Systematic Review of the occupational health hazards in banana plantation workers due to pesticides exposure in the Caribbean Region of Costa Rica from 1999 to 2014

Revisión sistemática de los riesgos a la salud por exposición ocupacional plaguicidas en trabajadores de las plantaciones bananeras de la Región Caribe de Costa Rica de 1999 al 2014

Edgar Mata¹, Andrés Robles², SukhDev Mishra³, P. Sivaperumal⁴

Mata, E; Robles, A; Mishra, SD; Sivaperumal, P. Systematic Review of the occupational health hazards in banana plantation workers due to pesticides exposure in the Caribbean Region of Costa Rica from 1999 to 2014. *Tecnología en Marcha*. Vol. 31, Número Especial Movilidad Estudiantil 5. Octubre 2018. Pág 122-133.

DOI: https://doi.org/10.18845/tm.v31.i5.4092



¹ Student at Instituto Tecnológico de Costa Rica, Costa Rica. E-mail: edjomaca@gmail.com.

² Engineer, professor and researcher at Instituto Tecnológico de Costa Rica. Costa Rica.

³ Scientist-B, National Institute of Occupational Health, Ahmedabad. India.

⁴ Scientist-D, National Institute of Occupational Health, Ahmedabad. India

Keywords

Occupational Exposure to Pesticides; Health effects; Banana Plantations; Costa Rica.

Abstract

Pesticides are highly used in Costa Rica especially in the Caribbean Region where numbers of banana plantations are located. Different studies have been conducted in the country especially in this region. The following research summarizes the scenario of the occupational exposure to pesticides in Costa Rica presented in studies conducted during the years 1999 to 2014. A comparison within the health effects and the pesticides in the banana plantations of the Caribbean Region of Costa Rica is also given.

Resumen

Los plaguicidas son usados en grandes cantidades en Costa Rica, especialmente en la Región Caribe donde se encuentran ubicadas una gran cantidad de plantaciones de banano. Se han realizado diferentes estudios en esta región del país. La siguiente investigación resume el escenario de la exposición ocupacional a plaguicidas en Costa Rica de acuerdo con estudios realizados durante los años 1999 al 2014. Se realizó también una comparación entre los efectos a la salud y los plaguicidas en las plantaciones de banano de la Región Caribe de Costa Rica.

Palabras clave

Exposición Ocupacional a plaguicidas; efectos en la salud; plantaciones de banano; Costa Rica.

Introduction

The word pesticide means to kill the pest, but also destroying, preventing, repelling or mitigating pests are part of its uses [1]. Costa Rica's usage intensity has no easy explanation regarding its multi variable factors involved. Different aspects faced by farmers like socioeconomic, for instance age, education, information sources, others; political-economical, as their contracts, credits, markets, others, and agroecological as parcel elevation, years of usage of the land, others, they all (but not only these ones) influence on pesticides usage at the field level [2].

Primarily used pesticides in Costa Rica and related health hazards to their exposure

Numbers of different varieties of pesticides are used according to the crops grown. According to the Instituto Regional de Estudio en Sustancias Tóxicas or Regional Institute for Toxic Substances Studies (IRET as in Spanish) [3], the mainly used pesticides in Costa Rica are Mancozeb, Glyphosate, 2,4-D, Tridemorph, Paraquat, Bromomethane, Metamsodium, Ethoprop, Diazinon, and Terbufos. Use of Mancozeb is highly prevalent in banana, plantain, vegetables, melon, ornamental plants, rice, fruit and beans crops. The Glyphosate is mainly used in banana, plantain, coffee, cane, fruits, palm, forests, pastures, palm heart and cotton crops. Other pesticide is the 2,4-D used for cane, rice, pastures, corn and palm. The Tridemorph is used in banana and plantain crops. The Paraquat is used in pineapple, potato, banana, plantain, coffee, vegetables, fruits and palm crops. The Bromomethane is used on melon and watermelon crops; the Metamsodium in melon and ornamental plants. The Ethoprop is mostly used for pineapple, banana, vegetables and cane crops; the Diazinon is used in pineapple, fruits, rice, vegetables, melon and ornamental plants crops; and the Terbufos are used in banana, plantain, corn and coffee crops.

