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Environmental Exposure to Glyphosate and Risk of Asthma in an Ecological Study

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Abstract

There is strong evidence of the link between asthma and occupational exposure to pesticides and even glyphosate in agricultural workers, but it is limited on asthma and environmental or residential exposure to these chemicals. This research analyzes the prevalence of asthma in an agricultural town with high use of pesticides, mainly glyphosate. Is an ecological study conducted in Monte Maíz, Argentina, composed of a chemical and environmental analysis to determine the burden of exposure to glyphosate and pesticides in general, and a crosssectional asthma study that uses the methodological criteria of the International Study of Asthma and Allergies in Childhood (ISAAC); the prevalence?s found in Monte Maíz are compared with the results of ISAAC in Argentine cities with low exposure to pesticides. In Monte Maíz area 975 tons of pesticides are sprayed (650 are glyphosate) that are also stored inside the town.

Index terms— asthma, environmental exposure, pesticides, glyphosate, environmental health.

1 Introduction

sthma is the most commonly occurring chronic childhood disease in the world (1,2). According to the Global Asthma Report 2014 (GAR 2014), 14% of the world's children and 8.6% of young adults experience asthma (3). Childhood asthma is particularly prevalent in Latin America, and the International Study on Asthma and Allergic Diseases in Children (ISAAC) has identified environmental contamination as a key factor in the region's elevated rates of the disease (1). The International Study of Asthma and Allergies in Childhood (ISAAC) surveyed a representative sample of 798,685 adolescents aged 13-14 years in 233 centres in 97 countries between 2000 and 2003. In ISAAC these adolescents were asked whether they had experienced wheeze, a symptom that is commonly attributable to asthma or use of bronchodilator aerosols.

Globally, too, exposure to environmental toxins explains the rise in asthma rates (4,5). Epidemiological studies reveal an association between pesticide exposure and increased prevalence of asthmas, while experimental testing has shown that certain pesticides generate immunological imbalances characteristic of asthma, fortifying the link between occupational exposure to pesticides and asthma, especially in farmers (6,7). However, there is a gap in knowledge with respect to asthma and residential environmental exposure to pesticides, especially glyphosate.

In Argentina, asthma is a serious health problem, causing more than 400 deaths and 15,000 hospitalizations annually (8,9). As elsewhere in South America, rates of pesticide application have increased dramatically in Argentina with the expansion of transgenic crops since the mid 1990s (10,11).

Transgenic crops now cover an area of 25 million hectares in Argentina. In 2013, 318,000 tons of pesticides were applied within the country's borders, including 250,000 tons of glyphosate (11). Most of these pesticides were applied in a region where about 12 million people reside. Concurrent with these changes, doctors in the region report a shift in the morbidity and mortality profile of rural populations (12). Along with other conditions, wheezing and asthma are now frequently detected.

Monte Maíz (Province of Córdoba) is a town located in the heart of Argentina's main agricultural region where inhabitants have expressed concern about an apparent increase in diseases that were previously perceived

as infrequent. A group of neighbors headed by their Mayor requested an evaluation of the health status of their local population from a research team at the Division of Medical Sciences of the National University of Córdoba (UNC).

In this context, a study was carried out in order to determine if there had been an increase in the prevalence of cancers, reproductive, endocrine and immunological problems, and asthma linked to a greater burden of exposure to pesticides. The objective was to analyze the environmental exposure to pesticides as a risk factor for the above-mentioned pathologies (and determine if any particular pesticide is preponderant), and to correlate environmental factors in order to develop a causality hypothesis. The results of the analysis of cancer and reproductive disorders have already been published (13,14), while those of asthma provide the basis for this article.

