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Correlation Between Pesticide Use in Agriculture and Adverse Birth Outcomes in Brazil: An Ecological Study

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Abstract This ecological study analyzed the association between pesticide use and prematurity, low weight and congenital abnormality at birth, infant death by congenital abnormality, and fetal death in Brazil in 2001. Simple linear regression analysis has determined a positive association between pesticide use and prematurity, low birth weight, and congenital abnormality. The association between pesticide use and low birth weight ($p = 0.045$) and, congenital abnormality ($p = 0.004$) and infant death rate by congenital abnormality ($p = 0.039$) remained after the adjustment made by the proportion of pregnant women with a low number of prenatal care visits.

Keywords Pesticides · Birth weight · Preterm birth · Birth defect

Brazil accounts for approximately 50% of the agricultural pesticides consumed in Latin America (Agencia Nacional de Vigilancia Sanitaria 2005). Its use increased after the implementation of agriculture financing in the 70's (Waissmann 2007) and, recently, with the implementation of the National Family Farm Program – PRONAF (Kageyama 2003). From 1995 to 2005, herbicides, insecticides, fungicides, and acaricides were, in decreasing order, the most consumed types of pesticides in the country especially in soy, sugarcane, cotton, corn, and citrus crops (Ministerio da Agricultura, Pecuaria e Abastecimento 2005). Exposure to agricultural pesticides in the Brazilian population has been monitored through the National Program for Food Residues Analysis – PARA, which was implemented in 2001. This program was able to identify nonauthorized agricultural pesticides or pesticide levels above the maximum limit permitted in food samples. Some pesticides detected by the PARA, such as endosulfan, acephate, chlorpyrifos, dichlorvos, and methamidophos (Agencia Nacional de Vigilancia Sanitaria 2009), are the active ingredients for the development of endocrine disruption and reproductive toxicity, therefore increasing risks of adverse events on the human fetus (Peiris-John and Wickremasinghe 2008).

Experimental studies have shown that many agricultural pesticides have an impact on production, release, transport, metabolism, and elimination of hormones that regulate homeostasis and other developmental processes (Woodruff et al. 2008). In the human species, the exposure of one or both parents to agricultural pesticides have been related to prematurity risk increase (Fenster et al. 2006), low birth weight (Whyatt et al. 2004), congenital abnormality (Bell et al. 2001), and fetal death (Longnecker et al. 2005), among other reproductive health problems.

This ecological study performed an exploratory analysis on the correlation between pesticide use and prematurity, low birth weight and congenital abnormality at birth, infant

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death caused by congenital abnormality, and fetal death in Brazil using the national information systems.

Materials and Methods

The study analyzed data from 26 Brazilian states, excluding the Federal District, which is an agricultural distribution center to other states.

A total of 3,115,474 live births, 61,943 deaths of under one-year-old infants, and 38,759 fetal deaths that were registered in the year of 2001 were analyzed. The data were obtained from the National Information System on Live Births (SINASC) and the National Mortality Information System (SIM), which were made available by the Minister of Health (Ministerio da Saude 2001a, b).

The main exposure variable was an indicator of pesticide use constructed by The Brazilian Institute for Geography and Statistics (IBGE), which expresses the intensity of pesticide use in crop areas in 2000. Data from the National Systematic Survey of Agricultural Production and from the National Association of Agricultural Defensive Industries (SINDAG) were used for the calculation of ratio between the quantities of agricultural pesticide (active ingredient) sold and consumed in 2000 and the Kg/ha/year cultivated area (Ministerio do Planejamento, Orçamento e Gestao 2002).

The outcome variables were percentage of prematurity (pregnancy age <37 weeks), low birth weight (<2,500 g), congenital abnormality at birth (defined according to the International Classification of Diseases, ICD-10), proportional mortality by congenital abnormality, infant death rate by congenital abnormality, and rate of fetal death (stillbirths; Table 1).

