Revista Facultad Nacional de Salud Pública Revista Facultad Nacional de Salud Pública

ISSN: 0120-386X ISSN: 2256-3334

Universidad de Antioquia

Benavides, John Alexander; Malagón-Rojas, Jeadran N.; Lagos, Luisa Fernanda; Bahia-Coelho, Thereza Christina; Vasquez-Lozada, Yenny Alejandra; Quintana-Cortés, Mónica Alejandra; Díaz-Gómez, Alejandra del Pilar; Hernández, Mario A.

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Revista Facultad Nacional de Salud Pública, vol. 41, no. 3, e05, 2023, September-December Universidad de Antioquia

DOI: https://doi.org/10.17533/udea.rfnsp.e351613

Available in: https://www.redalyc.org/articulo.oa?id=12076139005



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Intoxicación aguda por plaguicidas: Comparación de características epidemiológicas entre la población rural y urbana

Intoxicação aguda por agrotóxicos: comparação de características epidemiológicas entre a população rural e urbana

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Recibido: 24/10/2022. Aprobado: 25/07/2023. Publicado: 22/08/2023

Benavides JA, Malagón-Rojas JN, Lagos LF, Bahia TC, Vásquez A, Quintana MA, Díaz-Gómez AP, Hernández MA. Acute pesticide poisoning: Comparison of epidemiological characteristics between the rural and urban population. Rev. Fac. Nac. Salud Pública. 2023;41(3):e351613. DOI: https://doi.org/10.17533/udea.rfnsp.e351613

Abstrac

Objective: To analyze the behavior of pesticide poisoning in rural and urban populations associated with lethality in Colombia during 2007-2017. **Methodology:** Retrospective observational study that included: a descriptive cross-sectional study and an ecological design that analyzed aggregate measures of morbidity, mortality and risk attributable to the population in rural and urban areas. In the cross-sectional study,

the relative risk was estimated to measure the factors associated with lethality among intoxications using Poisson regression with logarithmic function. For the time series, the trends were established with simple linear regression and the seasonal decomposition was performed using the multiplicative model. Autocorrelations were tested using the Box-Ljung statistic. **Results:** Between 2007-2017; 89 490 cases were reported. The

Morbidity due to poisoning showed a higher proportion in the rural population 36.03 cases per 100 000; this indicator was three times higher than in urban areas (12,33 cases per 100 000). The mortality rates in rural and urban areas were 1,00 and 0,13 cases per 100 000, respectively. The relative risk of fatality in case of intoxication was associated with the intention of suicide in the rural population RR: 5.9 (95% CI: 5.0-6.9).

Conclusion: A higher proportion of lethality associated with these events occurred in populations living in rural areas and reporting cases of suicidal intent. In addition, morbidity and mortality due to pesticide poisoning had the highest proportion in rural areas and a growing trend over time.

-----Keywords: Rural Population, mortality, urban population, pesticides, poisoning

Resumen

Objetivo: Analizar el comportamiento de las intoxicaciones por plaguicidas en poblaciones rurales y urbanas asociadas a la letalidad en Colombia durante 2007-2017. Metodología: Estudio observacional retrospectivo que incluyó: un estudio descriptivo transversal y un diseño ecológico que analizó medidas agregadas de morbilidad, mortalidad y riesgo atribuibles a la población en áreas rurales y urbanas. En el estudio transversal se estimó el riesgo relativo para medir los factores asociados a la letalidad entre las intoxicaciones mediante regresión de Poisson con función logarítmica. Para la serie de tiempo, las tendencias se establecieron con regresión lineal simple y la descomposición estacional se realizó mediante el modelo multiplicativo. Las autocorrelaciones se probaron mediante el estadístico Box-Ljung. Resultados: Entre 2007-2017; Se notificaron 89 490 casos. La Morbilidad

