, and of greater or lesser clinical importance².

The etiology of congenital malformations is multifactorial, caused by complex interactions between genes and the environment, which modify normal embryofetal development, mainly during the organogenesis phase. In particular, environmental factors (e.g., pesticides, chemical toxins, infectious agents, maternal disease, and exogenous factors) can have pre-conception mutagenic action, teratogenic and postconception effects, periconceptional endocrine dysregulation, or epigenetic action. Regarding genetic causes, there are genetic chromosomal aberrations or dysgenesis.

The economy of many Brazilian cities is directly linked to agribusiness products, and this development model implies the increasing use of pesticides, which justifies concerns about the potential damage to public health in the medium and long term³.

But what are pesticides? They are synthetic chemical products used to kill insects, larvae, fungi, and ticks, under the justification of controlling diseases caused by these vectors and regulating vegetation growth, both in rural and urban environments. These are used in rural areas across numerous crops and in urban areas for the control of vector-borne diseases, but are potentially toxic to other organisms, including humans.

We know that the way humans are exposed to pesticides can vary, occurring environmentally through the air, consumption of residues in food and water, as well as occupationally during the application of inputs. In addition to these means of contamination and transmission, there is the problem of drift in pesticide applications, a serious agricultural problem that occurs when products are sprayed and reach extensive areas outside the intended location, contaminating soil, water, animals, and humans. Depending on the time they remain in the environment, pesticides can undergo transformations, that is, changes in their molecular structure, which can be mediated by light, temperature, chemical reactions (hydrolysis, oxidation, decarboxylation), or other biological agents (biodegradation). The more pesticides present, the smaller the number of microorganisms and the lower the biodegradation capacity. This situation extends the persistence time of the pesticide in the environment³⁻⁵. Temperature and crops also greatly influence the persistence of insecticides⁶⁻⁸.

The process of soil degradation caused by pesticides begins with sterilization - the elimination of flora and fauna - which contributes to erosion processes and increases the demand for the application of chemical products⁹. Micronutrient deficiencies, caused by the loss of biological activity in the soil, affect plant quality, making them susceptible to pests. This weakness demands increasingly higher and/or varied doses of pesticides, thus closing the cycle of soil contamination¹⁰.

Human exposure to pesticides can result in a wide range of chronic disorders, including some types of cancer, neurological, immunological, reproductive, teratogenic, and genotoxic effects. Some classes of pesticides, such as organochlorine substances and pyrethroids, have demonstrated the ability to alter the endocrine system, potentially interfering with the development of organs and tissues during the prenatal period¹¹.

The widespread use of pesticides raises public-health concerns regarding the safety of these products, possible health effects among exposed populations, potential associations with congenital anomalies, and the long-term consequences of exposure.

2. LITERATURE REVIEW

The proportional mortality rate due to congenital malformations has been progressively increasing and is among the leading causes of fetal mortality, representing a global problem affecting children worldwide⁴.

The definition of Congenital Malformation (CM), according to the Pan American Health Organization (PAHO), encompasses any defect in the constitution of an organ or set of organs that determines a structural or functional morphological anomaly, present at birth or not, caused by genetic,



environmental, or mixed factors. They can be classified as isolated or associated, physical or mental, simple or multiple, and of greater or lesser clinical importance. It can be identified during pregnancy, at birth, or a few days after birth. It can affect almost all parts of the baby's body, such as the heart, brain, feet, etc., compromising appearance, body function, or both.

According to the Pan American Health Organization (PAHO), approximately 8 million babies worldwide are born with this disease each year, and of that total, about 3 million die before their fifth birthday. In Latin America, congenital defects are responsible for 21% of deaths in children under 5 years old, and in the case of newborns, it is estimated that one in five dies during the first 28 days of life. In Brazil, congenital malformation is considered the second leading cause of death for babies and children - prematurity is the leading cause. Although not all congenital anomalies are fatal, many children who survive are at higher risk of long-term disabilities, requiring health and other support services to improve their quality of life.

Deaths can occur during the fetal stage (between 20-28 weeks) or when the fetus weighs more than 500 grams and is a product of conception before complete expulsion or extraction from the mother's body (WHO). An infant death is considered to be one that occurs within the first year of a child's life. Many factors can contribute to infant or fetal death, including maternal infections and diseases during pregnancy, trauma, placental, umbilical, amniotic, and uterine complications, and fetal growth restriction. Furthermore, fetal death can be related to multiple factors, including poverty, low education level, maternal age, overweight, medication use, smoking, drug use, diet, and contamination by external agents (pollution, pesticides).

2.1 Pesticides

Discussing pesticides and their potential effects on the environment and human health is complex, mainly because human exposure to them can occur environmentally, through the air, consumption via residues in food and water, as well as occupationally, during or after internal/external application. According to the National Cancer Institute (INCA), the average Brazilian citizen consumes 7.5 liters of poison per year due to the widespread use of pesticides. These numbers should raise significant public concerns regarding the safety of these products.

According to the World Health Organization (WHO), "[.] 20,000 deaths are recorded annually due to the consumption of pesticides [.]"¹²

According to INCA (Brazilian National Cancer Institute), "[.] exposure to pesticides can cause a number of diseases, depending on the product used, the exposure time and the amount of product absorbed by the body [.]"¹³

The economy of the city of Marialva-PR is directly related to agribusiness products, which are based on capital-intensive agriculture that utilizes energy and nonrenewable natural resources, harming the environment. This conventional model, in particular, involves the increasing use of pesticides, raising concerns about the potential damage to public health in the medium and long term, including congenital malformations³.