2 II.

3 Material and Methods

This ecological study was designed to test for possible correlation between residential exposure to pesticides and the prevalence of asthma in Monte Maíz by comparing local rates of disease with those measured by ISAAC in Argentine cities with low or no residential exposure to pesticides. The study comprises both an analysis of chemicals in the environment, and a cross-sectional study of asthma prevalence. The latter was carried out via the administration of a populational survey designed to georeference each datum acquired utilizing census radii from the National Census Institute (map in Figure 1). The presence or absence of asthma was recorded not according to existing medical diagnosis, but rather in accordance with ISAAC's previously validated survey instrument (15). ISAAC's questionnaire is based on questions such as whether the respondent experienced wheezing in the last year, or use of bronchodilator aerosols. This study's implementation of ISAAC's survey instrument facilitates comparison between the data generated elsewhere by ISAAC and the data generated in Monte Maíz.

The environmental analysis reviewed and georeferenced garbage dumps, industrial sites, grain stockpiles, and pesticide deposits in each census radius. Through the synthesis of information acquired from interviews with key informants (agronomists, farmers and pesticide applicators), pesticide application rates were determined to calculate the burden of exposure.

The burden of exposure was then verified by measuring quantities of the most commonly used pesticides in soil and volatile grain dust (from pulverized grain husk). Sampling was carried out by researchers from the Center for Environmental Research at the National University of La Plata. Pretreatment and analysis of the samples were carried out in accordance with international regulations using mass spectrometry and liquid chromatography (16,17).

The study area was Monte Maíz, a town of 7,788 inhabitants, located at 33º12'south latitude and 62º36' west longitude. The study population comprised all inhabitants of Monte Maíz, with a special focus on children 6 and 7 years old, and 13 and 14 years old from across the entire town. Children from these age groups were analyzed against the control population: children from those same age groups who live in three large Argentine cities (Buenos Aires, Rosario and Córdoba), who were evaluated by ISAAC. The data from this study has also been evaluated against the data on asthma prevalence reported by the Argentine Society of Pediatrics and Ministry of Health of the Nation (9).

In the statistical analysis, asthma was the dependent variable. The independent variables were sex, age, occupation, time living in the area of study, smoking, premature birth, radius of residence within the town, and education. Asthma prevalence rates were generated by age groups. To investigate the relationship between the variables, a multivariate study was carried out using principal component analysis. The association between asthma and independent variables was analyzed by Pearson's bivariate correlation. Contingency tables were created to measure the levels of risk in the most significant correlations, both with a 95% confidence interval. The INFOSTAT (UNC), SPSS and EPIDAT (PAHO) programs were used. Environmental and asthma maps were constructed using the Quantum GIS 2.4 program. This study was conducted in accordance with the Declaration of Helsinki and Law No. 9694 of the Province of Córdoba, which regulates human health research (19).The health surveys were carried out by students and professors of the UNC's medical program, and the environmental analysis was carried out by members of the School of Geography. All the teams worked simultaneously and the fieldwork was completed in October 2014.

4 III.

5 Results

6 a) Epidemiological Study

Every home in the town was visited by the survey teams. In some homes there was no one to answer and in 4.8% the inhabitants declined to respond to the survey. Data were collected from 4,959 people, some 62% of the population. Demographic composition is represented in table 1.

The general asthma rate of the population was 16.2%. Among them 22% were smokers and 4.3% reported a history of neonatal prematurity. The prevalence in the 18 to 40 year-old group was 12.6%, higher than that of the entire country (5.9%) according to the National Asthma Prevalence Survey of 2015 (19), with an OR:

2.32 (CI: 1.79 -3.01). In children aged 13 and 14, the prevalence was 39.9%, while in those aged 6-7 years it reached 52.4%.In three large Argentine cities, ISAAC detected a prevalence of asthma of 13.6% among children aged 13-14 (20). In Monte Maíz, children of the same age group had a prevalence of 39.9%, with an OR of 4.64 (CI: 3.26-6.60). The principal components analysis positively linked asthma with children, negatively with smokers, and found no association with any particular occupations. In Pearson's Bivariate Correlations there was a positive spatial relationship with the inhabitants of radii 16 and 17, but it had no bilateral significance with people with direct participation in agricultural activity (significance value: 0.295).

