entrosur
e-ISSN:2706-6800

Health effects in populations exposed to glyphosate: a review

Efectos en salud en poblaciones expuestas a glifosato: una revisión

Article resulting from a research project financed by Corporación Universitaria Minuto de Dios- UNIMINUTO

Fabian Jose Vera Vera
Master's Degree, Corporación Universitaria Minuto de Dios, Bogota, Colombia, fabian.vera@uniminuto.edu
https://orcid.org/0000-0002-8310-3843

Leidy Isabel Calderón Sierra
Master's Degree, Corporación Universitaria Minuto de Dios, Bogotá, Colombia, Leidy.calderon@uniminuto.edu,
https://orcid.org/0000-0002-1056-901X

http://centrosuragraria.com/index.php/revista
Published by: Edwards Deming Institute
Quito - Ecuador
April - June vol. 1. Num. 9 2021
Pages 71 - 91

RECEIVED: SEPTEMBER 18, 2020
ACCEPTED: JANUARY 08, 2021
PUBLISHED: APRIL 4, 2021

ABSTRACT

Glyphosate is a broad-spectrum herbicide that has been used primarily in the agricultural sector for pest control and eradication of illicit crops in drug-trafficking countries such as Colombia. According to the International Agency For Research On Cancer (IARC) this herbicide is classified as probably carcinogenic to humans, however, the world literature on the effects on human health presents a confusing and diverse picture. The objective of this review was to identify the possible health effects of exposure to herbicides with active ingredient glyphosate, following the recommendations of the Cochrane Collaboration for systematic reviews and the PRISMA guidelines for reporting the results. A literature search was performed in PubMed, MedLine, VHL Regional Portal, ProQuest, EBSCOhost databases, among others, using DECS and MESH search engines, all existing articles in the time period from 2007 to 2017 were examined. The case studies or case reports present results related to varied health effects associated with glyphosate, including pancreatitis, epidermal necrolysis and renal damage, clinical manifestations that were not documented in studies with other types of methodology. But other studies present statistical measures that indicate that exposure to glyphosate is a risk factor for health problems such as multiple myeloma, wheezing, non-Hodgkin's lymphoma, among others.
Keywords: glyphosate; Environmental Hazards Exposure; pesticides; toxicity; toxicity

RESUMEN

El glifosato es un herbicida de amplio espectro que ha sido usado principalmente en el sector agrícola para el control de plagas y la erradicación de cultivos ilícitos en países que trafican droga como Colombia. Según la International Agency For Research On Cancer (IARC) este herbicida es clasificado como probablemente carcinogénico para humanos, sin embargo, la literatura mundial sobre los efectos en la salud humana presenta un panorama confuso y diverso. El objetivo de esta revisión fue identificar los posibles efectos en salud por exposición a herbicidas con principio activo glifosato, se siguieron las recomendaciones de la colaboración Cochrane para revisiones sistemáticas y la guía PRISMA para el reporte de los resultados. Se realizó búsqueda de literatura en bases de datos PubMed, MedLine, Portal Regional de la BVS, ProQuest, EBSCOhost, entre otras, utilizando buscadores DECS y MESH, se examinaron todos los artículos existentes en el período de tiempo comprendido entre los años 2007 a 2017. Los estudios de caso o reportes de caso presentan resultados relacionados con efectos en salud variados asociados a glifosato, entre los que se encuentra pancreatitis, necrolisis epidérmica y daño renal, manifestaciones clínicas que no fueron documentadas en los estudios con otro tipo zde metodología. Pero otras investigaciones presentan medidas

estadísticas que indican que la exposición a glifosato es un factor de riesgo para problemas en salud como mieloma múltiple, sibilancias, linfoma No Hodgkin, entre otros.

Palabras clave: clave: glifosato; Exposición a Riesgos Ambientales; plaguicidas; toxicidad

INTRODUCTION

In the last ten years, the consumption of agrochemicals or pesticides worldwide grew by 93%, with Brazil being the main consumer of these products due to its model of agricultural expansion and economic development (Ferreira F, et al., 2016). The use of these substances is not only intended for pest control in crops, but is also used at the domestic level, in gardening, forestry work and animal production, among others, exposing in different ways a large number of people and generating potential risks to health and the environment (Karam et al. 2005).

Among the most common uses of glyphosate are gardening, agriculture, illicit crop control and weed control in forestry plantations, industrial complexes and railways. (Agencia EFE, 2016) and weed control in forestry plantations, in industrial complexes and railways, which brings this chemical compound uncontrollably close to different population groups, children, adolescents, the elderly, workers, among others, are in contact with the herbicide, without knowing the risks to which they are exposed. This is why the research has sought to know the possible effect that glyphosate has on living beings and the environment.

Glyphosate is a weak organic acid consisting of a glycine group and a phosphonomethyl group, the chemical name is N-(phosphonomethyl)glycine, this is the most widely used postemergence - systemic and non-selective herbicide worldwide.The main mechanism of action is to inhibit the activity of 5-enolpyruvyl shikimate 3-phosphate synthetase in plants and in several microorganisms, causing a reduction in the synthesis of proteins and other molecules leading to premature cell death (Solange 2011), humans use a different mechanism to perform protein synthesis, which in theory would not cause toxic effects, but several scientific studies expose negative health effects.