The main crops identified were table grapes, strawberries, lychees, avocados, tomatoes, vegetables, flowers, along with the production of soybeans, wheat, corn and pastures. All of these require the extensive use of pesticides in significant quantities¹⁴.

The grape production system currently practiced is highly dependent on the application of pesticides. In addition to the high use of pesticides, most producers do not bother to learn about the technological aspects related to product application and the control of diseases and weeds. This lack of interest is detrimental to human health and the environment, since it involves the use of toxic and harmful substances¹⁵.

Grape production is characterized by the extensive use of agrochemicals, especially fungicides, with an average of up to 2 applications per week. Drift that occurs during product spraying, as well as



leaching and surface runoff, transport pesticides to groundwater and surface water. The physicochemical properties of the agrochemicals, as well as the characteristics of the soils, are determining factors in this movement.¹⁶

In another study, contamination was proven, the study evaluated the potential for contamination of surface and underground waters by pesticides used in grape production, using the GUS Index (Groundwater Ubiquity Score) and the Goss method, through a survey of the main pesticides used in the region studied, through questionnaires verifying their toxicological and environmental classification, noting that more than 50% of the pesticides used in vineyard areas, whether certified or not, can cause a risk of contamination of water resources. Based on these models, some compounds used in grapevine management offer high and moderate potential for contamination of surface and groundwater.¹⁷

Even though some active ingredients, based on their acute effects, may be classified as moderately or slightly toxic, one cannot lose sight of the chronic effects that can occur months, years, or even decades after exposure, manifesting in various diseases such as cancers, congenital malformations, endocrine, neurological, and mental disorders. As an example, we have Carbendazim, which has already been withdrawn from several European countries due to its influence on genetic defects, its harmful effects on fertility and the fetus, and its extreme toxicity to aquatic life. In Brazil, within the program for analyzing pesticide residues in food, it was the most frequently found product between 2013 and 2015, and the third most prevalent in 2017 and 2018.¹⁸

In the city of Marialva, the most commonly used types of pesticides were herbicides, fungicides, and insecticides. These can cause various changes in the human body. For example, pesticides from the pyrethroid group, used in agriculture, in the domestic environment, and in public health campaigns as insecticides, are associated with several serious health effects.

Pyrethroid is a chemical compound similar to the natural substance pyrethrin (the active constituent of the flowers of the pyrethrum plant, better known as chrysanthemum), and is present in the formulas of many insecticides used, with a greater number of different active ingredients. Just look at the label of famous, wellknown, and widely used insecticides; they may have names like Transfluthrin, Deltamethrin, and Cypermethrin.

Cypermethrin, an agrochemical classified as highly toxic (class II), is toxic to rat embryos, including post-implantation fetal loss and visceral malformations¹⁹.

Similar effects - neonatal deaths and congenital malformations - have been described in humans in 60 cotton farmers¹⁹. The mutagenic and genotoxic potential of Cypermethrin has been demonstrated in different studies: chromosomal aberrations, micronucleus induction, sperm alterations, dominant lethal mutations and sister chromatid exchanges were observed in mice¹⁹.

In human lymphocytes treated with Cypermethrin, chromosomal aberrations and sister chromatid exchanges were also observed. In addition, Cypermethrin induced tumor promotion in mice and, when treated orally, changes in testosterone levels were observed with a consequent decrease in the number of spermatozoa, deleterious effects on reproductive organs, including after exposure in intrauterine life and also in rats exposed orally.¹⁹

Glyphosate is a systemic herbicide from the substituted glycine group that acts on cytochrome P-450, altering cell membrane synthesis in both plants and mammals. In plants, it interferes with the synthesis of the amino acids phenylalanine, tyrosine, and tryptophan. At low concentrations, it causes a deregulatory effect on the aromatase enzyme in human placental cells in vitro, reducing its activity and decreasing the expression of the StAR protein, evidencing an influence on malformations. Experimental assays with Wistar rats exposed orally demonstrated systemic toxicity and teratogenic effects, resulting in embryonic resorptions, stillbirths, and macroscopic skeletal malformations in fetuses.

¹⁹



2.2 Women's and Children's Health in Paraná/Marialva

In May 2012, the Governor of Paraná, Beto Richa, together with the State Secretary of Health at the time, Michele Caputo Neto, launched the Paraná Mother Network, aiming to improve the organization of care and assistance in prenatal, childbirth, postpartum, and monitoring the growth and development of children in their first year of life.

The intention was to reduce maternal and infant mortality through various actions, such as: organizing care processes, early reception of pregnant women in prenatal care, risk stratification and linking pregnant women, according to risk stratification, to the most appropriate hospital to attend to their delivery, as well as the training process for health professionals.

Following the State's proposal, the Municipal Health Department of Marialva observed the need for change in its municipal network, especially in women's and children's health care. To strengthen patient care and monitoring, nurses Patrícia Hernandez Soares (Family Health Strategy Coordination) and Débora C. M. Mori (Women's and Children's Health Coordination) were appointed. Upon assuming their coordination roles, with the assistance and participation of other Health Department employees, they developed and produced nursing protocols, provided training for doctors and nurses for Low-Risk Prenatal Care, decentralized prenatal care to Basic Health Units, standardized the first prenatal consultation with the nurse (including filling out the pregnant woman's card, registering her in the Prenatal SIS system, requesting tests according to protocol, performing rapid tests, stratifying the pregnant woman, referring her to a reference clinic when necessary, and scheduling a follow-up appointment with the doctor), implemented a monthly monitoring spreadsheet for pregnant women (allowing for the identification of care gaps), and implemented child health care in all health units. The municipality's gynecologists began to only provide care for high-risk pregnant women, as well as difficult-to-resolve cases and gynecological problems.