Resumo

Objetivo: Analisar o comportamento das intoxicações por agrotóxicos em populações rurais e urbanas associadas à letalidade na Colômbia durante 2007-2017. Metodologia: Estudo observacional retrospectivo que incluiu: estudo transversal descritivo e delineamento ecológico que analisou medidas agregadas de morbidade, mortalidade e risco atribuíveis à população em áreas rurais e urbanas. No estudo transversal, o risco relativo foi estimado para medir os fatores associados à letalidade entre as intoxicações por meio da regressão de Poisson com função logarítmica. Para as séries temporais, as tendências foram estabelecidas com regressão linear simples e a decomposição sazonal foi realizada usando o modelo multiplicativo. As autocorrelações foram testadas usando a estatística Box-Ljung. Resultados: Entre 2007-2017; 89.490 casos foram notificados. A Morbidade por

Introduction

Food production is mainly based on monocultures that limit the entire agroecosystem, produce an intense imbalance of homeostasis, and promote the appearance of different pests [1]. A control method for this production model is encouraging the intensive use of pesticides, which increases the exposure concentration of these products among farmers [2].

This exposure is usually linked to adverse health outcomes. Acute pesticide poisoning is the most frequent event associated with pesticide exposure because signs and symptoms occur quickly after exposure and present a high possibility of complications [3]. On the other hand, chronic exposure to pesticides is linked to a greater risk of presenting chronic neurological disorders, pathologies, such as cancer, and chronic kidney disease [4,5,6].

Even though there are no exact estimates, the World Health Organization (WHO) reported one million cases of unintentional severe poisoning per year worldwide, leading to approximately 20 000 deaths [7]. Seventy percent of these poisonings occurred due to occupational exposure. Additionally, one million hospitalizations were reported for suicide attempts using these substances. Of these suicide attempts, 300 000 resulted in death. However, a recent systematic review of the scientific literature published between 2006 and 2018 estimated that about 385 million cases of unintentional poisoning for pesticides occur annually worldwide including around 11 000 fatalities [8,9]. Additionally, the annual incidence of acute pesticide poisoning in agricultural workers has risen to 18,2 cases per 100 000 workers [7].

Some authors have indicated that suicidal intention and living in rural areas are the most frequent causes of death associated with pesticide poisoning. In Jiangsu, China, 38 513 poisoning cases were reported, of which 7891 were occupational pesticide poisonings in rural areas and 16 569 were suicides caused by poisoning [10]. In Nepal, 439 cases of suicide were reported, with almost 90% of the cases carried out by self-harm and 71,3% of the cases occurred in rural areas [11]. Furthermore, in Gujarat, India, approximately 70% of poisoning cases occurred in people living in rural areas, and more deaths happened from suicidal poisoning than accidental poisoning [12].

In Colombia, between 2008 and 2015, 209 823 cases of chemical poisoning were detected by the surveillance health system, first by pesticides (32,2%), followed by medications (30,1%) [13,14]. However, few studies on rurality and pesticide poisoning in Colombia have been performed. Additionally, no analysis on the behavior of mortality and morbidity has been carried out over time, and the estimation of risk factors associated with fatality

due to poisoning has not been established for pesticides. Furthermore, most national and international studies have not compared the distribution of pesticide poisonings between rural and urban areas to understand if there is an additional risk of poisoning due to differences in the rural context.

Furthermore, agricultural policies and markets have led to an increase in the number of hectares dedicated to monocultures, which requires greater pesticide usage to ensure productive harvests. The increase in pesticide usage implies higher exposures to these chemicals, increasing the risk for accidental and nonaccidental poisonings.

In this context, this work aimed to analyze the behavior of pesticide poisoning in rural and urban populations through time series and to determine the risk factors associated with fatal cases in Colombia during 2007-2017.

Methodology

Type of study

This is a retrospective observational study that included two components: a descriptive cross-sectional study that considered the individual the unit of analysis and an ecological design that analyzed aggregate as measures of morbidity and mortality of the population in rural and urban areas during 2007-2017.

Population

The population was constituted by the reported cases of exogenous intoxications compiled by the National Public Health Surveillance System (SIVIGILA) in the Chemical Substances Poisoning Surveillance System.