In the literature there are systematic reviews on possible health effects in humans caused by glyphosate such as the one conducted by Mink P and collaborators, this review found that most studies did not observe statistically significant positive differences between glyphosate and various outcomes studied, but for respiratory disease, asthma, bronchitis and wheezing, the results were varied, finding significant association for rhinitis, concluding that epidemiological studies do not support a causal association between glyphosate and any of the adverse health outcomes evaluated (2011).

In 2013 the publication by Kier & Kirkland concluded that glyphosate and its formulations do not pose a risk of producing heritable mutations in humans. Kirkland concluded that glyphosate and its formulations do not pose a risk of producing heritable mutations in humans, but does not rule out that at high or toxic doses it causes effects on DNA (Kier and Kirkland 2013), Niemann in (2015) analyzed the results of seven studies conducted in Europe and the United States and concluded that although amounts of glyphosate are detected in urine samples, the estimated exposure is below the Acceptable Daily Intake (ADI) or Acceptable Operator Exposure Levels (AOELs), which shows that exposure is documented, but not possible harm. Finally, a meta-analysis gathered 81 experimental studies on the relationship between glyphosate exposure and micronuclei formation, concluding that exposure to glyphosate and its formulations increases the frequency of micronuclei formation, which is related to cancerous processes (Ghisi, Oliveira, and Prioli 2016).

On the other hand, in 2015, the Agency for Research on Cancer (IARC) classified glyphosate as probably carcinogenic in humans (group 2A), based on the limited evidence of carcinogenicity specifically for the development of Non-Hodgkin's lymphoma, evidence from studies mainly in farmers in the USA, Canada and Sweden published in 2001, which increased interest in recognizing the real risks to which millions of people who have some kind of contact with the herbicide are exposed. Following the publication of the report, the National Narcotics Council in Colombia took the decision to suspend spraying, at the request of the Constitutional Court, for use on illicit crops. (El Espectador, 2015) .

The panorama in the country with respect to the use of glyphosate is diverse, it is used in different productive processes in addition to having a leading role in the control of illicit crops, from 1978 to 1982 it was used to fumigate marijuana crops in the Sierra Nevada, in 1984, the government funded a study to evaluate the convenience of the use of glyphosate, the conclusion was that it was not possible to establish the consequences. Despite this and in comparison with other pesticides, it was decided to use the herbicide for national security reasons, to spray poppy and cocaine crops, in 1994 began the struggle of people to avoid spraying with glyphosate because they were exposed to a chemical that was used in an indiscriminate manner, but until 2002 the ombudsman denounced damage to peasant and indigenous communities and requested a form of eradication more friendly to the environment and people. In 2015 the court forced the government to end aerial spraying of glyphosate. (El Espectador, 2015) .

The challenges that the use of pesticides has represented for research, motivated to systematically review the published literature on the possible health effects caused by pesticides, but glyphosate caused a great interest due to the particular use that has been given to it in several regions of Colombia. The main objective of this review is to determine

the possible health effects of glyphosate exposure in order to identify research priorities and create evidence that will contribute to make the best decision regarding the use of the chemical.

MATERIALS AND METHODS

The Cochrane Collaboration recommendations for systematic reviews were followed and the PRISMA (preferredreporting items forsystematicreviews and meta-analyses) guide was followed for the reporting of results (flowchart 1).

The choice of articles was made taking into account the following inclusion and exclusion criteria, in addition to the date of publication comprised between the years 2007 - 2017:

Inclusion criteria:

Methodological documents , articles in peer-reviewed journals.

Exclusion criteria:

-Summary , letters to the editor, comments, or editorials

Not available in full text

-Not published in English, Spanish or Portuguese language

Animal studies

In vitro studies

Study eligibility was assessed independently by two authors in a standardized manner. Disagreements were resolved by consensus. Articles were first screened by title and abstract, then full papers that met the inclusion criteria were selected, and finally the required information was extracted and the quality of the studies was assessed.

The characteristics of the included studies were extracted by a reviewer and presented in a standard format in Excel® 2010 that included the following variables: title, author, year, country, type of study, number of persons included, population, outcomes, intervention or comparator, observation time, study quality, financing or report of conflicts of interest.

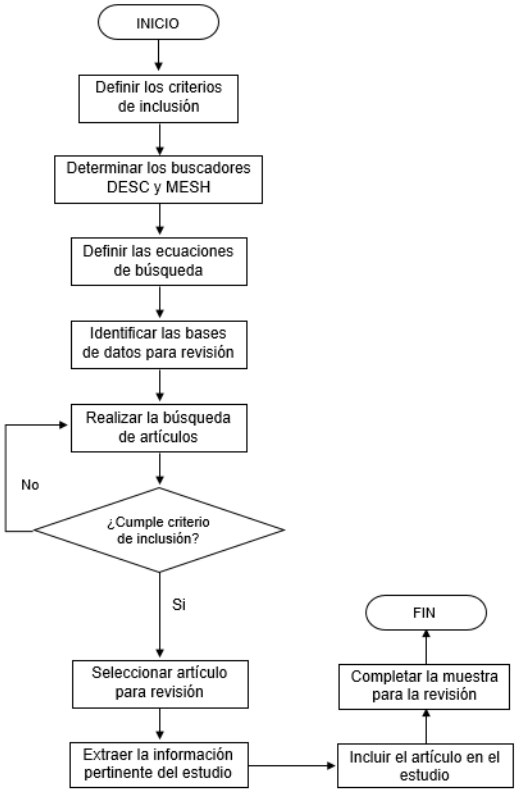

Figure 1. Flowchart for item selection

The systematic search for references was performed in the databases of Universidad del Rosario, using the search engines PubMed, MedLine, the Regional Portal of the VHL, ProQuest, EBSCOhost, BioMed Central, Scopus,ScienceDirect and Scielo, publications were searched between 2007 and 2017, the last search was performed on May 7, 2017.