Other factors were relevant, such as greater availability of prenatal consultations, actions developed by community health agents that favored women's adherence to prenatal care, and childhood vaccination, which had a coverage of 111.16% that year.

When evaluating the indicator for the SISPACTO agreement of 2017, a significant reduction in the absolute number of infant deaths was observed in 2016, which was zero, compared to 2015, which was ¹⁰. Due to this, the coordinators received a national award for successful experiences in the SUS (Brazilian Public Health System), but this did not completely change the scenario or for very long, with a progressive increase in the number of deaths over the years. This situation caused concern and worried the Women's and Children's Health Management, leading them to determine other causes related to fetal/infant deaths, thus resulting in the present study.

2.3 Agroecology and Health Promotion

Exploring the conceptual approach to Agroecology and Health Promotion, one perceives the proximity between these scientific and practical fields, based on their common guidelines that seek to stimulate democracy, promote citizenship, and strengthen the autonomy and community participation of social actors, recover traditional and popular knowledge and practices, in addition to promoting health, quality of life, and sustainability at the environmental, social, and economic levels. However, despite their connections, these two fields have not been in dialogue. Agroecology and its imminent action of promoting health in rural areas have not been discussed in Public Health and Health Promotion; in turn, these areas are not producing or sharing knowledge that could contribute to strengthening Agroecology as a health promotion strategy.

There are several discussions about healthy food and health. In the Dietary Guidelines for the Brazilian Population, there is much discussion about the importance of improving the population's dietary and nutritional standards and contributing to the promotion of health (MINISTRY OF HEALTH,

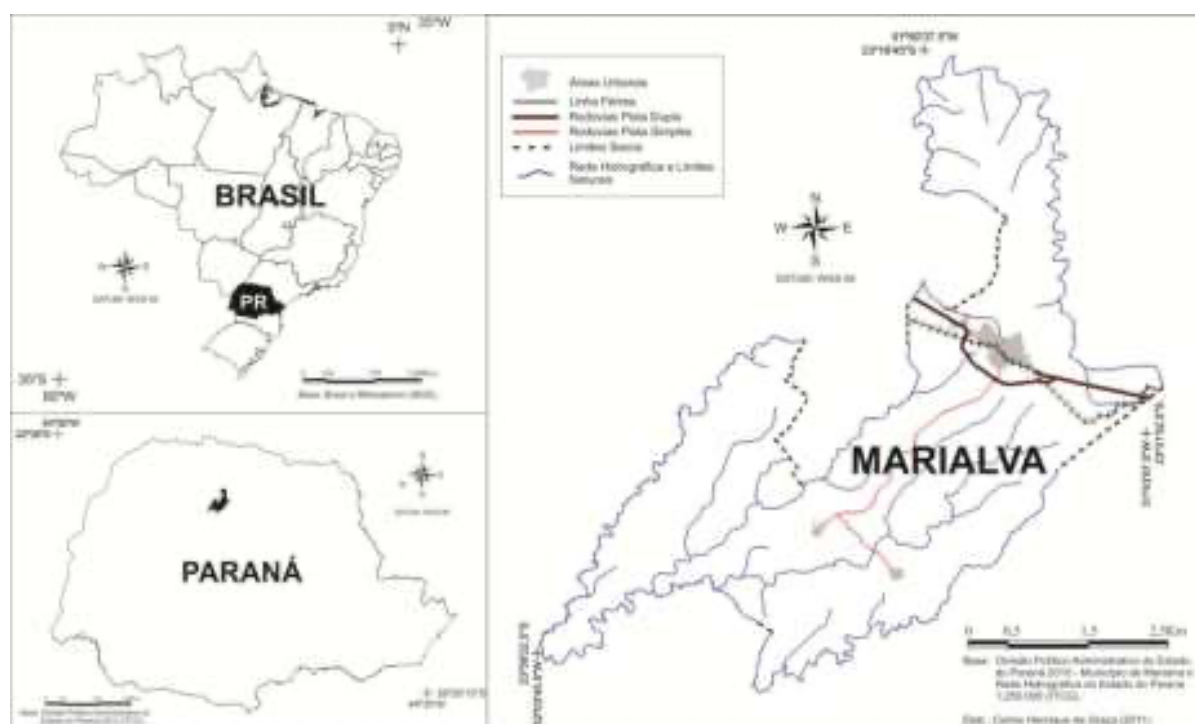


2014), however, in practice, agricultural plantations are still focused on quantity produced and not on quality.

3. METHODS

The study was conducted in the municipality of Marialva-PR, located in the North Central Paranaense Mesoregion, microregion of Maringá, known as the “Capital of Fine Grapes”. The municipality has a population of 41,851 inhabitants according to the 2022 Census, a territorial area of 475.564 km², and 44.4% of households have adequate sanitation. Agricultural establishments total 35,746 hectares, with 1,961 rural properties mapped by the agricultural census,²⁰ in addition to 2,172 properties included in the Rural Environmental Registry System (SICAR),²¹ with the Atlantic Forest as the predominant biome.