Data source

The information was compiled by the National Institute of Health between 2007 and 2017. These records came from all public and private hospitals and clinics in the country. The SIVIGILA collects the mandatory notifications of intoxication by chemical substances weekly. Each report constitutes an epidemiological week (a year is constituted by 52 epidemiological weeks).

Definition of the case and data curation

All the reported cases of exogenous intoxication involving a pesticide in Colombia between 2007 and 2017 were included. At the time of the development of this research, 2017 was the last year available for analysis. The database was reviewed, excluding duplicate cases. No imputation method was used to manage the missing data. The name of the pesticide was not included due to a loss of more than 20% of the data.

Variables

Sociodemographic, exposure, clinical outcome and place of occurrence of the poisoning (rural or urban) were analyzed. The Public Health Surveillance Protocol Poisoning by chemical substance from INS (2011, 2014 and 2017) was used as source of definition of external intoxication [15,16,17]. The definition remained unchanged during the described period of time. In addition, the definition of rural areas from the National Department of Statistics (DANE) was used: "rural areas are outside of the location of the county seat, which is characterized by the dispersed locations of houses and farms" [18].

In addition, the variable of cases with suicidal intentions was defined as all intoxication associated with self-inflicted injury behavior. Additionally, the variable of ethnicity was defined as intoxication in a person who belonged to an indigenous, gypsy, Raizal, Palenquero or Afro-Colombian group [18].

Statistical analysis

In the cross-sectional study, continuous variables were presented as proportions or means, with standard deviation. Then, a bivariate analysis was performed, comparing the variables with the place of occurrence (urban or rural), using a chi-square test. Statistical significance was defined as a p-value < 0,05. Statistical analysis was performed with SPSS software, version 25, licensed from EAN University.

The risk-related measures for lethality associated with pesticide poisoning were estimated using *Poisson* regression with a logarithmic function.

The dependent variable was fatal events due to pesticide exposure. The following independent variables were considered: sex, age, suicidal intention, ethnicity, place of occurrence, educational level, and clinical treatment. The *Poisson* regression model allowed us to estimate the risk of lethality, calculated from the beta exponent measurement. The RR was estimated for adjusted and unadjusted models [19].

Finally, each risk measure was evaluated stratifying by rural and urban areas. In addition, the measure of association of the interaction between the independent variables and the rural population were calculated, considering a significant $p_{int} > 0.05$. All models were adjusted for sex and age. Morbidity and mortality measures were adjusted for age by the indirect method with the WHO standard population [20].

For the ecological study, morbidity and mortality rates were estimated in the general population and in rural and urban areas. These measures were presented as proportions, where the numerator was the total number of cases of poisonings and fatal poisonings reported by the SIVIGILA. In addition, the denominator was the population estimate of the DANE for rural and urban

populations and each year of the time series [21]. Morbidity and mortality measures were adjusted for age by the indirect method [22].

Additionally, to establish the excess risk of mortality associated with pesticide poisoning in the population living in rural areas, the population attributable risk (PAR) and the corresponding 95% confidence intervals for each year were calculated [23]. The excess risk expresses the difference between mortality in the general population and mortality in the rural population.

Finally, the aggregated means were analyzed through an exploratory time series analysis, using the epidemiological week as the time unit. First, mortality, morbidity and PAR trends were described in the time period with a simple linear regression. Then, the coefficient (R²) was estimated for these indicators. The R² indicator provided information on the strength of the association and the direction of the relationship between mortality, morbidity, and PAR with time [24].

Subsequently, the time series was constructed using 52 epidemiological weeks for each year. Additionally, a seasonal decomposition was performed using the multiplicative model of the time periods. The data was presented as a graphical representation of the time series [22]. Additionally, a predictive time series model for one year was built. Finally, the trend component of the model was expressed with seasonal R².

Model fit tests

Different tests were used to evaluate the sensitivity of the models. In the case of Poisson regression, the chi-square goodness-of-fit test and the omnibus contrast were used [19]. In the case of the time series analysis, the independence of distribution was tested using the Box-Ljung test [21]. The Box-Ljung test allowed for the identification of the independence of the distribution.