The probability of suffering asthma was higher (OR: 1.43 [CI: 1.18 -1.72) for residents living near grain storage sites in the south-southwest direction in radii 16 and 17. The asthma prevalence rate in children 6-7 and 13-14 years-old in those sectors were 53.3% and 42.8% respectively, the highest among all the radii of the town.

7 b) Environmental analysis

The population of this region is concentrated in the town of Monte Maíz, which has quality drinking water and an adequate sewer network. Urban solid waste is accumulated in an open-air dump located 800 meters from the town, in which no occurrences of fire or combustion have been reported for more than five years. To the south of the town there are two metallurgical factories which produce agricultural equipment and use methane gas as fuel. Forests or grasslands on the periphery of the town have been replaced by crops. These crop fields, which are in many cases adjacent to homes, receive systematic applications of pesticides. The agricultural area of Monte Maíz comprises 65,000 hectares. Of these, 45,000 hectares are planted with transgenic soybeans and 20,000 hectares with transgenic corn (both glyphosate resistant). In the winter season, 15,000 hectares of wheat are sown. Agronomists and pesticide applicators interviewed report that soybean and corn crops consumed 10 kg of glyphosate and 5 kg of additional pesticides (including atrazine, 2-4D, chlorpyrifos, endosulfan, cypermethrin, and epoxiconazole) per hectare per year. As a whole, the area of study consumes 975,000 kg of pesticides annually, of which 650,000 kg are glyphosate. This constitutes a general environmental burden of pesticide exposure of 121 kg per person per year, and of glyphosate in particular of 81 kg per person per year. This environmental burden varies depending on individuals' occupational or residential proximity to agricultural activity. The national pesticide exposure burden is 7.9 kg per person per year, and 6 kg of glyphosate per year (see table **??**). In Monte Maíz there are huge silos and grain stores which release pulverized soy and corn into the air. A predominantly northeast to southwest bearing wind carries the dust towards radii 16 and 17(see location in Figure 2). Chemical analyses confirmed the high exposure estimated based on interview data. Glyphosate and ácido aminometilfosfónico (AMPA, its metabolite) were detected in 100% of the soil and dust samples. Glyphosate and AMPA concentrations exceeded concentrations of other pesticides in all samples, averaging concentrations of 505 and 607 ppb, respectively, followed by chlorpyrifos (14 ppb) and epoxiconazole (2.3 ppb) (see table 3).

The samples of the site square no. 6 (see map figure 2) contain 68 times more glyphosate than the soil of a cornfield of site no. 5. Samples from site No. 8, taken from the soil of the pedestrian path of a pesticide deposit, is where the highest concentrations of all pesticides were detected. As elsewhere, concentrations of glyphosate (3868 ppb) and AMPA (3192 ppb) far exceed concentrations of other pesticides, such as endosulfan II (338 ppb), and chlorpyrifos (242 ppb) (see in table 3).

8 Medical Research Volume XXI Issue I Version I

9 Discussion

In Monte Maíz, industrial pollution is minimal, there has been no combustion of waste in the landfill in the last 5 years, and a good standard of living prevails. However, with the proliferation of transgenic crop production since the mid 1990s, pesticide deposits have multiplied in the area, now numbering twenty-two.

At least 975,000 kilos of pesticides per year are applied in fields surrounding Monte Maíz, and concentrations found inside the town were several times higher than in the cultivated fields (see table 3), reflecting the fact that the town is the operational base for pesticide applications in the region.

We detected glyphosate in 100% of grain dust samples and its concentration was 20 times higher than other pesticides. Glyphosate was always found coexisting with other pesticides, revealing that its presence is not due to use in gardening.

Contamination with glyphosate in particular and with pesticides in general is predominant in this environment. The burden of residential exposure to glyphosate is 13.5 times greater than the average burden of the national population, and within the town this burden seems to be even greater in radii 16 and 17 where the grain dust impregnated with glyphosate is carried by the wind.