Moreover, pesticides, in general terms, have been associated to produce important negative effects on human beings. For instance, the mancozeb pesticide has been associated with decrease in the sperm account [4]. Also, it is associated with thyroid disruption as a reduction in plasma T4 levels. Moreover, different studies indicate that mancozeb causes important effects on different hematological parameters. All the effects have been studied in animals as well as in humans [4] [5] [6]. Glyphosate is a worldwide herbicide which has not only endocrine effects, but also toxic effects. These effects were demonstrated in DNA damage after certain conditions of exposure and pregnancy problems within farmers [7]. Furthermore, recent studies have demonstrated that cases of affecting young male farm workers in the Central American countries of Nicaragua, El Salvador, and Costa Rica are caused by exposure to glyphosate in combination of water hardness and nephrotoxic metals [8]. Studies executed in animals have demonstrated the toxic effects, renal tissue effects and endocrine disruption [9] [10]. There are not enough studies with evidence that 2,4-D pesticide is a potentially cause of death within workers exposed to this pesticide. However, it can be associated with reproductive toxicity effects due to the impaired functions on human sperm [11]¹[12]. Another highly used pesticide by different farmers all over the world is the Paraguat. This pesticide is associated with Parkinson's disease as recorded in widely publish literature. There is a big relation between this pesticide skin contact and inhalation and Parkinson's disease. As well as the exposure is increased the risk for developing the disease is higher [13] [14] [15]. Another widely used pesticide is the methyl bromide, also known as bromomethane because of its IUPAC name. Its toxicity is known for causing serious effects on central nervous system, that go from headache, nausea, disturbance, among others, to death due to respiratory or cardiovascular failure. This pesticide has a strong relation between adverse effects on the nervous system for which memory loss is one of the most important. It has also being shown as a potential tumor promoter in animals and human cells. For prostate cancer, different studies indicate an increased risk of developing due to its exposure [16] [17] [18]. Due to its fungicide, herbicide, insecticide and nematicide simultaneous properties, metam sodium is a soil pesticide extensively used. As many other pesticides, metam sodium has shown to have effects on the thymus and other parts of immune system, decreasing the size of thymus and also the activity of the system. Also, this pesticide has an influence on hormones as it is shown in the increased levels of a stress hormone. The lab studies are evidence of the association of being carcinogen and mutagene. It is shown in other studies the reduction in the possibility of pregnancy, effects in behaviour, possibility of anemia, developing asthma and liver damage [19] [20]. Different studies conducted in rats show that there is cell liver damage and increase of permeability of plasma membrane because of increase in activities of specific enzymes studied, due to Diazinon exposure [21] [22]. Other studies have shown how placental barrier and milk is a media to affect male offspring's reproductive functions at puberty and adulthood [23]. Another commonly used pesticide is the Terbufos, in different kind of crops. Its toxicity was demonstrated to be highly, even in small dosages, causing impacts like cardiovascular complication even at non-lethal doses [24]. Epidemiological studies show a strong relation between prostate and lung cancer, leukemia and non-Hodgkin's disease with the exposure to terbufos [25], [26].

Nevertheless, effects of some pesticides have not been studied in a broad and separate way, in general terms each pesticide have exhibited adverse effects when it comes to exposure. Since, it is complex to study of combined effects, many studies have shown pesticide effects as a whole. For instance, fertility problems in male have been conducted in several studies as

one of the effects to pesticide's exposure, not the same for the case of women. Even though, cases in women have demonstrated anomalies and congenital diseases in the newborns. The pesticides are also associated to be endocrine disruptors as it was written before. The repeatable intensity in short periods may also cause neurological effects and also the possibility of developing Parkinson's disease. Different studies, as well, suggest that especially organochloride and organophosphate pesticides can cause anxiety, concentration problems, memory loss and even depression. Cancer is also related to pesticide exposure [6]·[27]. Other studies point into the respiratory symptoms due to exposure to pesticides. Some of the effects for many pesticides used are wheezing and asthma symptoms. Handling pesticides, as in mixing or applying tasks, increase the risk of atopic asthma [28]·[29]. Actually, Costa Rica has been the highest pesticide consumer in the region of Central America for the last decades. Nevertheless, the high consumption has not been a great impulse for having a wide and well-studied topic in terms of occupational exposure to pesticides [30].

Methodology

Studies of occupational exposure to pesticides and health toxicity assessments on human health were identified from PubMed (from 1999 to 2016). The following terms were used as part of the search strategy: 'pesticide exposure Costa Rica' OR 'occupational hazard to pesticide Costa Rica ' OR 'agricultural health and Pesticides exposure Costa Rica' OR 'Pesticides exposure to workers Costa Rica'; limited to humans with no language restrictions. Abstracts were screened to identify those meeting our time period of interest criteria in Costa Rica. Publications from the1999 to 2016 which had health assessment components and effects of any pesticide were included. Studies which have inference in any of health system-respiratory, reproductive, dermatology, neurotoxicity, etc were mainly included. For the approximate measure of overall quality of the studies with clinical findings related to pesticide exposure and included in the review, ethical aspects of studies were carefully checked along with statement of a potential conflict of interest.

Results

Review of Methodology and statistical evidences

Table 1 summarizes different details taken into account in the articles conducted during 1999 to 2014. The information was organized by giving a number to the articles (a random number) in the first column and these papers can be identified by the given number in Figure 1. The next column specifies the population which was taken into account during the study. After this column, it is written the pesticide or pesticides which were studied in the article. For this case, some articles were studying only the pesticide exposure as a whole and not the exposure to a particular pesticide, so it can be read as "pesticide(s) not specified" or "wide list of pesticides". The column for method specifies the kind of assessment or way of analysis for the data collection used by the author(s). The last column specifies the author citation.