Ethical Considerations

This project used the records of the SIVIGILA public health vigilance database. To carry out the study, all the variables that allowed the identification of the cases were eliminated, which guaranteed confidentiality and data management, complying with the biomedical research regulations of the country.

Results

Between January 2007 and December 2017, 89 490 cases were reported to the SIVIGILA. A list of sociodemographic characteristics of the reported cases is presented in Table 1. A higher proportion of poisonings among men living in rural areas compared to those who lived in urban areas (66% vs. 49.9%: p < 0.001) was observed.

Regarding the types of cases, occupational exposure was found to be higher in rural populations (rural areas 26,3% vs. urban areas 9,6%, p < 0,001). Furthermore, suicidal intention was lower in rural areas than in urban

areas (67,7% vs. 47,9%). In addition, it was observed that fatal cases occurred more often in populations living

Table 1. Characteristics of Poisoning and Pesticides, Colombia, 2007-2017

	cs of poisoning by 2007-2017 period	Url	oan	Ru	ral	To	tal	р
		N	%	n	%	n	%	-
Cov	Feminine	25038	50,1%	13410	34,0%	38448	43,0%	000
Sex	Masculine	24957	49,9%	26085	66,0%	51042	57,0%	- ,000
	< 14	8269	16,5%	5194	13,2%	13463	15,0%	
Age groups (years old)	15 -39	33430	66,9%	26242	66,4%	59672	66,7%	_ ,000
,	40- 64	7184	14,4%	6971	17,7%	14155	15,8%	
	> 65	1104	2,2%	1085	2,7%	2189	2,4%	
Education level	Secondary or higher level	28023	56,1%	12758	32,3%	40781	45,6%	,000
	Basic level	21972	43,9%	26737	67,7%	48709	54,4%	
Belonging to an	No	46426	92,9%	34869	88,3%	81295	90,8%	- ,000
ethnic identity	Yes	3569	7,1%	4626	11,7%	8195	9,2%	,000
Marital status	Married or domestic partnership	19091	38,2%	18399	46,6%	37490	41,9%	,000
	Single	30904	61,8%	21096	53,4%	52000	58,1%	
Type of case with	No	16139	32,3%	20560	52,1%	36699	41,0%	00
suicidal intention	Yes	33856	67,7%	18935	47,9%	52791	59,0%	- ,00
Type of case as	No	45181	90,4%	29122	73,7%	74303	83,0%	
occupational exposure	Yes	4814	9,6%	10373	26,3%	15187	17,0%	,000
D	No	49440	98,9%	38383	97,2%	87823	98,1%	
Deadly case	Yes	555	1,1%	1112	2,8%	1667	1,9%	- ,000
Case of	Yes	30244	60,5%	19594	49,6%	49838	55,7%	
hospitalizing because of poisoning	No	19751	39,5%	19901	50,4%	39652	44,3%	,000
Type of case	Laboratory confirmation	2000	4,0%	1489	3,8%	3489	3,9%	
confirmation	Clinical confirmation	47478	95,0%	37677	95,4%	85155	95,2%	,002
	Epidemiological link	517	1,0%	329	0,8%	846	0,9%	-
	Respiratory	5431	10,9%	9038	22,9%	14469	16,2%	
-	Oral	38112	76,2%	22624	57,3%	60736	67,9%	
Exposure manner	Dermic/mucous	5587	11,2%	6956	17,6%	12543	14,0%	,000
	Other exposure	865	1,7%	877	2,2%	1742	1,9%	

in rural areas (rural 2,8% vs. urban 1,1%), with poor access to health services.

For the *Poisson* regression model, it was found that the risk of lethality for suicide intention was higher among the rural population risk: 5,9 (95% CI: 5,0–6,9) than in urban areas risk: 3,0 (95% CI: 2,3–3,8). (p_{int} < 0,001). The risk of lethality of ethnic and low educational levels had a significant association, increasing lethality in both rural and urban areas (Table 2).