Terms relevant to the subject matter, objectives and scope of the review were selected and entered into the DeCS and MeSH search engines, thus selecting the most appropriate descriptors.

DECS: toxicity, toxicity test, impacts on health, environmental exposure, pesticide exposure, occupational exposure.

MESH: humans, occupational exposure, herbicides, toxicity, toxicity tests, environmental exposure.

The following search equations were constructed from these terms

Glyphosate

Glyphosate "AND" cancer

Glyphosate "AND" Impacts of health
Glyphosate "AND" human risk
Glyphosate "AND" toxicity
Glyphosate "AND" environmental exposure
Glyphosate "AND" human exposure
Glyphosate "AND" occupationalexposure
Glyphosateherbicides

RESULTS

Twenty-three articles were selected (see Table 1) to be analyzed and included in the systematic review, the vast majority of the references found did not meet the inclusion and exclusion criteria, in addition to finding a large number of studies in vitro, in animals and in plants.

The systematic review contains studies of methodological diversity, the most common methodology used in the investigations was case studies (n=6), followed by case-control studies and retrospective data investigations with participation of 5 for each, in addition to analyzing descriptive studies and meta-analysis and a cohort study (Table 1).

Case studies or case reports present results related to varied health effects associated with glyphosate, in Venezuela González et al, in 2014, reported the case of an individual who was diagnosed with acute pancreatitis associated with glyphosate use because the already known etiology did not fit the patient's clinical history, in India they reported a suicide attempt where the subject ingested a dose of the herbicide and subsequently presented toxic epidermal necrolysis and acute kidney damage (Indirakshi et al. 2017), a case similar to the study developed in Thailand by Sribanditmongkol et al. where the patient was diagnosed with erosion of tissues including mucous membranes and linings of the gastrointestinal and respiratory tracts (2013). In Ireland they studied blood and urine samples from 13 cases of glyphosate poisoning, clinical results confirmed high blood glyphosate concentrations with a mean value of 61 mg / L (range 0.6-150 mg / L) and 4146 mg / L (range 690-7480 mg / L) respectively in mild-moderate poisoning and fatal cases. Among the signs and symptoms of the patients were oropharyngeal ulceration, nausea, vomiting, respiratory distress, cardiac arrhythmia, hyperkalemia, impaired renal function, cardiovascular shock and multiple organ failure (Zouaoui et al. 2013), a study that agrees with the one conducted in Korea by Han and collaborators where similar symptomatology was documented (2016).

Finally in the United States William Shaw reported an association between autism and the presence of high levels of glyphosate in urine, parents of triplets noticed a change in the behavior of two of the children who were diagnosed with autism and were subjected to

various tests including glyphosate in urine, the 3 children had significantly elevated urinary glyphosate with respect to the reference value, the study concluded that the elevation of glyphosate corresponded to an intake of food with glyphosate in addition to an individual susceptibility (2017).

Retrospective data studies were not conclusive to establish cause-effect relationship with the use of glyphosate, a study conducted in the United States found no association between reported cumulative days of glyphosate use and suffering from multiple myeloma, the study does not attribute the use of the herbicide as a risk for the disease (Sorahan,T 2015), on the other hand an investigation found how the exacerbation of asthma was inversely associated with the use of glyphosate (OR CI = 0.5, 95% 0.3, 0.8) but presented apparently contradictory results because it considers glyphosate as a substance that exacerbates asthma in patients with a history of allergies (Henneberger et al. 2014). Another such study conducted in the United States by Slarger and co-workers found that 74% of pesticide applicators reported at least one episode of rhinitis in the past year. The herbicides 2,4-D, glyphosate , the insecticide diazinon and the fungicide benomyl were positively associated with rhinitis and the association of 2,4-D and glyphosate was limited to individuals who used both compounds in the past year (OR 1.42, 95% CI 1.14 to 1.77) (2009). In 2017 a similar study conducted in the United States looked for the presence of wheezing in individuals using glyphosate, finding a statistically significant relationship between current glyphosate use and the presence of allergic wheezing (OR 1.56 CI 95% 1.19, 2.03), and non-allergic wheezing (OR 1.24 CI 1.07, 1.44), people who manifested prolonged use of the herbicides 2,4-D and Glyphosate showed higher prevalence of allergic wheezing (Hoppin et al. 2017).