 Table 1. Details of studies conducted in Costa Rica during the period of 1999 to 2014 (latest study) related to

Occupational Exposure to Pesticides

No.	Population / Source	Target Pesticide(s)	Method	Reference
1	66 Handlers in Coffee, banana and palm farms.	Paraquat	Biological sampling: 24 hour urine sample collection	[31]
2	10 chayote farms, 11 heart of palm farms and 10 ornamental flowers	Bifentrina, Cihalotrina, 2,4-D, Deltametrina	Algorithm Quantitative Approach Method (AQAM), Fluorescent Tracer Technique (FTT), Absorbant Patches Technique (APT)	[32]
3	451 pregnant women	Mancozeb	Biological Sampling: ETU concentration in urine samples	[33]
4	Case-control:: 27 workers exposed and 27 controls.	DDT	17 neurobehavioral tests and complimentary questionnaires and clinical examinations.	[34]
5	Case-control: 69 indigenous women and 58 controls.	Cholpyrifos, Terbufos, Paraquat	Questionnaire to evaluate exposure and symptoms; Spirometry Tests to evaluate FVC (Forced Vital Capacity) and FEC (Forced Expiratory Capacity)	[35]
6	Case-control: 78 poisoned workers (54 with organophosphate and 24 carbamate) and 130 non-poisoned workers.	Organophosphates, Carbamates	Brief Symptoms Inventory (BSI) Standardised questionnaire	[36]
7	Case-control: 301 cases of leukemia childhood and 582 controls.	List of pesticides including: 2,4-D , Glyphosate, Paraquat, Carbofuran, Mancozeb, Terbufos, Deltamethrin, Malathion, Aldrin and others.	Parental face to face interview.	[37]
8	Data from National Tumor Registry (NTR) database, 2000 census, Pesticide Exposure Indicator Data.	Pesticides not specified	Ordinary Least Squares (OLS) regression	[38]
9	Case-control: 20 farmers (long term employment in banana farms) and 20 controls	Pesticides not specified	Standard chromosome aberration assay, Challenge assay and Fluorescent in situ hybridization (FISH) assay.	[39]

Continúa...

Continuación

10	Phase 1: *n=400; Phase 2: *n=361; Phase 3: *n=144/163	Pesticides not specified	Three Tier Screening Process. Phase 1: Dementia and Parkinson's Disease screening. Phase 2: Mini Mental States Exam and United Parkinson's Disease Rating Scale Phase 3: Clinical exam by neurologist	[40]
11	Costa Rican import data	Active ingredients of imports	Analysis of data	[41]
12	Cancer Registry, Population census, Agricultural census, Indicator PEI (Pesticide Exposure Indicator)	Wide list of pesticides	Analysis of data	[42]
13	Literature Review	Poisoning cases	Literature Review	[43]
14	Restrospective study: banana plantation workers (most employed between 1976 and 1979)	DBCP	Analysis of data: Standarized Mortality Ratios (SMRs), Expected Deaths and Stratified analysis	[44]
15	Occupational pesticide-related illness and injuries Data (1993-1996) from National Institute of Insurance (INS)	Pesticides depends on cases	Analysis of data	[45]
16	30 most used pesticides in Costa Rica	30 most used pesticides in Costa Rica	Impact Assesment of Chemical Toxics (IMPACT) (2002) model and Dynamic Model for Pesticides Residues in Plants.	[46]

Workers at Risk in banana plantations in Caribbean Region, Costa Rica

It was observed [4] that paraquat levels in banana field workers were significantly higher during the spraying day than the days before and after of spraying [31]. The arithmetic mean of urinary paraquat level for handlers was $6.3(\pm 10.45)\mu g/24h$. As commonly assumed that exposure is mainly limited to the handling of paraquat, same was observed in this study as only 4 out of 53 non-handlers were exposed to paraquat during spray. Another study conducted with pregnant women living near banana plantations concluded that they have elevated urinary ETU concentration. The probable source for this elevated concentration is the mancozeb spraying by aircraft, as well as occupational and environmental factors. Even none of the women from the study reported applying mancozeb herself. More than 72% of women had an Estimated Dose Intake (EDI_{chronic}) above the Reference Dose (RfD) of 0,08µg/Kg/day according to US EPA. Women living within 48m from the plantation had 45% higher urinary ETU concentration than the ones who lived more than 565m away [33]. A cross-sectional study conducted with indigenous women suggested no association shown between respiratory

