POSSIBLE CORRELATION BETWEEN CHRONIC HERBICIDES EXPOSURE AND OCCURRENCE OF HEPATOCELLULAR CARCINOMA IN DELTA AREA OF EGYPT

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ABSTRACT

Herbicides, known as weed killers, used to kill unwanted plants, leaving the desired crop relatively unharmed. They are widely used in agriculture and account for about 70% of all agricultural pesticide use. Among environmental factors hypothesized to increase the risk of hepatocellular carcinoma (HCC) are exposures to pesticides. Because a major segment of the population in Egypt is employed in agriculture, raising the possibility that exposure to pesticides is an additional risk factor for (HCC), which is the most common malignant tumors worldwide. So, the present work studied the possible association between some herbicides exposure used at least within the past 12 months as (2,4,5-trichlorophenoxyacetic acid) and (N- glycerine isopropyl ammonium) and occurrence of (HCC) in some delta areas in Egypt. The study was conducted from the 1st of January 2014 to 1st of July 2015. It involved 100 cases were recruited from Hepatology, Gastroenterology and infectious disease of Al-Azhar University Hospital (New Damietta). In addition to 50 subjects served as a control group. After free informed consent to participate in this study and within one hour after arrival to Hepatology, Gastroenterology and Infectious Disease Hospital, 10 mL of blood were collected and the serum was divided into three aliquots. One for extraction of (2,4,5-trichlorophenoxyacetic acid and N- glycerine isopropyl ammonium) residues by using high performance liquid chromatography (HPLC) and two of which were stored at -8C° for the following assays to all subjects, (HCV and HBV) and serum alpha-fetoprotein. Cases and controls were subjected to a standardized questionnaire. Clinical examination to all groups with a special attention to; manifestation of liver disease, then diagnosis of (HCC) by; abdominal ultrasonography, computerized tomography and magnetic resonance imaging beside histopathology for confirmation of some case were done. In general (HCC) in the present study, has a strong possible correlation with exposure to some herbicide (2,4,5-trichlorophenoxyacetic acid) (70.0%) and (N- glycerine isopropyl ammonium) (80.0%) which is statistically significant and hepatitis c virus is positive in (80.0%) and to some degree hepatitis B virus is positive in (40.0%) which acts as additive effects for HCC especially among rural area, which constitutes (95.0%) of the present sample.

INTRODUCTlON

Pesticides are substances or mixture of substances intended to prevent, destroy, repel or mitigate any kind of pests (Gilden et al., 2010). Numerous human and other animal studies evidenced side effects of pesticides (Hawthorne and Dively, 2011). The toxicology of mixtures can not be fully understood without knowing the differential cytotoxicity of the various compounds on human (IFEN, 2011). Pesticides possess a complex of specific features that distinguish them from other chemical agents used by their intentional introduction into the environment and their unavoidable exposure, the possibility of exposure of large contingents of populations and their high biological activity (Hawthorne and Dively, 2011).

Some researchers have considered pesticides as possible epigenetic carcinogens through one or several mechanisms, including spontaneous initiation of genetic changes, cytotoxicity with sustained cell proliferation, oxidative stress, inhibition of apoptosis, inhibition of intracellular communication and formation of activated receptors (Rakitsky et al., 2000).

Pesticides are classified into: herbicides, insecticides, fungicides, rodenticides, pediculocides, and biocides (Hawthorne and Dively, 2011). There is concern of possible carcinogenicity of herbicides especially hepatocellular carcinoma as 1,638 genes related to liver-toxicity, were analyzed by Agilent Human array to characterize each chemicals (Howard et al., 2012). Hepatocellular carcinoma (HCC) is the most common primary cancer of liver and its incidence has increased in Japan and several portions of the developing world, arising mainly in patients with chronic liver disease (Hawthorne and Dively, 2011). In the United States the incidence increased from 1.4 per 100,000 population for the period from 1976-1980 to 2.4 per 100,000 for the period from 1991-1995 (El-Serag and Mason, 2004). Worldwide, more than 80% of the risks for HCC are attributable to chronic infections with hepatitis B and C viruses (HBV and HCV) (Chen et al., 1997).