Figure 1. Location of Marialva in Brazil and Paraná, 2021.

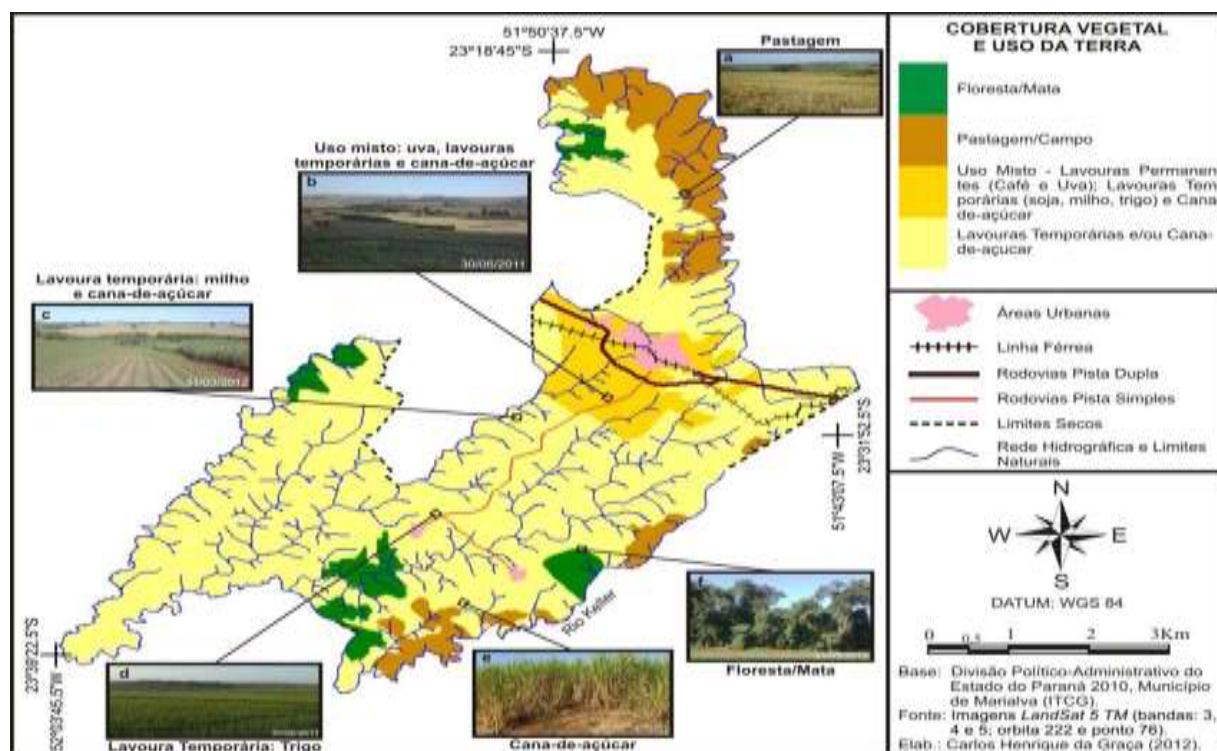


Source: Municipality of Marialva (2024).

The municipality of Marialva is located within two hydrographic basins: the Ivaí and the Pirapó. The Ivaí basin is important due to its hydraulic potential and the extent of its area in the overall composition of the hydrographic basins. Because of its intensive agricultural use, it is virtually associated with lands with greater soil suitability, thus presenting itself as one of the most critical in terms of the absence of native vegetation cover, requiring urgent measures for vegetation recovery. The Pirapó basin, on the other hand, was almost entirely occupied by artificial pasture, natural fields, areas of intensive agriculture, and small areas of forest cover. However, the soil characteristics of the region facilitated the modernization of agriculture aimed at intensive and extensive grain production to generate surpluses. This situation led to a rapid elimination of forests for agricultural occupation of the land and was the starting point for environmental imbalance, causing serious erosion problems. As a consequence, silting of waterways and deterioration of water sources that supply cities and serve other purposes occurred and continue to occur today. A large part of the basin is occupied by intensive agriculture.



Figure 2. Vegetation cover and land use in Marialva-PR.

Source: Graça et al. (2014).²³

There are several types of crops present in the city, encompassing large and small producers. The small producers are characterized by family farming with the cultivation of fruits such as table grapes, strawberries, lychees, avocados, tomatoes, as well as vegetables and flowers. The most significant is still the planting of table grapes, but other productions have been growing in recent years. Large producers follow the trend of the rest of Brazil with the production of commodities (soybeans, wheat, corn) and pastures.

For the present study, a quantitative, ecological approach was followed, covering the years 2015 to 2020 in the following order: bibliographic survey, collection of information from databases covering the periods from 2015 to 2020, SIM (Mortality Information System), SINASC (Live Birth Information System), TABNET (Information Technology at the Service of the SUS), SIAGRO (Monitoring System for the Trade and Use of Pesticides in the State of Paraná), ADAPAR (Paraná Agricultural Defense Agency), IBGE (Brazilian Institute of Geography and Statistics), and IPARDES (Paraná Institute for Economic and Social Development).

The death rates due to congenital malformation were obtained through the TABNET information system, using vital statistics data, and mortality from 2015 to 2020 by ICD. 10. Next, infant deaths are selected, followed by fetal deaths, following the same step-by-step process.