To conclude in one study, an association was found between having rheumatoid arthritis and having reported long-term use of any pesticide, analyses for specific pesticides show a sensitivity of diagnosed cases between rheumatoid arthritis and glyphosate use (OR = 1.4; 95% CI: 1.0, 2.1), in sensitivity analyses of cases diagnosed after the first 2 years of follow-up (n = 96), associations of rheumatoid arthritis with any specific pesticide use were confirmed (OR = 1.6; 95% CI: 1.0, 2.4) (Parks et al. 2016).

These allow the study of the possible relationship of the factors associated with a disease, this type of studies were presented by researchers from several countries. (García de la Torre, Sandoval Bosch, Gómez Muñoz, & de la Guardia González, n.d.). These types of studies were presented by researchers from several countries.

A research conducted by Fortes in Italy and Brazil in farmer patients using various types of pesticides, found association between the use of glyphosate, mancozeb and maneb and the risk of cutaneous melanoma (OR 2.58, 95% CI, 1.18 - 5.65), simultaneous exposure to both

pesticides and sunlight, increased the statistical relationship (OR 4.68 95% CI 1.29-17.0) (2016).

On the other hand in Sri Lanka the urinary excretion of various metals and glyphosate in patients with agricultural nephropathy (SAN) was examined and compared with the result of 2 groups without the disease, the results show how the median urinary concentrations of Sb, Cd, Pb, Mn, Ti and V in patients and controls exceed the reference range provided by the Mayo clinic in Rochester, the median unadjusted creatinine value of all other heavy metals and glyphosate in urine is higher in patients with the disease and in controls from SAN endemic areas, the Kruskal-Wallis test showed significant difference in unadjusted creatinine excretion for heavy metals and glyphosate except for Al, As, Cu, Mo, Ti and Zn between the groups of people living in endemic area without the disease and in people from the non-endemic area, urinary excretion of heavy metals and glyphosate is remarkably high in people living in endemic areas compared to those living in non-endemic areas, the data support the toxicological origin of FNS being present in people from specific geographical areas (Jayasumana, Gunatilake, and Siribaddana 2015), in that country another research conducted by Channa et al. looked for factors associated with chronic kidney disease of unknown etiology (CKDu) and among them drinking safe drinking water (OR 2.52, 95% CI: 1.12-5.70), history of recent consumption of abandoned well water (OR 5.43, 95% CI 2.88-10.26) and glyphosate use (OR 5.12 95% CI 2.33-11.26), overall subjects who sprayed glyphosate were four times more likely to have CKDu compared to people without the history (Jayasumana, Paranagama, et al. 2015).

In Sweden, it was studied whether herbicide exposure is a risk factor for non-Hodking lymphoma, finding a positive relationship (OR 1.72, 95% CI 1.18-2.51) equal to that found with respect to glyphosate exposure reported by 29 cases and 18 controls (OR 2.02, 95% CI 1.10 to 3.71), the above defined for an exposure period of less than 10 years and for a longer latency period, the association increased to (OR 2.26, 95% CI 1.16 to 3.71).02, 95% CI 1.10-3.71) the above defined for an exposure period of less than 10 years and for a longer latency period, the association increased to (OR 2.26, 95% CI 1.16-4.40) (Eriksson et al. 2008).

Meta-analyses allow to know in a summarized way what is the great part of evidence that exists on a given topic, one of the meta-analyses included was concerned with looking for the risk between the use of glyphosate and the suffering of lymphohematopoietic cancer, the results are presented in relative meta risks finding positive but marginal associations, for Hodgkin's lymphoma (meta-RR = 1.3, 95% CI 1.0-1.6, based on six studies) and for multiple myeloma (meta-RR = 1.4; 95% CI = 1.0-1.9; four studies), there was no statistical significance for leukemia and Hodgkin lymphoma (Chang and Delzell 2016), these results are in agreement with another meta-analysis developed by Schinasi and Leon which concludes that yes there

is a strong meta RR estimate but higher meta RR estimates were associated with non-Hodgkin lymphoma subtypes, furthermore there was a positive association between exposure to organophosphates, glyphosate, and B-cell lymphoma (CI 2.0, 95%: 1.1 to 3.6, CLR: 3.2) there is no consistent evidence against whether pesticide exposure in occupational agricultural settings may be important determinants of lymphoma (Schinasi and Leon 2014).

In contrast, a review by Mink and co-authors on glyphosate exposure concluded that they did not find a consistent pattern of positive associations indicating a causal relationship between glyphosate exposure and the types of cancers studied in different population groups or any specific cancer (Mink et al. 2012).

A study evaluating the effects of glyphosate in illicit crop eradication zones in Colombia looked for individuals who reported within 5 days of spraying

signs of pesticide intoxication, being headache, dizziness, profuse sweating, blurred vision, pruritus and erythema the most common symptoms, these people underwent study of glyphosate and other biomarkers finding that 42 individuals had glyphosate levels and of these none exceeded the permitted range, 64.3% of these people reported occupational use of glyphosate. A statistically significant relationship was found between the use of terrestrial (manual) glyphosate and the levels of this herbicide in urine (OR=2.54; 95%CI 1.08-6.08), while for amino-methyl-phosphonic acid there was no significant relationship (OR=0.24; 95%CI 0.02-4.47) (Varona et al. 2009).

Another study conducted in Brazil by Faria agrees with the symptoms of poisoning, but although 98.3% of the respondents used glyphosate, the study only attributed 11% of the poisonings to this herbicide (Faria, Rosa, and Facchini 2009).