symptoms and exposure to pesticides. The prevalence of cough, asthma and atopic symptoms was similar between exposed and unexposed women. Like these symptoms, the study found no association between them and the personal protective equipment or clothes worn by the women. Wheezing was more prevalent in exposed group, and increased wheezing associated among nonsmokers exposed to chlorpyrifos and terbufos with OR = 6.7, 95% CI: 1.6, 28.0 and OR = 5.9, 95% CI:1.4, 25.6, respectively [35]. Another study conducted with women, relates the breast cancer incidence with exposure to pesticides by the use of the Pesticide Exposure Index (PEI); it gives an approach to the extension and intensity per This index showed for women younger than 45 years an increase of 3% in breast districts. cancer incidence when moving to the next decile of pesticide exposure; while for women of 45 years or more the associated increase was of 29%. The PEI was statistically significant and associated with breast cancer incidence. Other factors were taken into account, for example at younger ages breast cancer can be explained by genetic factors. It was related the access to health care services with lower breast cancer incidence, and low socioeconomic status with high rates of breast cancer. Another association was given which suggests breast cancer explained according to the different areas in the country [38]. Other than highly prevalent breast cancer in Costa Rica, additional types of cancer have also been hypothesized to be associated to exposure of pesticides in females. Another paper [42] studied the risk of different cancers in rural areas and urban areas as well, for which it was founded that there were specific types of cancer at higher risk in rural areas. In the Caribbean Region, the Standardize Incidence Ratio (SIR) was higher for respiratory cancers in both genders, and ovary and prostate cancers; in this area dibromochloropropane, chlorothalonil and mancozeb are examples of pesticides which are used. Also, the hypothesis of association of use of the pesticide Paraguat and skin cancer was consistent with other studies. One more study relates the pesticide exposure with cancer in Costa Rica region. The Standardized Mortality Ratios (SMRs) was calculated and showed elevated SMRs in penile cancer, Hodgink's Disease in men and cervical cancer, which are consistent with other studies. In the case of testicular cancer and Parkinson 's disease among men and lung cancer for women have not been reported previously [44]. Other studies are related to effects in the nervous system, like one which found that occupational exposure to DDT is associated to a permanent decline in neurobehavioral functions, as well as an increase in neuropsychological and psychiatric symptoms (odds ratio for Q16 3*98 [95% CI 1*02 – 15*63] and for brief symptom inventory 7*25 [1*87 – 27*78]). The exposed group showed a 20% poorer performance [34]. Another study [40] found that the exposure to pesticides is associated to a high risk of diagnosis of Parkinson's Disease (PD). Exposed participants were 2.6 times more likely than those who were not occupationally exposed to pesticides, to have prevalent Parkinson's Disease. The tests for neurological disease were performed poorer by occupationally exposed to pesticides participants. Out of 144 participants examined by neurologist (third and last phase), 33 were diagnosed with possible or probable PD, 13 with different types of Parkinsonism and 15 with essential tremor. Only 9 cases were expected as prevalent cases of PD. From the same group of participants evaluated by neurologist, 14 were diagnosed with Alzheimer's Disease (AD) and 27 with Mild Cognitive Impairment (MCI), but linear regression did not showed high risk of diagnosis with occupational exposure to pesticides (p=0.70). The expected AD prevalence was of 21 cases, so diagnosis were less than expected, and for MCI the prevalence was not calculated. Other study [36] is consistent with number of published reports where neuropsychological effects like depressive symptoms and high prevalence of suicidal thoughts are related to organophosphates overexposure, but not for carbamate. It was found that psychological distress symptoms are related to organophosphate past poisoning. Also, these organophosphate poisonings are related in eight out of nine symptom dimension. The symptoms increased with the number of past poisonings and higher prevalence of suicidal

thoughts in workers poisoned compared to never poisoned workers. Exposure of parents to twenty six different pesticides was studied [37] by a population-based case control study of childhood leukemia. The number of fathers exposed was more than the number of mothers, but high exposure varies within the pesticide. The highest correlations between exposure intensity during active application (I) and time (A) was for deltamethrin (0.80), Aldrin (0.79), fluazifop (0.73) and carbofuran (0.71). The effects of offspring are related to xenobiotics in parents, like genetic alterations in sperm or ovum. This study did not assessed direct exposure of children or transplacental exposure of fetus.

Furthermore, cytogenetic effects were studied [39] and founded that farmers with "unfavorable" metabolizing genes had an increased possibility of adverse biological effects than controls and farmers with "favorable" genes by inheritance. Also, the standard aberration chromosome assay showed that the banana farmers had an increased level in chromosome abnormalities and the challenge assay showed significantly abnormal DNA repair responses. Both of the assessments suggest that the workers were exposed to genotoxic agents, which are the effect of interactions among the pesticides. An additional study on pesticide that related injury and illness was conducted with data from 1993 to 1996. It was estimated that 78% of reports were from banana farmers, from which 90% of the incidents were workers of less than 50 years and 5% were from children between 12 and 17. The 11% of reports from 1993 were from women, and in 1996 it increased to 17%. According to the pesticide related illness, it decreased from 4.0 per 100 in 1993 to 2.6 per 100 in 1996. During the year of 1996, the herbicide related injuries and illness incidence was considerably lower (1.2 versus 0.8 herbicide-related incidents per 100 banana plantation workers, RR96/93=0.6, 95% CI 0.5-0.8), which was associated with a reduction in the usage of paraguat. From this herbicide related incidents, 71% are associated with paraguat, but substitutes for herbicides do not remain harmful due to the doubling incidence of injuries related to herbicides other than paraguat during 1996. Also, is important to highlight the increase in reported allergies (RR 96/93 = 11.0, 95% CI 1.4-85.2). Overall, the pesticide related illness and injuries decreased around 20% from 1993 to 1996 [45].

The exposure of workers to pesticides depends on the access they have to them. High usage of pesticides is a problem in the region of Central America, where an increase of around 5000 cases of poisonings were reported from 1992 to 2000; an average of 6 to 20 acute poisonings per 100.000. The majority of this poisonings are caused by certain pesticides like organophosphates and carbamates, endosulfan and paraquat [43].