In urban areas, the nonhospitalized population had a protective factor for lethality (RR: 0,856 (95% CI: 0,72–1,018): However, these associations were not statistically significant. conversely, the risk of dying was higher among the people who resided in rural areas who were not hospitalized (RR: 1,51 (95% CI: 1,34–1,7)). This difference of receiving hospital care and living in rural areas was statistically significant ($p_{int} < 0,001$) (Table 2). Nevertheless, it was observed that the population older than 65 years living in urban areas had an RR of 4,3 (95% CI: 3,2–5,7).

Cases of suicidal intention for people living in rural areas who reported ethnic belonging showed a greater RR: 8,6 (95% CI 6,9–10,6) compared to the same population in the urban areas, RR: 5,2 (95% CI % 3,7–7,4) (p_{int} < 0,001) (Table 2).

In addition, the accumulated rate of morbidity in the general population for all time periods was 24,18 cases per 100 000 inhabitants adjusted per age. In rural areas, the accumulated rate of morbidity was 36,03 cases per 100 000 inhabitants (Figure 1A). This indicator was three times higher than that in urban areas (12,33 cases per 100 000). The accumulated mortality rate for all cases was 0,57 cases per 100 000 inhabitants. The mortality rates in rural and urban areas were 1,00 and 0,13 cases per 100 000, respectively. In addition, an upward mortality and morbidity trend was found in the time periods in rural areas ($R^2 = 0.65$ and 0.16, respectively) (Figure 1B). Finally, there was a notable difference in the behavior of the mortality rate according to the place of occurrence of the event. The PAR was 69,6% (95% CI 54,2-89,3%). Additionally, an increasing trend of this indicator was observed throughout the time period $(R^2=0,2498)$ (Figure 1C).

Regarding the time series analysis, there was no evidence of a seasonal factor in mortality and morbidity because this indicator did not vary more than 20% between time periods. Additionally, an exponential smoothing model was selected only for morbidity in rural areas, because this indicator adjusted for distribution independence (p: Ljung-Box Q: 0,180); this model showed an upward trend ($R^2 = 0,279$) (Figure 2).

Discussion

Table 2. Factors associated with suicide and crude and adjusted Relative Risk (RR) in rural and urban populations

			Rural	area					Urbar	Urban area			
Factor	RR unadjusted	IC 95% lower	IC 95% higher	RR adjusted*	IC 95% Iower	IC 95% higher	RR unadjusted	IC 95% lower	IC 95% higher	RR adjusted*	IC 95% Iower	IC 95% higher	PINT
Suicide	5,371	4,590	6,285	5,906	5,028	6,937	2,790	2,204	3,531	3,000	2,366	3,805	<0,001
Ethnic identity	1,870	1,614	2,166	1,870	1,613	2,167	1,786	1,383	2,306	1,847	1,430	2,385	<0,001
No Hospitalization	1,481	1,314	1,670	1,514	1,341	1,708	0,876	0,737	1,042	0,856	0,720	1,018	<0,001
Low Education Level	1,303	1,141	1,488	1,332	1,164	1,524	1,626	1,375	1,922	1,568	1,324	1,857	<0,001
Older than 65 years	2,234	1,742	1,742 2,865	2,340	1,822	3,006	4,578	3,441	6,091	4,307	3,227	5,749	<0,001
Suicide and ethnic identity (interaction)	7,803	6,290	9,681	8,601	6,915	10,698	4,686	3,325	6,604	5,258	3,722 7,429	7,429	<0,001

Adjusted for age and sex

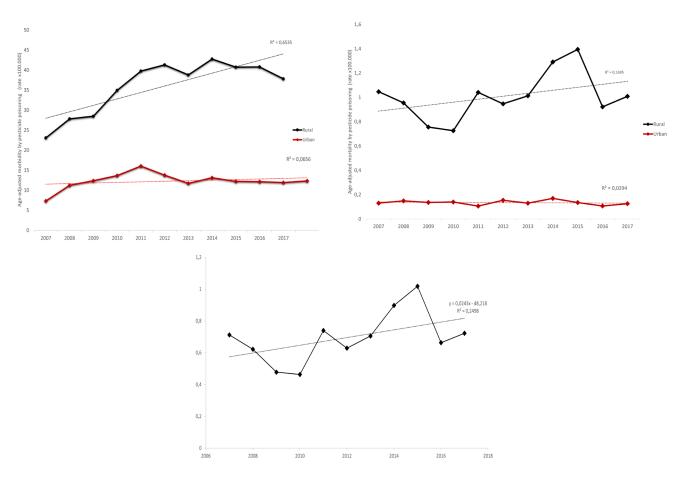


Figure 1. A) Morbidity by pesticide poisoning in rural and urban areas. B) Mortality by pesticide poisoning in rural and urban areas C) Risk attributable to mortality rural areas, 2007-2017