Finally, a cohort study conducted in Colombia was included in the review because it sought a statistical association between the time it took women to become pregnant and living in regions at risk of exposure to glyphosate due to the eradication of illicit crops. The study included women of childbearing age living in regions where there was an aerial spraying program. The study found that women from Valle de Cauca took longer to become pregnant (OR 0.15, 95% CI 0.12, 0.18) compared to the control regions Boyacá and Sierra Nevada, but the study did not associate time to fertilization with glyphosate use or exposure (Sanin et al. 2009).

Table 1. *General information*

Authors / Year	Country	Type of study	Sample size	Target	Characteristics Population / Region	Results
Fortes et al. 2016	Italy	Case-control study	n=800 (399 cases and 401 controls)	To examine the association between occupational pesticide exposure and cutaneous melanoma,		Risk of cutaneous melanoma and any pesticide (OR 2.58; 95% CI: 1.18-5.65) Pesticide exposure and sun (OR=4.68; 95% CI: 1.29-17.0).
Hohenadel et al. 2011.	Canada	Case-control study	n= 2019. Cases n= 513 and controls n= 1506.	To investigate the relationship between NHL and the use of pesticides and some combinations of pesticides.	Data collected from hospitals in six Canadian provinces, using telephone interviews and provincial health insurance records.	(OR [one pesticide] = 1.30, 95% CI = 0.90-1.88, OR [two to four] = 1.54, CI = 1.11-2.12 OR [five or more] = 1.94, CI = 1.17-3.23).
Varona et al. 2009	Colombia	Descriptive cross-sectional study.	n= 112 individuals	Explore the possible effects of glyphosate and other pesticides on human health as a result of	Individuals in areas sprayed with glyphosate and other pesticides in Huila, Tolima, Putumayo, Guaviare,	Statistically significant relationship between terrestrial (manual) glyphosate use and levels of this

				aerial spraying.	Santander, Antioquia, Magdalena and La Guajira.	herbicide in urine (OR=2.54; 95%CI 1.08-6.08).
Hennebe rger et al. 2013	United States	Retrospe ctive data study	n=926 pesticide applicators.	Investigate whether exacerbatio n of symptoms is associated with agricultural exposures.	Participants were pesticide applicators with (respiratory problems and wheezing in the last 12 months) prior to the study.	Exacerbation of asthma was inversely associated with current use of the herbicides glyphosate (OR= 0.5, 95% CI=95% 0.3, 0.8) and paraquat (OR= 0.3, 95% CI 0.1, 0.9).
Parks et al. 2016	United States	Retrospe ctive	n= 24293, of which n= 275 cases and n= 24018 noncases	Examining association s between RA and pesticides or other agricultural exposures among wives of licensed pesticide applicators in the Agricultural Health Study.	Women spouses of pesticide applicators from the Agricultural Health Study.	AR remained associated with glyphosate (OR = 1.4; 95% CI: 1.0, 2.1). In sensitivity analyses after the first 2 years of follow-up (n=96), we confirmed associations of incident AR with any specific pesticide use (OR = 1.6;

						95% CI: 1.0, 2.4) and maneb/man cozeb (OR = 3.2; 95% CI: 1.3, 8.1), whereas the association was similar for glyphosate, although no longer statistically significant (OR =1.4; 95% CI: 0.9, 2.1).
Chang E, Delzell E. 2016.	United States	Systematic Review and Meta-Analysis	n= 19 items	Rigorously examine the relationship between glyphosate exposure and the risk of lymphohematopoietic cancer, NHL, HL, multiple myeloma and leukemia.	This study included epidemiological studies in humans that reported quantitative measures of association between glyphosate and different types of cancer.	Meta-RR for association between any versus no glyphosate use and risk of NHL (meta-RR = 1.3, 95% CI = 1.0-1.6, based on six studies) and MM (meta-RR = 1.4; 95% CI = 1.0-1.9; four studies). Associations were statistically null for HL (meta-RR =

						1.1; 95% CI = 0.7 to 1.6; two studies), leukemia (meta-RR = 1.0; 95% CI = 0.6-1.5; three studies), and NHL subtypes except B beta-cell lymphoma (two studies each).
Mink et al. 2012	United States	Systematic review	n= 21 studies	To evaluate whether glyphosate exposure is causally associated with cancer risk in humans.	Epidemiological literature evaluating glyphosate exposure and cancer risk in humans.	Our review did not find a consistent pattern of positive associations indicating a causal relationship between cancer (in adults or children) and cancer (in adults or children). children) or any site-specific cancer and glyphosate exposure.
Eriksson et al. 2008	Sweden	Population-based case-	n= 1926, of which n= 910 were	Evaluating pesticide exposure as	Men and women exposed to	Exposure to herbicides with (OR)