Conclusions

A mean of 6.3(±10.45)µg/24h was found in the urine collected from people in a period of 24 hours [31]. Moreover, the literature review, shows that high exposure to Paraquat is associated with Parkinson's Disease [13], [14], [15]. Also, pregnant women had high ETU concentration in their urine due to mancozeb exposure [33]. More than 72% of women had an Estimated Dose Intake (EDIchronic) above the Reference Dose (RfD) of 0,08µg/Kg/day according to US EPA. The literature review shows that mancozeb exposure is related to thyroid disruption, effects in hematological parameters and reproductive effects; studies have support in results shown in animals and humans [5], [6], [4]. Different kinds of cancers were associated with pesticides exposure. For instance, the breast cancer in women [38]; respiratory cancer in both genders, ovary and prostate cancer where dibromochloropropane, chlorothalonil and mancozeb were used and the hypothesis of relation between skin cancer and paraquat was

consistent with other studies [42]. Also, penile cancer cervical cancer, testicular cancer and lung cancer in women was associated with pesticide exposure. Moreover, Hodgkin's disease in men was related to pesticides exposure as well [44]. According to epidemiological studies cited before, there is strong relation between prostate and lung cancer and non-Hodgkin's disease with exposure to terbufos [25], [26] which is one of the most used pesticides in Costa Rica and is used in banana crops [3]. Effects in the central nervous system due to pesticides exposure are consistent with this review. Moreover, Parkinson's disease is related to pesticides exposure, and prevalence is 2, 6 times more likely to happen in exposed people [40], [44]. Also, the DDT (an organochlorine type pesticide) is related to permanent decline in neurobehavioral functions, increase in neuro psychological and psychiatric symptoms [34] and organophosphate pesticides were related to neuro phsycological effects, depression and suicidal thoughts, were prevalence is higher for poisoned workers [36]. The reproductive toxicity was related [37] where leukemia in offsprings was studied. It was related the parents exposure to pesticides to this effect on their children. Cytogenetic effects were studied in different assessments [39]. These assessments related changes in genes of the workers, which suggest that they were exposed to genotoxic agents, as an effect of the interaction of pesticides. An increase in poisoning cases where reported from 1992 to 2000 in the whole region of Central America, where Costa Rica belongs [43]. Most of these cases were due to organophosphates and carbamates, endosulfan and paraquat.

Acknowledgement

The main author, Edgar Mata, would like to recognize his family's support which encouraged him to go abroad. Also, special thanks to Instituto Tecnológico de Costa Rica, professors and personnel who helped out with the process of going to India.

In India, special thanks to Soumya Swaminathan madam, ICMR Director; Dr Sunil Kumar, NIOH director; Chacko sir and Shruti mam; all the departments visited including Biostatistics department and Pesticides department; personnel from NIOH Regional Centers in Bangalore and Kolkata and all the NIOH personnel who showed the best of India in terms of academics and culture.

References

- [1] D. K. Singh, "Toxicology: Agriculture and Environment," 2012. [Online]. Available: https://books.google. co.in/books?hl=en&lr=&id=4Z_HmFR5CCcC&oi=fnd&pg=PP1&dq=pesticide+chemistry+and+toxicology+& ots=VasS-PtZmp&sig=1iNa2Uhv1hpQJ-fI97U3_tIFy7s#v=onepage&q=pesticide%20chemistry%20and%20 toxicology&f=false.
- [2] R. Galt, "Toward an integrated understanding of pesticide use intensity in Costa Rican vegetable farmers," Human Ecology, vol. 36, pp. 655-677, 2008.
- [3] Instituto Regional de Estudios en Sustancias Tóxicas (IRET), "Importación de plaguicidas en Costa Rica: 2007-2009 [Pesticides imports in Costa Rica: 2007-2009].," 2011. [Online]. Available: http://cep.unep.org/repcar/ informacion-de-paises/costa-rica/Impoortaciones_07-09_REPCar.pdf.
- [4] P. Khan and S. Sinha, "Ameliorating effect of vitamin C on murine sperm toxicity induced by three pesticides (endosulfan, phosphamidon and mancozeb)," 1996. [Online]. Available: https://watermark.silverchair.com/11-1-33.pdf?token=AQECAHi208BE49Ooan9kkhW_cy7Dm3ZL_9Cf3qfKAc485ysgAAAaswggGnBgkqhkiG9w0-BBwagggGYMIIBIAIBADCCAY0GCSqGSIb3DQEHATAeBgIghkgBZQMEAS4wEQQME2wRL5QVhor5TKIy AgEQgIIBXgbUktw6sG4F-TXgVdX4md4jq5wYVgm4OKnOURgoGDbUwAH.