In GAR 2014, the global prevalence of asthma for people 18-45 years-old is recorded at 8.6%, placing Argentina slightly below average (3).However, 18-45 year-old residents of Monte Maíz experience an asthma rate more than double that. Using a methodology identical to that employed in this study (21), ISAAC reports an asthma prevalence of 13.6% for children aged **??**3-14 years (20). The most recent publication of the Argentine Society of Pediatrics recognizes a national prevalence of 16.4% in children aged 6-7 years and 10.9% in those aged 13-14 years (9). Among the 307 children surveyed in Monte Maíz the prevalence of asthma is three times higher (52.4% and 39.9% for the 6-7 year-old group and 13-14 year-old group respectively)(see Table **??**).

Confounding variables such as smoking and premature birth were not linked to asthma in any of the statistical methods applied. For example, smoking was present in 22% of the residents of Monte Maíz who use bronchodilators, but in up to 75% in studies of asthma and wheezing in the city of Buenos Aires (22). In Monte Maíz, the inhabitants directly linked to agriculture no correlation with asthma arose, and the affected inhabitants were residential reflecting environmental exposure and no occupational exposure.

The high prevalence of asthma in this population with heavy exposure to glyphosate and other pesticides is consistent with the strong link between pesticides and asthma (23,24) including recent studies which specifically link glyphosate with asthma (25,26).The cluster of asthma symptoms in sectors R16 and R17, which both receive wind that sheds glyphosate-laden grain dust from silos, suggests a dose-response relationship. These data are congruent with local studies that found a prevalence of wheezing and rhinitis in 49% of people living near the silos (27).

The cause of asthma appears to be a combination of genetic predisposition with infections and / or environmental exposure to inhaled substances and particles (4,5). A cohort study in children with residential exposure to organophosphate pesticides found that they damage lung function as much or more than cigarette smoke (28). In the Children's Health Study, early exposure to herbicides increased the risk of asthma 4.5 times (29) and a recent ecological study of organic farms vs. conventional farms (those using pesticides) found more wheezing in children living on or near conventional farms (30).

Low molecular weight chemicals, such as herbicides, can induce occupational asthma (31). According to Jarvis' SAR (structure-activity relationship) model, the glyphosate risk index is 0.6257, which supports its potential to induce asthmatic symptoms (32).

Experimental studies on the effects of inhalation of glyphosate in rats indicated that it caused wheezing, reduced ciliary activity, and produced thick nasal secretion even at low levels of exposure, according to studies dating back more than 20 years, before its current levels of heavy use (33,34). More recently Kumar et al. demonstrated that rats exposed to glyphosate-rich air samples (collected on farms or air with added glyphosate) display increased eosinophil and neutrophil counts, mast cell degranulation, and interleukin production in their airways, confirming the role of glyphosate in the pathogenesis of asthma (35).

In short, previous studies provide plausibility to the findings of this study: a high prevalence of asthma in a population environmentally exposed to glyphosate. The weakness of this study is its observational and ecological design, which is insufficient to make categorical causal statements. Nor can it rule out the ecological fallacy. Finally, data from the control population were taken in 2003 and those of Monte Maíz in 2014, although ISAAC phase III did not find significant differences between phase I and phase III also made 10 years later (36).

ISSAC showed wide variability in global asthma rates and in Latin America the range was between 8.6 and 32.1% in children aged 6-7 years or between 6.6 and 27% in those aged 13-14 years (20), but in Monte Maíz it reached 39.9% and 52.4% respectively. Overall, compared to the Argentine cities studied by ISAAC, the data from Monte Maíz express a risk more than 4 times greater (OR: 4.64 with CI of 3.26 -6.60), which indicates an ecological factor beyond any natural variability of the population.

V.

10 Conclusion

The findings suggest a link between environmental exposure to glyphosate, and to a lesser extent, other pesticides, with high asthma prevalence. This population-environmental study demonstrates the co-occurrence of asthma and environmental exposure to glyphosate, while experimental studies support the plausibility of this association.