The proportion and outcome rates per state were standardized for maternal age through the direct method considering the standard of age group distribution of mothers registered by SINASC. Records without information on weight at birth (0.1%), pregnancy duration (1.6%), congenital abnormality (11.1%), number of prenatal care visits (3.8%), maternal age (SINASC: 0.4%; SIM: 23.7%), and cause of death (10.0%) were excluded from the analysis.

A bivariate analysis was initially performed through the method of simple linear regression to test the association between the pesticide use variable and the outcomes. Considering the possible effect of prenatal care on the occurrence of the outcomes, the correlation between the exposure variable and the outcomes was adjusted by the proportion of pregnant women with a low number of prenatal care visits (0–3 visits) in a model of multiple linear regression. Regression coefficient (beta) and the Pearson correlation coefficient (r) were estimated. The normal distribution of the outcomes values was evaluated through the Kolmogorov–Smirnov test.

As Sao Paulo has a high value of pesticide use indicator (Table 2), the data analysis was performed including or not the state of Sao Paulo and comparing to other states, no significant difference was found in the beta and p values, except for the variable "percentage of prematurity" when Sao Paulo was included ($p = 0.028$). For that reason, data analysis was performed including São Paulo.

Statistical analyses were accomplished by the Minitab 14.0 and Stata SE 10.1 softwares. The significance level of 5% was considered. This study was approved by the ethics committee of Research of the Instituto de Medicina Integral Prof. Fernando Figueira – IMIP under the registration number of 1,515/2009.

Table 1 Definition of health and exposure indicators used in the analysis

Indicator	Description
Pesticide use (kg/ha/year)[1]	Ratio between the quantity of agricultural pesticide (active ingredient) used in 2000 and the area cultivated in kg/ha/year
Pregnant women with a low number of prenatal care visits (%)[2]	Live births infants whose mothers had 0–3 prenatal care visits in 2001
Prematurity (%)[2]	Live births with pregnancy duration below 37 weeks (×100) in 2001
Low birth weight (%)[2]	Live births with weight below 2,500 g (×100) in 2001
Congenital abnormality at birth (%)[2]	Live births with congenital abnormality according to chapter XVII (Q00-Q89) of CID-10 (×100) in 2001
Proportional mortality by congenital abnormality (%)[3]	Deaths by congenital abnormality among all deaths in under 1 year old infants (×100) in 2001
Infant death rate by congenital abnormality (per 1,000 live births)[2,3]	Deaths in under 1 year old infants caused by congenital abnormality in all live births (×1,000) in 2001
Rate of fetal death (per 1,000 live births)[2,3]	Fetal deaths of all live births and stillbirths (×1,000) in 2001

Sources [1] Ministerio do Planejamento, Orçamento e Gestao (2002); [2,3] Ministerio da Saude (2001a, b)

Table 2 Pesticide use distribution and magnitude of outcomes by States. Brazil, 2001