		control study.	cases and n= 1016 were controls.	a risk factor for non-Hodgkin's lymphoma.	glyphosate. The mean and median age of the cases was 60 and 62 years, and in the controls it was 58 and 60 years, respectively.	1.72, 95% (CI) 1.18-2.51. Glyphosate exposure with OR 2.02, 95% CI 1.10 to 3.71 and with> 10 years latency period or 2.26, 95% CI 1.16 to 4.40. General insecticides gave OR 1.28, 95% CI 0.96 to 1.72 and impregnation agents OR 1.57, 95% CI 1.7 to 2.30.
Hoppin et al. 2017	United States	Prospective study	n= 22134 men	To assess the association of currently used pesticides with allergic and nonallergic wheezing among male farmers.	Data on male workers from the Agricultural Health Study from the North Carolina and Iowa regions.	Allergic wheezing 62% glyphosate use OR 1.56 CI (1.19, 2.03), non-allergic wheezing 61% glyphosate use OR 1.24 CI (1.07, 1.44) P valuecontrast 0.120, being significantly

							associated with both types of wheezing.
Leah S, Maria E. 2014	Switzerland	Systematic review and meta-analysis	n= studies	44	Investigate the depth of literature on the relationship between specific pesticide chemicals and NHL.	Agricultural workers and their families, from populations in the United States and Europe.	. There was a positive association between exposure to the organophosphate herbicide, glyphosate, and B-cell lymphoma (CI 2.0, 95%: 1.1 to 3.6, CLR: 3.2).

The possible health effects due to exposure to glyphosate are diverse but not conclusive, this is attributed to the fact that most studies do not only evaluate exposure to glyphosate as a risk factor but to other types of pesticides or specific situations that are part of the lifestyles and environment of the participants. This was found in the review conducted by Mink et al., 2012 where it is concluded that the literature used does not present a pattern of associations that indicate a causal relationship between any disease and exposure to glyphosate, arguing that most associations are weak (Mink et al. 2011). Rome 2017, determine that the lack of quantitative assessments of exposure and the design of studies to determine dose-response relationships were common weaknesses in epidemiological investigations of health risks posed by exposure to glyphosate (Paumgartten 2017), being a deficiency found in the present review.

Within the studies analyzed, there are results of statistical measures that indicate that exposure to glyphosate is a risk factor for health problems such as multiple myeloma, wheezing, non-Hodgkin's lymphoma, among others, these associations are either weak or are presented in terms of mixtures with other pesticides, which considerably weakens the result. Reviews of epidemiological studies conducted by Mink and collaborators (Mink et al. 2011) (Mink et al. 2011) conclude that they did not find strong statistical associations between health problems or cancer and glyphosate, but neither do they completely rule out the

potential of glyphosate to cause harm. In the reviews, the authors recommend that research should be conducted to determine the cause-effect relationship in order to establish the true consequences caused by exposure to this herbicide.

Since there is limited and inconclusive evidence on the effects caused by glyphosate on human health, the precautionary principle must be applied for the protection of people. This principle is used in cases where there is no prior knowledge, there is little knowledge or the magnitude of the damage has not been established in the medium or long term, but the evidence is sufficient to determine that the exposure has a potential to cause damage to health and the environment.

The history of the use of glyphosate in Colombia is broad, complex and somewhat complicated, because the use of the herbicide has become an important point in the political landscape of the country, due to the importance it has had in the eradication of illicit crops, but at the same time, because of the consequences on populations and the environment that are attributed to its use, This is why it is considered pertinent to continue with the creation of scientific evidence that objectively guides decisions regarding the use not only of glyphosate but also of other chemical substances, in order not to cause harm to people who in different ways are exposed to contact with the chemical.

CONCLUSIONS

The search for a causal relationship has been a major problem when it comes to research. For this particular case, the studies included in the review have not been conclusive in establishing concrete negative effects that affect the health of individuals exposed to glyphosate, but neither do they completely rule out that the use of the chemical or being in contact with it does not cause health effects. In the case reports, it is shown how these presented health problems with different degrees of severity after having some type of exposure to glyphosate, it is clear that, when ingesting the substance with the intention of self-injury, intoxication is experienced by the oral intake of high doses of the chemical, but in the other cases it is not clear which factors of the individual played an important role in the development of the effects already described. The vast majority of the research included in the study used surveys as a method of collecting information, based on clinical manifestations referred by the persons included in the studies, leaving aside the importance of diagnostic tests to search for the causal relationship. Respiratory system diseases such as asthma and respiratory symptoms such as wheezing were the health effects that presented the most frequent statistical association in the studies analyzed, in contrast to carcinogenic processes which, despite being so extensively studied, do not conclude whether exposure to glyphosate is or is not a risk factor for acquiring the disease, due to the discrepancy in the conclusions.

REFERENCES

EFE Agency. (May 05, 2016). Colombia re-authorizes spraying of illicit crops with glyphosate. Agencia EFE. Retrieved 2016 Sep 25, 2016, from https://www.efe.com/efe/america/sociedad/colombia-vuelve-a-autorizar-la-fumigacion-de-cultivos-ilicitos-con-glifosato/20000013-2916862#

Barros-Bastidas, C., & Turpo, O. (2020). Research training and its impact on the scientific production of education faculty at a public university in Ecuador. Publicaciones, 50(2), 167-185. doi:10.30827/publicaciones.v50i2.13952.

hang, Ellen T., and Elizabeth Delzell. 2016. "Systematic Review and Meta-Analysis of Glyphosate Exposure and Risk of Lymphohematopoietic Cancers." *Journal of Environmental Science and Health - Part B Pesticides, Food Contaminants, and Agricultural Wastes* 51(6):402-34.