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[1]

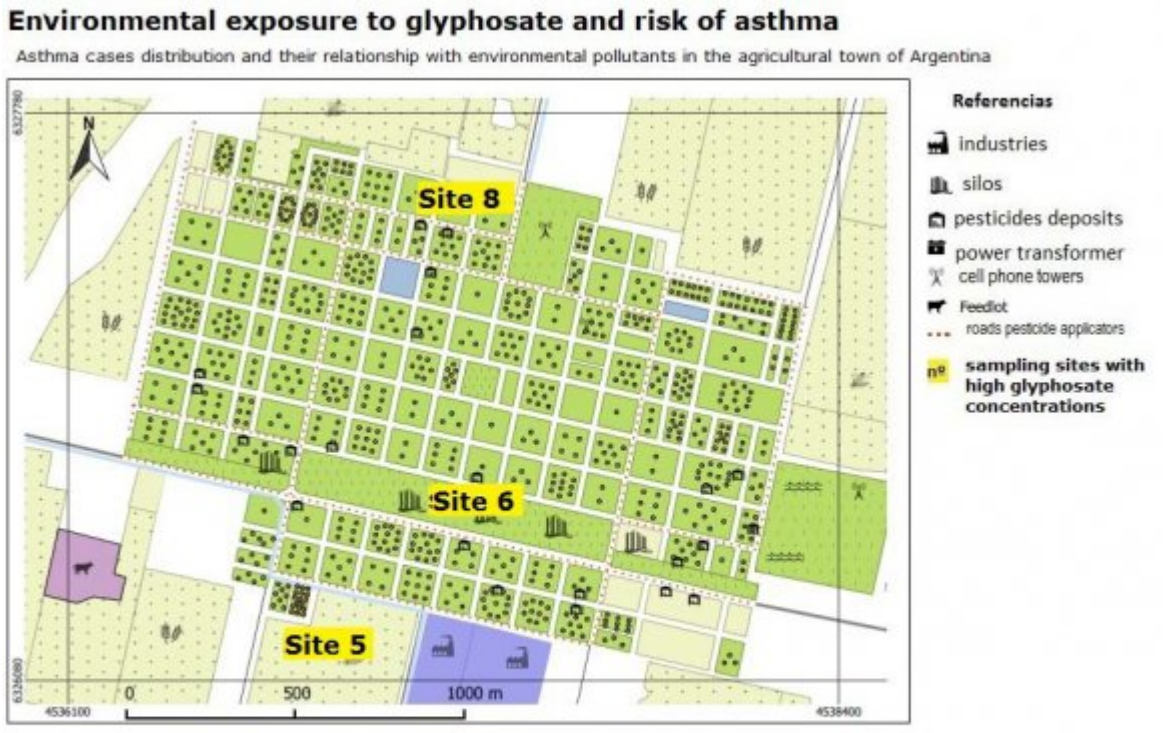

Figure 1: A

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Figure 2: Figure 1 :