Region/state	Pesticide use (Kg/ha/2000)[1]	Pregnant women with a low number of prenatal care visits (%)[2]	Prematurity (%)[2]	Low birth weight (%)[2]	Congenital abnormality at birth (%)[2]	Proportional mortality by congenital abnormality (%)[3]	Infant death rate by congenital abnormality (per 1,000 live births)[2,3]	Rate of fetal death (per 1,000 live births)[2,3]
Northern Region								
Rondonia	0.78	18.30	4.89	5.43	0.36	8.06	0.62	7.91
Acre	0.02	44.16	4.80	6.22	0.18	7.25	0.87	10.12
Amazonas	0.11	30.95	5.79	6.30	0.47	9.94	1.89	10.61
Roraima	2.71	24.93	5.02	6.69	0.17	20.93	2.14	8.95
Para	0.45	24.85	6.36	6.07	0.35	6.55	1.19	10.92
Amapa	0.46	36.34	5.95	8.07	0.25	10.35	1.72	11.27
Tocantins	0.71	23.61	5.82	6.43	0.32	7.62	1.29	12.02
Northeast Region								
Maranhao	0.70	32.92	6.96	6.78	0.21	8.67	1.34	11.87
Piaui	0.21	20.14	4.47	6.31	0.15	7.56	1.13	12.86
Ceara	0.13	15.13	5.16	6.46	0.28	6.99	0.67	6.64
Rio Grande do Norte	0.46	16.96	5.71	7.35	0.47	11.01	1.11	9.53
Paraiba	0.34	13.11	6.38	6.08	0.68	7.25	0.47	6.22
Pernambuco	1.37	20.63	4.90	7.03	0.70	8.63	1.66	10.91
Alagoas	1.90	31.63	4.01	6.26	0.33	4.77	0.61	9.80
Sergipe	0.58	18.77	4.79	7.29	0.32	4.59	0.64	13.95
Bahia	0.99	28.00	6.24	7.26	0.30	6.71	0.75	8.21
Southeast Region								
Minas Gerais	2.87	12.49	6.52	9.14	0.52	11.70	1.17	8.38
Espirito Santo	1.76	12.41	5.14	7.60	0.37	12.80	1.18	8.34
Rio de Janeiro	2.71	10.74	6.92	9.03	0.62	15.20	2.31	11.52
Sao Paulo	8.05	7.17	7.11	8.98	0.61	16.72	1.44	9.39
Southern Region								
Parana	3.44	7.04	6.37	8.25	0.57	16.08	2.35	10.17
Santa Catarina	3.03	9.46	5.96	7.80	0.66	18.03	1.73	6.18
Rio Grande do Sul	2.62	13.38	7.49	8.95	0.79	17.09	1.81	8.07
Midwest Region								
Mato Grosso do Sul	4.03	11.64	7.57	6.72	0.45	13.86	2.94	15.42
Mato Grosso	3.33	10.56	5.21	6.24	0.53	9.68	1.30	9.99
Goias	4.22	10.71	5.76	7.20	0.42	17.13	1.97	8.81

Sources [1] Ministerio do Planejamento, Orçamento e Gestao (2002); [2,3] Ministerio da Saude (2001a, b)

Results and Discussion

The pesticide use indicators and the outcome rates by regions and states are shown in Table 2. The greatest consumers of agricultural pesticides are the States of Sao Paulo (Southeast region), Goias, and Mato Grosso do Sul (Mid-West region), with pesticide use values above 4 kg/ha/year. The percentage of prematurity varied from 4.0% in the State of Alagoas to 7.6% in Mato Grosso do Sul, whereas the low birth weight percentage varied from 5.4% in the State of Rondonia to 9.1% in Minas Gerais. The lowest percentage of congenital abnormality at birth was found in the State of Piaui (0.2%) and the highest in the State of Rio Grande do Sul (0.8%). Proportional mortality by congenital abnormality varied between 4.6% in Sergipe and 21.0% in Roraima. The lowest rate of infant death by congenital abnormality registered was 0.5/1,000 live births in the State of Paraiba and the highest 2.9/1,000 live births in Mato Grosso do Sul. The States of Mato Grosso do Sul (15.4/1,000 live births), Sergipe (14.0/1,000 live births), and Piaui (12.9/1,000 live births) showed the highest fetal death rates.

Table 3 presents the results of the crude and adjusted linear regression analyses between pesticide use and the outcomes investigated. A statistically significant positive correlation between pesticide use and low birth weight was observed in the bivariate analysis (beta = 0.31; 95% CI: 0.11–0.51; $p = 0.004$). This association remained with a positive correlation ($r = 0.31$) after adjustment in the multiple linear regression model (beta = 0.26; 95% CI: 0.006–0.52; $p = 0.045$).

Pesticide use was positively associated to proportional mortality by congenital abnormality in under one-year-old infants (beta = 1.71; 95% CI: 0.95–2.46; $p < 0.001$) as well as infant death rate by congenital abnormality (beta = 0.17; 95% CI: 0.04–0.29; $p = 0.012$) as determined by bivariate statistics. The correlations between pesticide use and both outcome variables remained, with r values ranging from 0.24 to 0.49 after adjustment by the variable "proportion of pregnant women with a low number of prenatal care visits."