El Espectador. (May 17, 2015). The tangled history of glyphosate. *El Espectador*. Retrieved May 17, 2017, from https://www.elespectador.com/noticias/politica/la-enredada-historia-del-glifosato/

Eriksson, Mikael, Lennart Hardell, Michael Carlberg, and Måns Åkerman. 2008. "Pesticide Exposure as Risk Factor for Non-Hodgkin Lymphoma Including Histopathological Subgroup Analysis." *International Journal of Cancer* 123(7):1657-63.

Faria, Neice Müller Xavier, José Antônio Rodrigues da Rosa, and Luiz Augusto Facchini. 2009. "Poisoning by Pesticides among Family Fruit Farmers, Bento Gonçalves, Southern Brazil." *Revista de Saude Publica* 43(2):335-44.

Ferreira Crneiro, F., L. Silva Augusto, R. Rigotto, K. Friedrich, and A. Campos Búrigo. 2016. *Dossier ABRASCO An Alert On The Impacts Of Agrotoxins On Health*. 2016th ed. Rio de Janeiro.

Fortes, Cristina, Simona Mastroeni, Marjorie Segatto, Clarissa Hohmann, Lucia Miligi, Lucio Bakos, and Renan Bonamigo. 2016. "Occupational Exposure to Pesticides with Occupational Sun Exposure Increases the Risk for Cutaneous Melanoma." *Journal of Occupational and Environmental Medicine* 58(4):370-75.

Gamboa Romero, M. A., Barros Morales, R. L., & Barros Bastidas, C. (2016). Childhood aggressiveness, learning and self-regulation in primary school children. LUZ, 15(1), 105-114. Retrieved from https://luz.uho.edu.cu/index.php/luz/article/view/743

Chang, Ellen T., and Elizabeth Delzell. 2016. "Systematic Review and Meta-Analysis of Glyphosate Exposure and Risk of Lymphohematopoietic Cancers." *Journal of Environmental Science and Health - Part B Pesticides, Food Contaminants, and Agricultural Wastes* 51(6):402-34.

El Espectador. (May 17, 2015). The tangled history of glyphosate. *El Espectador*. Retrieved May 17, 2017, from https://www.elespectador.com/noticias/politica/la-enredada-historia-del-glifosato/

Eriksson, Mikael, Lennart Hardell, Michael Carlberg, and Måns Åkerman. 2008. "Pesticide Exposure as Risk Factor for Non-Hodgkin Lymphoma Including Histopathological Subgroup Analysis." *International Journal of Cancer* 123(7):1657-63.

Faria, Neice Müller Xavier, José Antônio Rodrigues da Rosa, and Luiz Augusto Facchini. 2009. "Poisoning by Pesticides among Family Fruit Farmers, Bento Gonçalves, Southern Brazil." *Revista de Saude Publica* 43(2):335-44.

Ferreira Crneiro, F., L. Silva Augusto, R. Rigotto, K. Friedrich, and A. Campos Búrigo. 2016. *Dossier ABRASCO An Alert On The Impacts Of Agrotoxins On Health*. 2016th ed. Rio de Janeiro.

Fortes, Cristina, Simona Mastroeni, Marjorie Segatto, Clarissa Hohmann, Lucia Miligi, Lucio Bakos, and Renan Bonamigo. 2016. "Occupational Exposure to Pesticides with Occupational Sun Exposure Increases the Risk for Cutaneous Melanoma." *Journal of Occupational and Environmental Medicine* 58(4):370-75.

García de la Torre, G. S., Sandoval Bosch, E., Gómez Muñoz, M. L., & de la Guardia González, G. (n.d.). *Access Medicine*. Retrieved June 01, 2017, from Chapter 8: Case-control studies: https://accessmedicina.mhmedical.com/content.aspx?bookid=1464&sectionid=101050213

Ghisi, Nédia de Castilhos, Elton Celton de Oliveira, and Alberto José Prioli. 2016. "Does Exposure to Glyphosate Lead to an Increase in the Micronuclei Frequency? A Systematic and Meta-Analytic Review." *Chemosphere* 145:42-54.

Han, Joseph, Hantae Moon, Youngki Hong, Songhee Yang, Won joon Jeong, Kwang Sik Lee, and Heesun Chung. 2016. "Determination of Glyphosate and Its Metabolite in Emergency Room in Korea." *Forensic Science International* 265:41-46.

Henneberger, Paul K., Xiaoming Liang, Stephanie J. London, David M. Umbach, Dale P. Sandler, and Jane A. Hoppin. 2014. "Exacerbation of Symptoms in Agricultural Pesticide Applicators with Asthma." *International Archives of Occupational and Environmental Health* 87(4):423-32.

Hoppin, Jane A., David M. Umbach, Stuart Long, Stephanie J. London, Paul K. Henneberger, Aaron Blair, Michael Alavanja, Laura E. Beane Freeman, and Dale P. Sandler. 2017. "Pesticides Are Associated with Allergic and Non-Allergic Wheeze among Male Farmers." *Pestisida* 125(4):535-43.