Data on the sale and consumption of pesticides were obtained through the Pesticide Trade and Use Monitoring System of the State of Paraná (SIAGRO).

Statistical and demographic data for the period from 2015 to 2020 were obtained from the Brazilian Institute of Geography and Statistics (IBGE) and the Paraná Institute for Economic and Social Development (IPARDES).

The analyses were ecological and used year as the unit of observation. Exponential regression models were fitted in R version 4.2.0, and statistical significance was assessed at the 5% level. The coefficient of determination (R^2) was interpreted as the proportion of observed variance in the annual

outcome index explained by each fitted model. Because the data were aggregated at the municipal level, the estimates were interpreted as ecological associations and not as evidence of individual-level exposure or causal effects.

4. RESULTS AND DISCUSSION

Analyses of statistical data on infant/fetal mortality, congenital malformations, and pesticide use are presented in the tables and figures below.

Table 1. Fetal deaths due to congenital malformations in Marialva-PR, 2015-2020.

Indicator	2015	2016	2017	2018	2019	2020	Total
Fetal deaths	0	-	0	0	0	0	0

Source: MS/SVS/CGIAE - Mortality Information System (SIM).

Table 2. Infant deaths due to congenital malformations in Marialva-PR, 2015-2020.

Indicator	2015	2016	2017	2018	2019	2020	Total
Infant deaths	4	0	0	2	4	7	17

Source: MS/SVS/CGIAE - Mortality Information System (SIM).

Table 3. Pesticide use and infant/fetal deaths due to congenital malformations in Marialva-PR, 2015-2020.

Variable	2015	2016	2017	2018	2019	2020
Total pesticides (t)	1,332.0	516.3	440.5	450.2	456.9	490.8
Herbicides (t)	488.6	296.2	266.9	280.0	294.1	315.3
Insecticides (t)	328.5	69.9	53.4	70.0	70.9	71.3
Fungicides (t)	255.1	57.9	48.3	49.8	46.5	59.7
Other pesticides (t)	259.9	92.4	72.0	50.5	45.4	44.5
Infant/fetal deaths due to congenital malformations	4	0	0	2	4	7

Source: SIAGRO/ADAPAR (2022) and SIM.

Table 4. Live births, infant deaths, and infant mortality rate in Marialva-PR, 2015-2020.

Year	Live births	Infant deaths	Infant mortality rate per 1,000 live births
2015	498	10	20.08
2016	543	0	0.00
2017	493	5	10.14
2018	487	5	10.27
2019	555	8	14.41
2020	551	9	16.33
Total/period	3,127	37	11.83

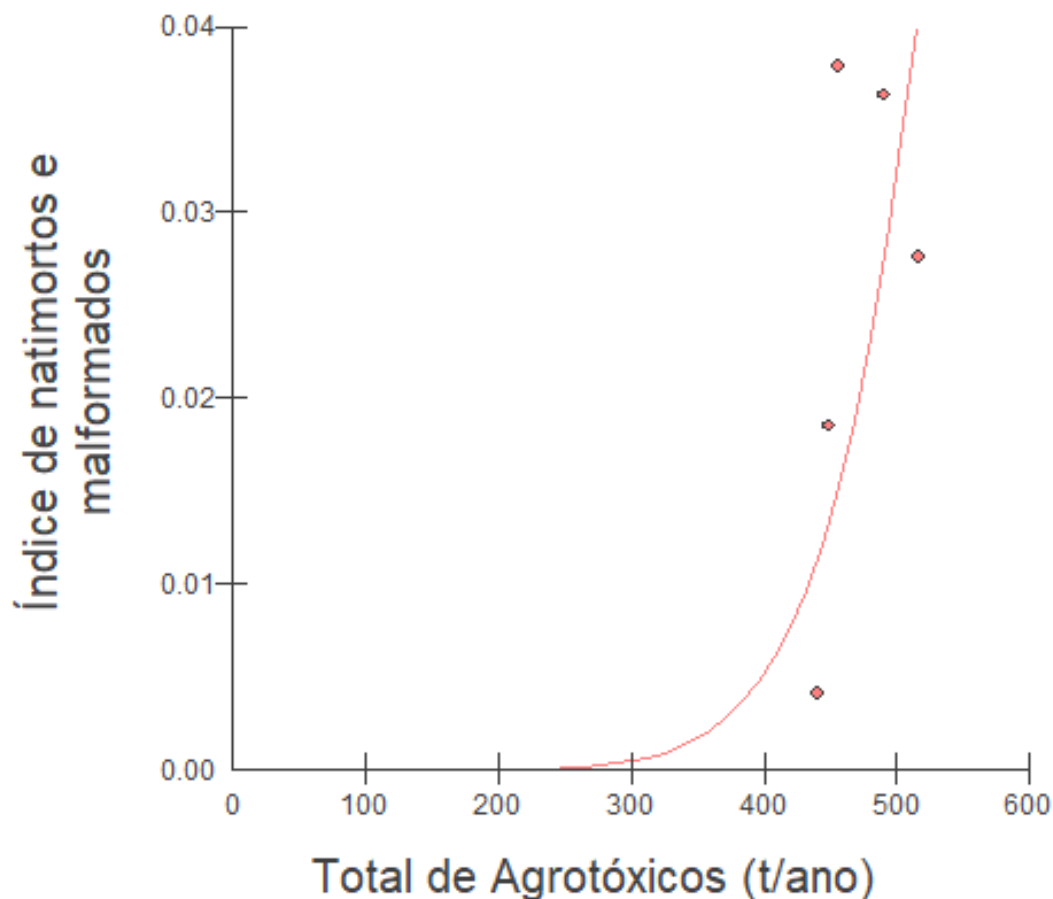
Source: SESA-PR, SIM/SINASC. Rates recalculated as infant deaths/live births x 1,000.