- [5] R. Madarapu and B. Prakhya, "In vitro myelotoxic effects of cypermethrin and mancozeb on human hematopoietic progenitor cells," 2015. [Online]. Available: http://web.a.ebscohost.com/ehost/pdfviewer/ pdfviewer?sid=acc83f7c-4e0f-4dea-ae4e-b0cb7985b827%40sessionmgr4007&vid=0&hid=4206.
- [6] I. Baños, "Exposición a pesticidas: su influencia negativa en la fertilidad masculina en Cuba [Exposure to pesticides: its negative influence in masculine fertility in Cuba]," 2009. [Online]. Available: https://ebookcentral. proquest.com/lib/itcrsp/reader.action?docID=3198631.
- [7] A. W. Campbell, "Glyphosate: Its Effects on Humans," 2014. [Online]. Available: https://www.researchgate.net/ publication/261800913_Glyphosate_Its_Effects_on_Humans.
- [8] E. Haskovic, M. Pekic, M. Focak, D. Sulvejic and L. Mesalic, "Effects of glyphosate on enzyme activity and serum glucose in rats Rattus norvegicus," 2016. [Online]. Available: https://www.degruyter.com/downloadpdf/j/ acve.2016.66.issue-2/acve-2016-0018/acve-2016-0018.pdf.
- [9] H. Karimi, L. Novin and M. Poor, "Effect of the herbicide Glyphosate on renal tissues in adult female rats," 2013.
 [Online]. Available: http://web.a.ebscohost.com/ehost/pdfviewer/pdfviewer?sid=d537c6e1-465e-44ac-906d-5771a4b84563%40sessionmgr4006&vid=1&hid=4206.
- [10] N. Omran y W. Salama, "The endocrine disruptor effect of the herbicides atrazine and glyphosate on Biomphalariaalexandrina snails," 2013. [En línea]. Available: http://web.a.ebscohost.com/ehost/pdfviewer/ pdfviewer?sid=f13a5977-9fa0-410e-b528-1dae3fb4dc0e%40sessionmgr4007&vid=1&hid=4206.
- [11] C. Burns, K. Beard and C. J.B, "Mortality in chemical workers potentially exposed to 2,4-dichlorophenoxyacetic acid (2,4-D) 1945–94: an update," 2000. [Online]. Available: http://oem.bmj.com/content/oemed/58/1/24.full. pdf.
- [12] Z. Tan, J. Zhou, H. Chen, Q. Zhou, S. Weng, T. Luo and Y. Tang, "Toxic effects of 2,4-dichlorophenoxyacetic acid on human sperm function in vitro," 2016. [Online]. Available: http://web.a.ebscohost.com/ehost/pdfviewer/ pdfviewer?sid=36fbdb5d-6f5b-4920-a23a-778b2a88b212%40sessionmgr4008&vid=1&hid=4206.
- [13] A. León, "Enfermedad de Parkinson por exposición ocupacional a paraquat [Parkinson's Disease because of Paraquat occupational exposure]," 2012. [Online]. Available: http://www.medigraphic.com/pdfs/imss/im-2012/ im126n.pdf.
- [14] B. Ritz, A. Manthripragada, S. Costello, S. Lincoln, M. Farrer, M. Cockburn y J. Bronstein, «Dopamine Transporter Genetic Variants and Pesticides in Parkinson's disease,» 2009. [En línea]. Available: http://web.a.ebscohost. com/ehost/pdfviewer/pdfviewer?sid=3ff27b8d-556d-46ec-9601-04d36e167d15%40sessionmgr4006&vid=1& hid=4212.
- [15] G. Chester and B. Woollen, "Studies of the occupational exposure of Malaysian plantation workers to paraquat," 1981. [Online]. Available: http://oem.bmj.com/content/oemed/39/1/23.full.pdf.
- [16] L. T. Budnik, S. Kloth, M. Velasco-Garrido and X. Baur, "Prostate cancer and toxicity from critical use exemptions of methyl bromide: Environmental protection helps protect against human health risks," 2012. [Online]. Available: https://ehjournal.biomedcentral.com/articles/10.1186/1476-069X-11-5.
- [17] F. Deschemps and J. Turpin, "Methyl bromide intoxication during grain store fumigation," Occupational Medicine, vol. 46, no. 1, pp. 89-90, 1996.
- [18] G. M. Calvert, C. A. Mueller, J. M. Fajen, D. W. Chrislip, J. Russo, T. Briggle, L. E. Fleming, A. J. Suruda and K. Steenland, "Health Effects Associated With Sulfuryl Fluoride and Methyl Bromide Exposure Among Structural Fumigation Workers," 1998. [Online]. Available: http://ajph.aphapublications.org/doi/pdf/10.2105/ AJPH.88.12.1774.
- [19] C. Cox, "Metamsodium," Journal of Pesticide Reform, vol. 26, no. 1, 2006.
- [20] M. Deguigne, L. Lagarce, D. Boels and P. Harry, "Metam sodium intoxication: the specific role of degradation products – methyl isothiocyanate and carbon disulphide – as a function of exposure," Clinical Toxicology, vol. 49, no. 5, 2011.
- [21] H. AbdElmonem, M. Abbas and A. Mahmoud, "Combined Effects of Ribavirin and Diazinon on Hepatic, Pancreatic, and Kidney Biomarkers in female albino rats," 2016. [Online]. Available: http://www.thejaps.org. pk/docs/v-26-04/28.pdf.
- [22] P. Lari, K. Abnous, M. Imenshahdiidi, M. Rashedinia, M. Razavi and H. Hosseinzadeh, "Evaluation of diazinoninduced hepatotoxicity and protective effects of crocin.," 2013. [Online]. Available: http://web.a.ebscohost. com/ehost/pdfviewer/pdfviewer?sid=706c90e4-5e40-4725-8f1f-292f63ffe7c7%40sessionmgr4007&vid=1&h id=4214.
- [23] S. Jayachandra and U. D'Souza, "Prenatal and postnatal exposure to diazinon and its effect on spermatogram and pituitary gonadal hormones in male offspring of rats at puberty and adulthood," 2014. [Online]. Available: https://www.ncbi.nlm.nih.gov/pubmed/24502214.