Indirakshi, J., A. Sunnesh, M. Aruna, M. Krishna Reddy, A. Kumar, V. Sarat Chandra, B. Sangeetha, D.... Katyarmal, R. Ram, and V. Siva Kumar. 2017. "Toxic Epidermal Necrolysis and Acute Kidney Injury Due to Glyphosate Ingestion." *Indian Journal of Critical Care Medicine* 33(1):167-69.

Jayasumana, Channa, Sarath Gunatilake, and Sisira Siribaddana. 2015. "Simultaneous Exposure to Multiple Heavy Metals and Glyphosate May Contribute to Sri Lankan Agricultural Nephropathy." *BMC Nephrology* 16(1):0-7.

Jayasumana, Channa, Priyani Paranagama, Suneth Agampodi, Chinthaka Wijewardane, and Sarath Gunatilake. 2015. "Drinking Well Water and Occupational Exposure to Herbicides Is Associated with Chronic Kidney Disease, in Padavi-Sripura, Sri Lanka." 1–10.

Karam, Miguel Ángel, Guadalupe Ramírez, L. Patricia. Bustamante Montes, and Juan Manuel Galván. 2005. "Pesticides and Population Health." *Science Ergo Sum* 11(3):246-54.

Kier, Larry D., and David J. Kirkland. 2013. "Review of Genotoxicity Studies of Glyphosate and Glyphosate-Based Formulations." *Critical Reviews in Toxicology* 43(4):283-315.

Mink, Pamela J., Jack S. Mandel, Jessica I. Lundin, and Bonnielin K. Sceurman. 2011. "Epidemiologic Studies of Glyphosate and Non-Cancer Health Outcomes: A Review." *Regulatory Toxicology and Pharmacology* 61(2):172-84.

Mink, Pamela J., Jack S. Mandel, Bonnielin K. Sceurman, and Jessica I. Lundin. 2012. "Epidemiologic Studies of Glyphosate and Cancer: A Review." *Regulatory Toxicology and Pharmacology* 63(3):440-52.

Niemann, L., Sieke, C., Pfeil, R., & Solecki, R. (2015). A critical review of glyphosate findings in human urine samples and comparison with the exposure of operators and consumers. Journal Fur Verbraucherschutz Und Lebensmittelsicherheit, 10(1), 3-12. doi:10.1007/s00003-014-0927-3.

Parks, Christine G., Jane A. Hoppin, Anneclaire J. De Roos, Karen H. Costenbader, Michael C. Alavanja, and Dale P. Sandler. 2016. "Rheumatoid Arthritis in Agricultural Health Study Spouses: Associations with Pesticides and Other Farm Exposures." *Environmental Health Perspectives* 124(11):196.

Paumgartten, Francisco José Roma. 2017. "Glyphosate Exposure, Cardiovascular Diseases and Cancer Risks." *Journal of Public Health and Emergency* 1(May):15-15.

Sanin, Luz Helena, Gabriel Carrasquilla, Keith R. Solomon, Donald C. Cole, and E. J. P. Marshall. 2009. "Regional Differences in Time to Pregnancy among Fertile Women from Five Colombian Regions with Different Use of Glyphosate." *Journal of Toxicology and Environmental Health - Part A: Current Issues* 72(15-16):949-60.

Schinasi, Leah, and Maria E. Leon. 2014. "Non-Hodgkin Lymphoma and Occupational Exposure to Agricultural Pesticide Chemical Groups and Active Ingredients: A Systematic

Review and Meta-Analysis." *International Journal of Environmental Research and Public Health* 11(4):4449-4527.

Shaw, William. 2017. "Elevated Urinary Glyphosate and Clostridia Metabolites with Altered Dopamine Metabolism in Triplets with Autistic Spectrum Disorder or Suspected Seizure Disorder A Case Study." *Integrative Medicine (Boulder)* 16(1):50-57.

Slager, R. E., J. A. Poole, T. D. LeVan, D. P. Sandler, M. C. R. Alavanja, and Jane A. Hoppin. 2009. "Rhinitis Associated with Pesticide Exposure among Commercial Pesticide Applicators in the Agricultural Health Study." *Occupational and Environmental Medicine* 66(11):718-24.

Solange, María. 2011. "Impacto Del Glifosato y Algunos de Sus Formulados Comerciales Sobre El Perifiton de Agua Dulce." *Acta Toxicológica Argentina* 19(2):87-88.

Sorahan, Tom. 2015. "Multiple Myeloma and Glyphosate Use: A Re-Analysis of US Agricultural Health Study (AHS) Data." *International Journal of Environmental Research and Public Health* 12(2):1548-59.

Varona, Marcela, Gloria Lucía Henao, Sonia Díaz, Angélica Lancheros, Álix Murcia, Nelcy Rodríguez, and Víctor Hugo Álvarez. 2009. "Evaluación de Los Efectos Del Glifosato y Otros Plaguicidas En La Salud Humana En Zonas Objeto Del Programa de Erradicación de Cultivos Ilícitos." *Biomedica* 29(3):456-75.

Zouaoui, K., S. Dulaurent, J. M. Gaulier, C. Moesch, and G. Lachâtre. 2013. "Determination of Glyphosate and AMPA in Blood and Urine from Humans: About 13 Cases of Acute Intoxication." *Forensic Science International* 226(1-3):20-25.