Across the 3,127 live births recorded from 2015 to 2020, 37 infant deaths occurred, corresponding to 11.83 deaths per 1,000 live births. Of these deaths, 17 were attributed to congenital malformations, representing 45.9% of infant deaths and 5.44 deaths per 1,000 live births. The value of 17 is consistent with the annual counts in Table 2 (4 + 0 + 0 + 2 + 4 + 7).



The underlying causes among the infant deaths attributed to congenital malformations included ICD-10 codes Q43, Q89.8, Q89.7, and Q89.2. In 2015, four deaths were recorded; in 2018, two; in 2019, four; and in 2020, seven.

Figure 3. Index of stillbirths and congenital malformations according to total pesticide use.



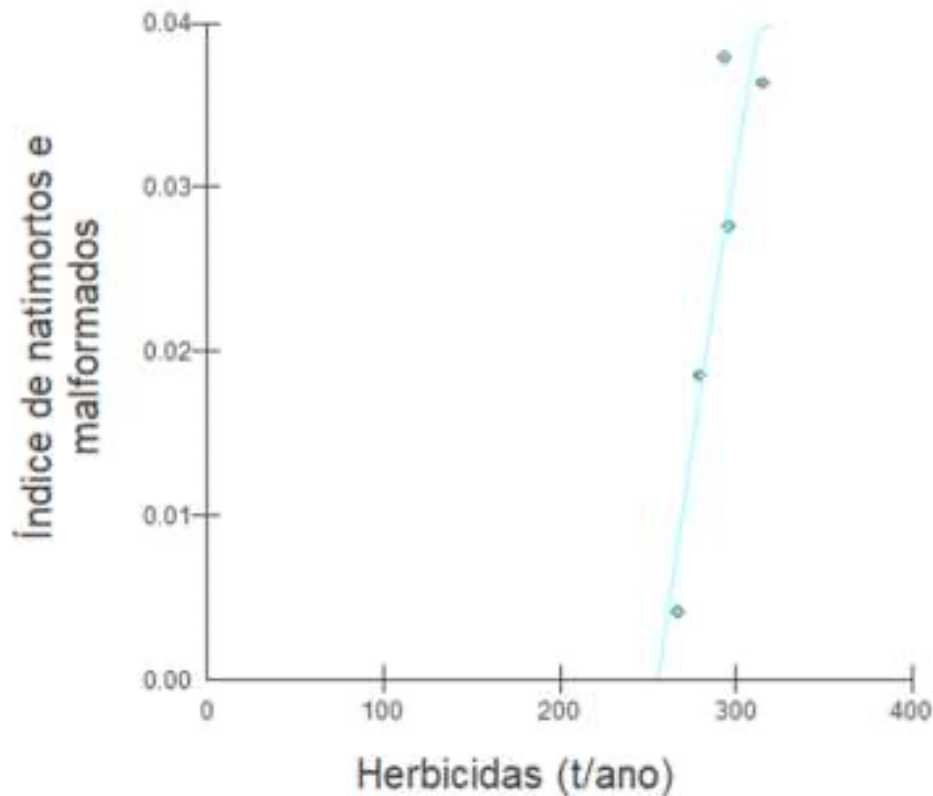
Source: the author (2024).

The exponential model for total pesticide use yielded $R^2 = 0.39$, indicating that 39% of the observed variance in the annual stillbirth and congenital-malformation index was explained by the fitted model. However, the association was not statistically significant ($p > 0.05$). Therefore, the observed pattern should be interpreted as exploratory and does not support the claim that total pesticide use directly influenced the outcome. The remaining 61% represents variance not explained by this model and cannot be attributed to specific unmeasured factors without additional analysis.

Although some annual observations between approximately 400 and 500 t/year coincided with higher outcome values, the small number of annual observations and the non-significant p-value preclude identifying an exposure threshold or a causal effect. Studies conducted in other settings have reported associations between maternal pesticide exposure and congenital malformations; however, those findings do not establish causality for the aggregate pattern observed in Marialva.²⁴



Figure 4. Stillbirth and congenital-malformation index according to herbicide use.