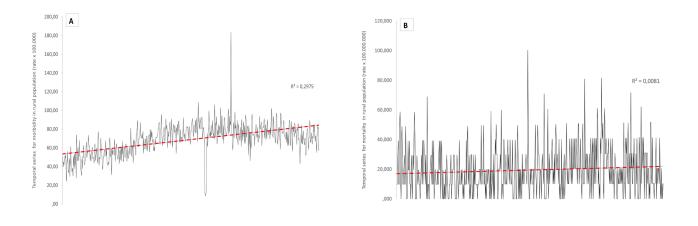


Figure 2. A) Trend for Morbidity, Colombia, 2007-2017 B) Trend for Mortality, Colombia, 2007-2017.

The objective of this work was to analyze pesticide poisoning in rural and urban populations through a time series analysis and estimate the relative risks associated with lethality in Colombia. More than 87 000 cases of exogenous intoxication were found during 2007–2017. To our knowledge, this is one of the largest reported record series of acute pesticide poisoning [7].

A seasonal factor was not observed in the time series analysis. Nevertheless, a growing trend in morbidity and mortality was observed, mainly in rural areas.

An increase in the population attributable risk of mortality was observed among rural populations. Additionally, an increased risk of lethality related to pesticide poisoning was found associated with living in rural areas and ethnicity. These results were similar to those of several studies, including that of Wang and associates [25], who performed a descriptive cross-sectional study in the province of Jiangsu, and reported 38 513 cases of pesticide poisoning over 12 years. Out of the cases reported in that study, 71,69% were due to suicidal intention, but the report did not study the difference between rural and urban populations. The study by Gyenwali and associates [11], a descriptive epidemiological study, found 439 cases of acute pesticide poisoning from 12 districts of Nepal, of which 89,5% were due to suicidal intention; 71,3% occurred in rural residents and 37,8% reported ethnic belonging.

Additionally, a positive interaction was found between suicidal intention and living in a rural region with an increase in lethality for pesticide poisoning. These results are comparable with some reports from the literature that describe the practice of taking pesticides as a usual method of suicide in rural areas [26]. In Gujarat, India, of 1092 identified poisoning cases, 69,59% were in rural areas, and 42,94% were by suicide, in Malaysia, a total of 11 087 pesticide poisoning cases were recorded and 93.6% of cases of intentional pesticide poisoning were caused by suicide attempts [12,27]. In addition, the WHO indicates that suicide has increased in agricultural workers due to poor harvests [28].

A high proportion of cases of suicidal intention due to acute pesticide poisoning was reported, particularly in rural areas. This may be explained by the easy access to pesticide products in the rural context. Troya and associates [29] showed that access to pesticides can be identified as a suicide risk factor in rural areas. Likewise, in Latin America, it has also been stated that the characteristics of suicides in rural areas include the use of pesticides as a common method [30]. Finally, several studies reported high suicide and lethality rates for suicide with pesticides in ethnic populations [31,32]. Therefore, the WHO and The Food and Agriculture Organization highlight the effects of restrictive measures against the use of pesticides. For example, programs adopted in countries such as Sri Lanka, where prohibition and se-

vere restriction of pesticides led to a 70% reduction in suicides, and an estimated 93 000 lives were saved between 1995 and 2015 [28].

Studies have documented the increase in suicide cases in the population with chronic exposure to pesticides in recent years [33,34,35]. This suggests that future research with prospective designs should consider the chronic and acute exposure to pesticides, the thoughts and behaviors in different ethnic groups, and the social factors associated with suicide in rural populations.