- [24] S. Nurulain, M. Shafiullah, J. Yasin, A. Adem, J. Al Kaabi, S. Tariq, E. Adeghate and S. Ojha, "Terbufos-sulfone exacerbates cardiac lesions in diabetic rats: sub acute toxicity study," 2016. [Online]. Available: http:// web.a.ebscohost.com/ehost/pdfviewer/pdfviewer?sid=83700e04-7644-4320-ba20-18696cd23271%40session mgr4010&vid=1&hid=4214.
- [25] M. R. Bonner, B. A. Williams, J. A. Rusiecki, A. Blair, L. E. B. Freeman, J. A. Hoppin, M. Dosemeci, J. Lubin, D. P. Sandler and M. C. Alavanja, "Occupational Exposure to Terbufos and the Incidence of Cancer," 2010. [Online]. Available: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2935663/pdf/nihms-232228.pdf.
- [26] S. Koutros, L. Freeman, J. Lubin, S. Heltshe, G. Andreotti, K. Barry, C. Delavalle, J. Hoppin, D. Sandler, C. Lynch, A. Blair and M. Alavanja, "Risk of Total and Aggressive Prostate Cancer and Pesticide Use in the Agricultural Health Study," 2012. [Online]. Available: http://aje.oxfordjournals.org/content/177/1/59.full.pdf+html.
- [27] J. Hoppin, D. Umbach, London S, M. Alavanja and D. Sandler, "Chemical predictors of wheeze among farmer pesticide applicators in the Agricultural Health Study," American Journal of Respiratory and Critical Care Meidicne, vol. 165, no. 5, pp. 683-689, 2002.
- [28] N. M. X. Faria, L. A. Facchini, A. Gastal Fassa and E. Tomasi, "Pesticides and respiratory symptoms among farmers," 2005. [Online]. Available: http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0034-89102005000600016.
- [29] J. Hoppin, D. Umbach, L. Stephanie, P. Henneberger, G. Kullman, M. Alavanja and D. Sandler, "Pesticides and Atopic and Nonatopic Asthma among Farm Women in the Agricultural Health Study," 2007. [Online]. Available: https://www.atsjournals.org/doi/full/10.1164/rccm.200706-8210C#readcube-epdf.
- [30] C. Wesseling, A. Aragón, L. Castillo, M. Corriols, F. Chaverri, E. De La Cruz, M. Keifer, P. Monge, T. Partanen, C. Ruepert and B. Van Wendel de Joode, "Consideraciones sobre plaguicidas peligrosos en América Central [Considerations on hazardous pesticides in Central America]," Manejo Integrado de Plagas y Agroecología, vol. 68, pp. 7-18, 2003.
- [31] K. Lee, E. Park, M. Stoecklin-Marois, M. Koivunen, S. Gee, B. Hammock, L. Beckett y M. Schenker, «Occupational Paraquat exposure of agricultural workers in large Costa Rican farms.,» International Archives of Occupational and Environmental Health, vol. 82, pp. 455-462, 2009.
- [32] L. Medina, M. Rodríguez y P. Zamora, «Comparison of pesticides dermal exposure methods in a sample of flowers, palm hearts and chayote producers in Costa Rica,» Tecnología en Marcha, nº Special Number, pp. 5-21., 2013.
- [33] B. Van Wendel, A. Mora, L. Cordoba, J. Cano, R. Quesada, M. Faniband, C. Wesseling, C. Ruepert, M. Oberg, B. Eskenazi, D. Mergler and C. Lindh, "Aerial Application of Mancozeb and Urinary Ethylene Thiourea (ETU) concentrations among Pregnant Women in Costa Rica: The Infants Environmental Health Study (ISA)," Environmental Health Prespectives, vol. 122, no. 12, pp. 1321-1328, 2014.
- [34] B. VanWendel, C. Wesseling, H. Kromhout, P. Monge , M. Garcia and D. Mergler, "Chronic nervous-system effects of long-term occupational exposure to DDT," The Lancet, no. 357, pp. 1014-1016, 2001.
- [35] K. B. Fieten, H. Kromhout, D. Heederik and B. van Wendel de Joode, "Pesticide Exposure and Respiratory Health of Indigenous Women in Costa Rica," 2009. [Online]. Available: https://academic.oup.com/aje/article/169/12/1500/169555.
- [36] C. Wesseling, B. Van Wendel, M. Keifer, L. London, D. Mergler and L. Stallones, "Symptoms of psychological distress and suicidal ideation among banana workers with a history of poisoning by organophosphates or n-methyl carbamate pesticides," 2010. [Online]. Available: http://oem.bmj.com/content/67/11/778.long.
- [37] P. Monge, T. Partanen, C. Wesseling, V. Bravo, C. Ruepert and I. Burstyn, "Assessment of Pesticide Exposure in the Agricultural Population of Costa Rica," The Annals of Occupational Hygiene, vol. 49, no. 5, pp. 375-384, 2005.
- [38] C. Santamaria, "The Impact of Pesticide Exposure on Breast Cancer Incidence. Evidence from Costa Rica.," Población y Salud en Mesoamérica, vol. 7, no. 1, 2009.
- [39] W. Au, C. Sierra Torres, N. Cajas Salazar, B. K. Shipp and M. S. Legator, "Cytogenetic Effects from Exposure to mixed pesticides and the influence from genetics Susceptibility," 1999. [Online]. Available: https://www.ncbi. nlm.nih.gov/pmc/articles/PMC1566563/pdf/envhper00511-0117.pdf.
- [40] K. Steenland, C. Wesseling, N. Roman and J. Juncos, "Occupational pesticide exposure and screening tests for neurodegenerative disease among an elderly population in Costa Rica," Environmental Research , vol. 120, pp. 96-101, 2013.
- [41] V. Bravo, T. Rodríguez, B. van Wendel de Joode, N. Canto, G. R. Calderón and M. Turcios, "Monitoring Pesticide Use and Associated Health Hazards in Central America," 2011. [Online]. Available: http://www.tandfonline. com/doi/abs/10.1179/107735211799041896.