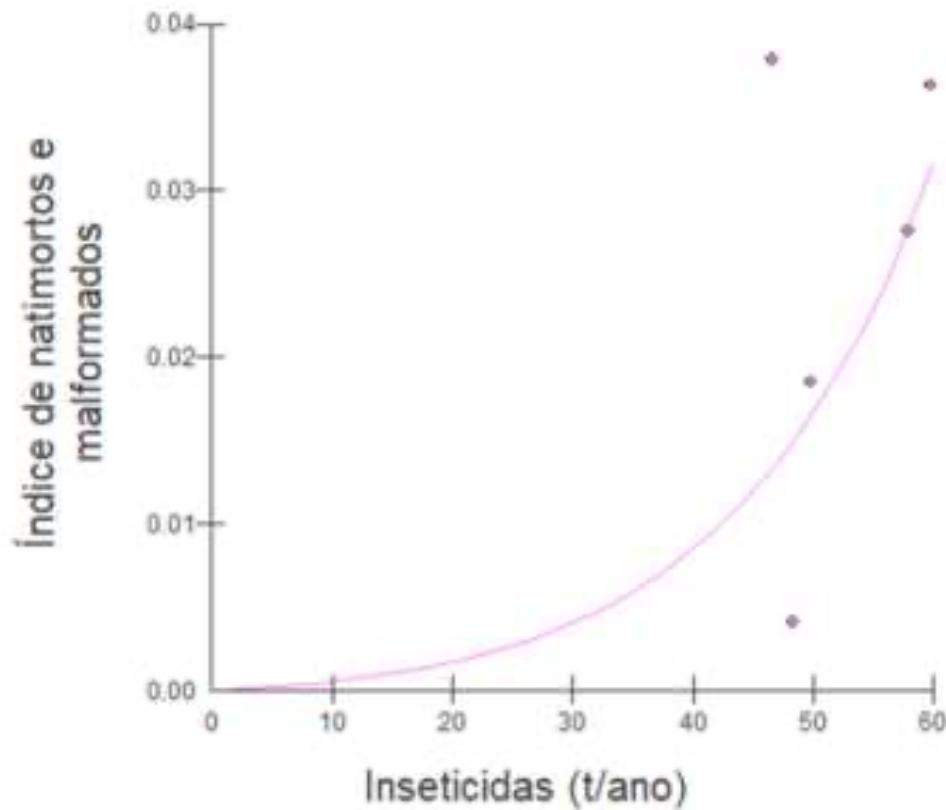
Source: the author (2024).

The herbicide model was statistically significant ($p < 0.05$) and had $R^2 = 0.80$. Thus, 80% of the observed variance in the annual outcome index was explained by the fitted exponential model. This finding indicates an ecological association with strong model fit, but it does not demonstrate individual maternal exposure or establish causality.

These findings are consistent with literature describing the toxic and teratogenic potential of several pesticide classes, including organophosphates, carbamates, pyrethroids, and organochlorines.²⁵



Figure 5. Stillbirth and congenital-malformation index according to insecticide use.



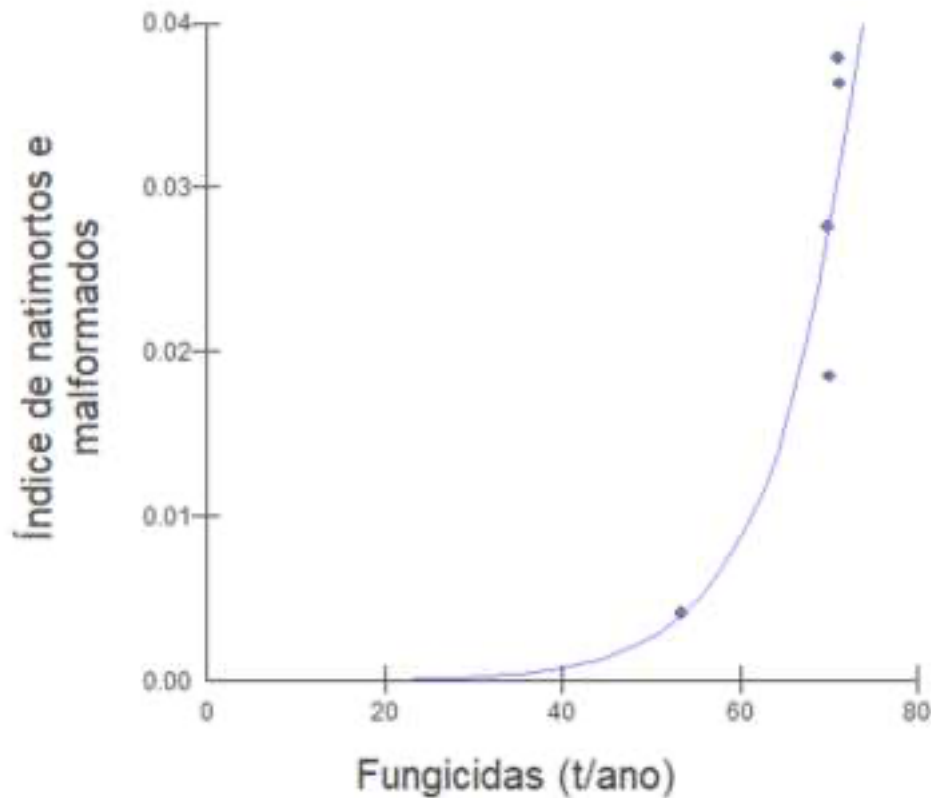
Source: the author (2024).

The insecticide model had $R^2 = 0.17$, meaning that it explained 17% of the observed variance in the annual outcome index. This was the lowest model fit among the three principal pesticide classes evaluated. Because R^2 does not test statistical significance or causality, this result should be interpreted only as a descriptive measure of model fit.

Previous research has described endocrine-disrupting substances in some pesticides and their potential relationship with congenital malformations in intensively agricultural municipalities.¹ These external findings provide biological and epidemiological context but do not establish causality in the present ecological analysis.



Figure 6. Stillbirth and congenital-malformation index according to fungicide use.