One of our main findings was an increasing trend of suicidal behavior, especially in rural areas, but this trend did not have an association with seasonality. This may be explained by the fact that Colombia has rainy and dry seasons. This allows farmers to have intensive farming practices during the entire year that require a greater usage of pesticides. Growing pesticide commercialization has been observed in Colombia during the last ten years [36]. In contrast, some studies carried out on farmers from nontropical areas have reported an increase in suicide cases during the summer period [25,37].

In addition, our analysis showed an increased risk of lethality in reported cases that occurred in rural areas and for those who did not receive medical attention. The lack of medical attention in rural areas has been highlighted as a determinant of poor clinical outcome in these areas [28].

An accumulated mortality rate of 0,57 cases per 100 000 inhabitants was observed in the 2007 – 2017 period. In contrast, other studies in a similar time period have reported decreasing trends in mortality for populations in India and Germany [25,37]. However, a higher mortality rate was reported for the populations in El Salvador and Nicaragua in a similar period [38]. Finally, a study carried out in Colombia using death certificates to determine deaths from pesticide poisoning, reported 4835 deaths between 1998 and 2011, and an age-adjusted rate of 2,38 deaths per 100 000 inhabitants with annual death averages higher than our findings and a decreasing trend in mortality since 2002 [14].

Our study had several limitations. First, there are limitations related to the source of the information. This study was based on records from epidemiological surveillance systems for patients who received medical attention. This may introduce a record bias. This disparity shows a potential source of underregistration for fatal and nonfatal events, especially for cases of unintentional mild work-related poisoning. Furthermore, these data are not associated with ICD-10 codes, introducing an additional bias in the analysis. In addition, the definition of intoxication of the Surveillance Protocol Poisoning by chemical substance from INS 2011 and 2017 was used for our study. The definition remained almost unchanged during the described period of time. Nevertheless, the definition and protocol for the external poisoning from 2007 to 2010

wasn't available and this may represent a bias in the data collected in these period of time.

Second, it was not possible to establish which products were involved in suicidal intentions. There was a lack of information related to the active ingredient associated with poisoning in more than 20% of the reported cases. Although Colombia has adopted the Globally Harmonized System since 2015, information related to the active ingredient in the product is not often known by rural farmers. Workers and relatives tend to report the popular names of chemical products, which can vary from region to region. This implies a limitation for clinical attention and the surveillance system.

Finally, a common bias of time-series studies includes confusion resulting from measured and unmeasured time, affecting the relationship between the main exposure and the result. We tried to control this bias by including additional explanatory variables in the regression model. However, this research did not have access to medical records to include additional variables that may have affected the outcomes.

In conclusion, the mortality and morbidity for pesticide poisonings in rural areas of Colombia have shown a trend of increase throughout the period 2007-2017. A higher risk of lethality associated with these events occurred in rural populations belonging ethnic. And, in population was reported as suicidal intent. These results can be used by health and academic institutions to prevent non-occupational and occupational poisoning by pesticides. The Surveillance Protocol Poisoning by chemical substance should include a differential rural and ethnic perspective that should be included in the public policy instruments. In addition, it should be tacked into account that the clinical guidelines may consider sociodemographic aspects in order to prioritize management of referral to specialized clinical centers. Finally, the surveillance may include a preventive actions through the local health and safety committees and health bureaus.

Funding source

The authors wish to thank the Ministry of Science. Technology and Innovation for the financial support provided through project code 1223-777-57906 - contract 619-2018. The main author wishes to thank the Coordination for the Improvement of Higher Education Personnel of Brazil (CAPES) for the doctoral scholarship

Conflicts of interest statement

All authors declare that they have no conflicts of interest.

Declaration of responsibility

The authors are responsible for all information provided in the document. There is no responsibility of the institution of affiliation of the authors and of the financiers.

Declaration of contribution by authors

All the authors contributed to the research with the generation of the research idea, the study design and the implementation of the program in each of the academic units; data collection, and together with all the authors worked on the draft of the article, and the critical review of its content.

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