Although a positive correlation between pesticide use, percentage of congenital abnormality at birth (beta = 0.04; 95% CI: 0.007–0.08; $p = 0.022$), and percentage of prematurity (beta = 0.22; 95% CI: 0.02–0.42; $p = 0.028$) has been observed in the bivariate analysis, these associations disappeared after adjustment by the "proportion of pregnant women with a low number of prenatal care visits." No correlation between pesticide use and fetal death rate (beta = −0.06; 95% CI: −0.570 to 0.459; $p = 0.827$) was found.

The data suggest a possible impact of agricultural pesticide consumption on the rates of low birth weight and infant mortality because of congenital abnormality in Brazil. The estimate is that for each unit of increase in the indicator value of agricultural pesticide consumption (Kg/ha/year), there is an average increase of 0.3% in the percentage of low weight, an average increase of 1.5% in the proportional mortality by congenital abnormality, and an average elevation of 0.17/1,000 live births in the rate of infant death by congenital abnormality.

These results should be interpreted with caution because of possible inconsistent data in the information systems used, and the possibility that results at an aggregate level are not reflecting at an individual level must be considered as well.

Although the effect of pesticide exposure on fetal growth is not yet conclusive in humans (Peiris-John and Wickremasinghe 2008), the association between paternal or maternal exposure to agricultural pesticides and adverse outcomes in the offspring have been demonstrated in experimental studies in animals (Woodruff et al. 2008). In humans, the exposure of one or both the parents to various chemical groups has been related to low birth weight (Whyatt et al. 2004).

The data showed a relation between pesticide use and deaths due to congenital malformations. Teratogenic effects

Table 3 Crude and adjusted regression analysis (by number of prenatal care visits) in association with pesticide use (kg/ha/2000) and adverse reproductive outcomes. Brazil 2001

Indicators	Crude analysis			Adjusted analysis		
	Beta	r	p-value	Beta	r	p-value
Prematurity (%)[2]	0.22	0.44	0.028	0.18	0.45	0.151
Low birth weight (%)[2]	0.31	0.55	0.004	**0.26**	**0.56**	**0.045**
Congenital abnormality at birth (%)[2]	0.04	0.45	0.022	0.01	0.65	0.664
Proportional mortality by congenital abnormality (%)[3]	1.71	0.70	<0.001	**1.52**	**0.70**	**0.004**
Infant death rate by congenital abnormality (per 1,000 live births)[2,3]	0.17	0.49	0.012	**0.17**	**0.49**	**0.039**
Rate of fetal death (per 1,000 live births)[2,3]	−0.06	0.04	0.827	0.18	0.24	0.580

Bold values represent statistically significant

Sources [1] Ministerio do Planejamento, Orçamento e Gestao (2002); [2,3] Ministerio da Saude (2001a, b)

resulting from agricultural pesticide exposure have been observed in urogenital, cardiac, nervous, and musculoskeletal systems (Thulstrup and Bonde 2006). Although the results of the studies in the human populations are controversial, some have determined relationship between an occupational or domestic exposure to agricultural pesticides and the increased genetic malformation risk in fetuses of different population groups (Dolk et al. 1998). Among the ecological studies investigating agricultural pesticide exposure and specific congenital malformations, there are divergences on the findings for the nervous, circulatory, urogenital, and musculoskeletal systems and labial and palate clefts (Nurminen 1995).

Fetal death and prematurity rates were not correlated to pesticide consumption in this study, although some epidemiological studies have determined such an association (Longnecker et al. 2005; Fenster et al. 2006). This result could be reflecting failure in the monitoring of fetal deaths, as well as the low accuracy of data on gestational age obtained by the health care services in the country.

This study reinforces the evidence of the possible effect of agricultural pesticide exposure in the occurrence of low birth weight and congenital abnormality in Brazil, as indicated by Perera et al. (2003) and Thulstrup and Bonde (2006). Large observational prospective studies are required to further evaluate the impact of pesticides on reproductive health. Furthermore, the monitoring of populations exposed to agricultural pesticide needs to consider adverse outcomes in the concept, such as congenital malformations and low birth weight.

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