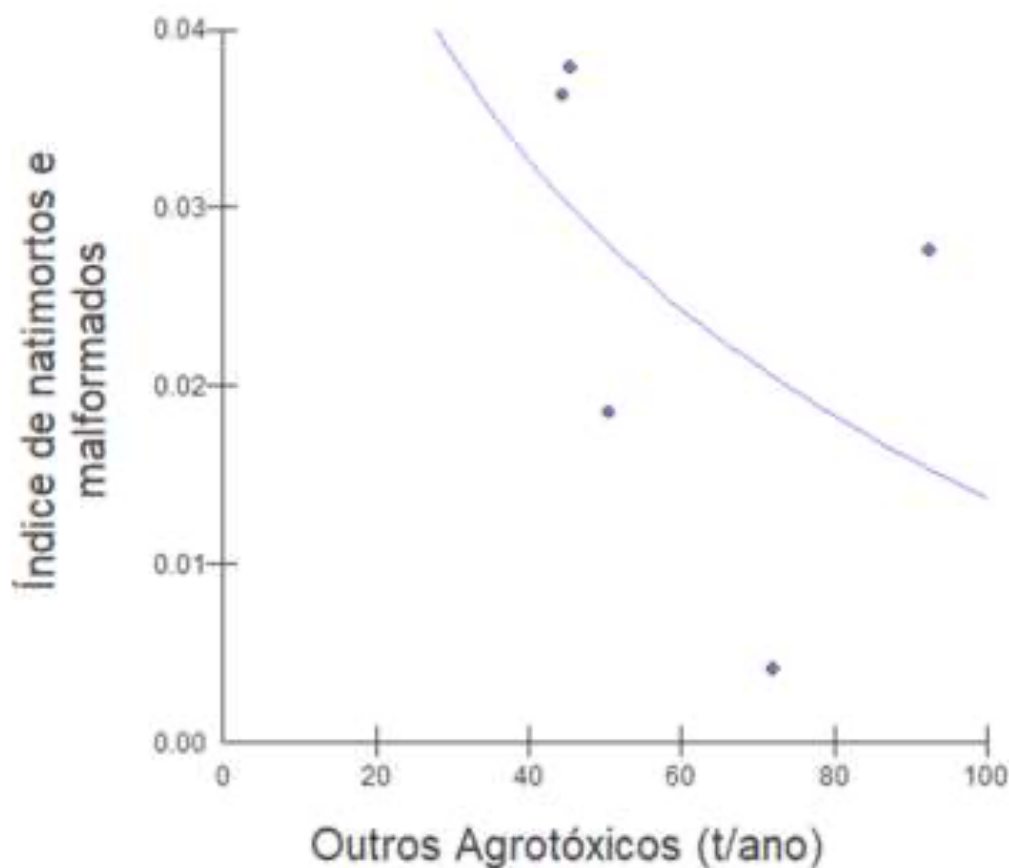


Source: the author (2024).

The fungicide model had $R^2 = 0.93$ and therefore explained 93% of the observed variance in the annual outcome index, representing the highest model fit among the pesticide classes evaluated. Nevertheless, no p-value for this model was reported in the available analysis, and a high R^2 alone does not establish statistical significance, a harmful effect, or causality.

Bourson et al.²⁶ reported that dietary exposure to pesticide residues before and during pregnancy may be associated with genetic instability and chromosomal alterations. Such evidence supports continued surveillance and hypothesis-driven studies, while the present aggregate results require cautious interpretation.

Figure 7. Stillbirth and congenital-malformation index according to other pesticide classes (nematicides, acaricides, etc.).



Source: the author (2024).

The group comprising other pesticide classes did not show a statistically significant association with the annual outcome index. Because each R^2 was obtained from a separate model, the coefficients must not be added or interpreted as components of a single 100% total.

Table 5. Relative comparison of model fit by principal pesticide class.

Pesticide class	R^2	Variance explained by fitted model	Statistical-significance information
Fungicides	0.93	93%	Highest fit; p-value not reported
Herbicides	0.80	80%	p < 0.05
Insecticides	0.17	17%	Lowest fit; p-value not reported

Note: Models were fitted separately; percentages are not additive. R^2 describes model fit and does not, by itself, demonstrate statistical significance or causality.

4.1 Limitations

This study has important limitations. First, it included only six annual observations, which limits statistical power and makes model estimates sensitive to individual years. Second, municipal pesticide-use data are aggregate measures and cannot be treated as individual maternal exposure. Third, the



analyses did not adjust for potential confounders such as maternal age, prenatal care, smoking, socioeconomic conditions, occupational exposure, comorbidities, or changes in notification and diagnostic practices. Consequently, associations observed at the municipal level may not apply to individuals, and causal interpretations would constitute ecological fallacy.

5. CONCLUSION

In this ecological analysis of Marialva from 2015 to 2020, fungicide and herbicide models had the highest coefficients of determination ($R^2 = 0.93$ and $R^2 = 0.80$, respectively), whereas the insecticide model had lower fit ($R^2 = 0.17$). The overall-pesticide model was not statistically significant ($p > 0.05$), and the herbicide model was reported as statistically significant ($p < 0.05$). Because statistical significance was not reported for all class-specific models, R^2 values must not be used as evidence of significance or causality.

The results indicate exploratory ecological associations rather than direct effects of pesticides on individual pregnancies. Aggregate exposure data, the small number of annual observations, unmeasured confounding, and the risk of ecological fallacy limit causal inference. Nevertheless, the findings support continued environmental and health surveillance in a municipality with intensive agricultural activity and justify future studies using individual-level exposure assessment, larger time series, and multivariable adjustment.

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