- [42] C. Wesseling, D. Antich, C. Hogstedt, A. Rodríguez and A. Ahlbom, "Geographical differences of cancer incidence in Costa Rica in relation to environmental and occupational pesticide exposure," International Journal of Epidemiology, no. 28, pp. 365-374, 1999.
- [43] C. Wesseling, M. Corriols and V. Bravo, "Acute pesticide poisoning and pesticide registration in Central America," Toxicology and Applied Pharmacology, vol. 207, pp. 697-705, 2005.
- [44] J. Hofmann, J. Guardado, M. Keifer y C. Wesseling, «Mortality among a Cohort of Banana Plantation Workers in Costa Rica,» International Journal of Occupational and Environmental Health, vol. 12, nº 4, pp. 321-328, 2006.
- [45] C. Wesseling, B. Van Wendel and P. Monge, "Pesticide-related illness and injuries among banana workers in Costa Rica: A comparison between 1993 and 1996," International Journal of Occupational and Environmental Health, vol. 2, no. 7, p. 90.97, 2001.
- [46] S. Humbert, M. Margni, R. Charles, O. Torres, A. Quiros and O. Jolliet, "Toxicity assessment of the main pesticides used in Costa Rica," Agriculture Ecosystems and Environment, vol. 118, pp. 183-190, 2007.
- [47] J. Beard, D. M. Umbach, J. A. Hoppin, M. Richards, M. C. Alavanja, A. Blair, D. P. Sandler and F. Kamel, "Pesticide Exposure and Depression among Male Private Pesticide Applicators in the Agricultural Health Study," Environmental Health Perspectives, 2014, p. 9.
- [48] V. Bravo Durán, E. de la Cruz Malavasi, G. Herrera Ledezma and F. Ramírez Muñoz, "Uso de plaguicidas en cultivos agrícolas como herramienta para el monitoreo de peligros en salud [Agricultural pesticides used as a tool for monitoring health hazard]," [Online]. Available: http://www.revistas.una.ac.cr/index.php/uniciencia/ article/view/4960/4754.
- [49] M. Dosemeci, M. C. Alavanja, A. S. Rowland, D. Mage, S. Hoar Zahm, N. Rothman, J. H. Lubin, J. A. Hoppin, D. P. Sandler and A. Blair, "A Quantitative Approach for Estimating Exposure to Pesticides in the Agricultural Health Study," 2002. [Online]. Available: https://academic.oup.com/annweh/article/46/2/245/136333.
- [50] D. Gunnel, M. Eddleston, M. Phillips and F. Konradsen, "The global distribution of fatal pesticide self-poisoning: Systematic review.," BMC Public Health, vol. 7, no. 357, 2007.
- [51] Ministry of Health of Costa Rica, «Analisis de situacion de salud, Costa Rica [Analysis of health situation, Costa Rica],» 2014. [En línea]. Available: https://www.ministeriodesalud.go.cr/index.php/vigilancia-de-la-salud/analisis-de-situacion-de-salud/2618-analisis-de-situacion-de-salud-en-costa.
- [52] World Health Organization (WHO), "Suicide, suicide attempts and pesticides: a major hidden public health problem," 2006. [Online]. Available: http://web.a.ebscohost.com/ehost/pdfviewer/pdfviewer?sid=b69deb69-a775-457b-b794-bda0ab068ac8%40sessionmgr4008&vid=1&hid=4201.