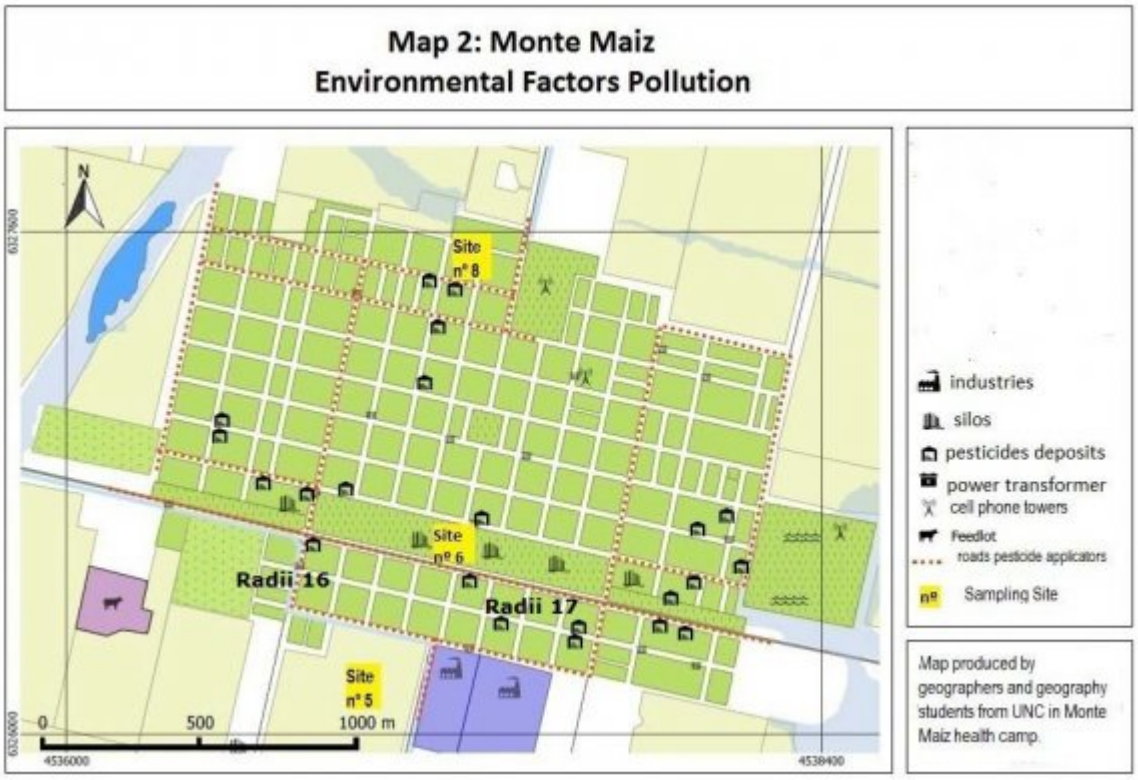

Figure 3:

Figure 4:

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Characteristics

Figure 5: Table 1 :

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Pesticides utilization rates (everything)	15 kilos / ha/ year
glyphosate utilization rates	10 kilos/ha/year
glyphosate resistant cultivated hectares	65.000 hectares
Total pesticides used per year	975.000 kilos
Total glyphosate used per year	650.000 kilos
Pesticide burden in Monte Maíz	121 kilos /inhabitants /year
Glyphosate burden in Monte Maíz	81 kilos /inhabitants/year
Total pesticides Argentina 2013	371.000.

Figure 6: Table nº 2

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Figure 7: 000 kilos Total glyphosate in Argentina 2013 240.000.000 kilos Pesticide burden in Argentina 2013 7,9 kilos por persona Glyphosate burden in Argentina 2013 6 kilos por persona

3

S: Site sampling Glifosato		AMPA	2.4 D	Atrazina	Clorpirifos	Endosulfan I	Endosu
S1 drinking water network	< 2 ppb	< 2 ppb	< 1 ppb	< 0.5 ppb	DNC	DNC	DNC	< p
S5 crop field soil	41 ppb	116 ppb	< 5 ppb	6.4 ppb	242 ppb	< 1,5 ppb	2.2 ppb	5 p
S6 children's playground soil	2792 ppb	797 ppb	S/D	S/D	4.4 ppb	< 1,5 ppb	< 1,5 ppb	4 p
S6 children's playground grain husks from silos	505 ppb	607 ppb	S/D	S/D	14 ppb	DNC	< 1,5 ppb	I
S8 pesticides deposits soil	3868 ppb	3192 ppb	128 ppb	52.5 ppb	150.4 ppb	17.5 ppb	338 ppb	1 p

Reference S located sampling site (S 5, S6 and S8) in map of Figure 3. DNC: Detectable no quantifiable. Center for Environmental Research, Faculty of Exact Sciences of National University of La Plata.

Figure 8: Table 3 :

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Volume XXI Issue I Version I
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Figure 9: Table n o 4 :

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.2 Conflict of interest:

The authors declare they have no actual or potential competing financial interests.

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