Among environmental factors hypothesized to increase the risk of HCC are exposures to pesticides (Gilden et al., 2010). During the past decade, the potential for chlorophenoxy herbicides to cause certain forms of cancers in humans has become under increasing scrutiny. The initial focus was principally directed to two member of this family of herbicides, 2,4,5-trichlorophenoxyacetic acid (2,4,5-T) and N-(Herophonomethyl) glycerine isopropyl ammonium, trade name in Egypt are; Herphossate 48%, Baron 48%, Glialka 48% and Round up 48% presumably had been shown to be an animal carcinogen (Eriksson et al., 2014).

The aim of the present work was to study the possible association between herbicides exposure (2,4,5-trichlorophenoxyacetic acid and N- glycerine isopropyl ammonium) and occurrence of hepatocellular carcinoma in area of delta in Egypt (Kafr Elshikh, Mansoura and Damietta).

PATIENTS AND METHODS

Study population

A cases-control study was conducted from the 1st of January 2014 to 1st of July 2015. After obtaining informed consent form 100 cases were recruited from the department of hepatology, gastroenterology and infectious diseases in Al-Azhar University Hospital (New Damietta) and 50 healthy volunteers as a control group after taking informed valid consent to participate in this study with no history of smoking, alcohol intake or herbicides exposure.

Cases and control were eligible if they were above the age of 20, had a residence in Egypt for more than one year, and were physically and mentally capable of understanding and completing the questionnaire.

Once informed consent was obtained, ten milliliters of blood were collected from each subject by venipuncture. The questionnaire contained inquiries about the following items:

a) Sociodemographic data:- (sex, age, region of current residence "urban or rural" and residential history),
b) Personal habits (current smoking and alcohol intake within the last 30 days),
c) Medical history (history of bilharziasis, intake of oral anti-shistosomiasis therapy or blood transfusions),
d) Family history of cancer,
e) History of occupational exposure to (2,4,5-trichlorophenoxyacetic acid) and (N- glycerine isopropyl ammonium) pesticides, petroleum products, and other chemicals) within at least the past 12 months and
f) Agricultural activities (working or helping in agriculture, history of exposure to herbicides, types of crops grown and wearing protective clothes).

Clinical examination

With special attention to; manifestation of liver disease including signs of HCC as: cachexia or loss of weight, itching, ascites, edema lower limbs, jaundice and Glasgow Coma Score (GCS).

Investigations

Cases were recruited with a provisional diagnosis of HCC; they were included in this study only if they had a definite or probable diagnosis of HCC by; abdominal ultrasonography (US) to study the pattern of the liver and size of its focal lesion and pattern of spleen, biliary tree, portal venous system, presence or absence and the

degree of ascites, both kidneys and any abnormality present, computerized tomography (CT) and magnetic resonance imaging (MRI) to confirm the diagnosis.

Haematoxiline and eosin-stained sections were reviewed by the pathologist to confirm a definite case of HCC. Non malignant cases were excluded from this study.

Cases were classified as having a definite diagnosis of HCC if there was documentation of pathology evidence of malignancy or alpha-fetoprotein (AFP) above 1000 ng/ml or AFP above 450 ng/ml plus evidence of single mass from ultrasound or CT. While cases were classified as having a probable diagnosis of HCC if they had an isolated finding of AFP above 450 ng/ml or an isolated finding of a large mass on doppler ultrasound, CT or MRI.

Laboratory assays

Serum was separated and the divided into three aliquots;

a) According to method of (Verebey et al., 1998), one milliliter of blood was inserted in a 50 mL flask for extraction of 2,4,5-trichlorophenoxyacetic acid and N- glycerine isopropyl ammonium). Hexane (6 mL) and acetone (3 mL) were added, and the contents were shaken at room temp for 30 min using a mechanical shaker. The extract was centrifuged for 10 min at 2000 rpm and the clear top layer of hexane was collected in a clean test tube. The remaining portion was again extracted twice using same processes and the hexane fractions were added to the previous solvent fractions. Clean up of the samples was done by column chromatography. Elute was collected in a 100 ml beaker and hexane was evaporated to concentrate the samples. The concentrated residues were dissolved in hexane for further analysis.
b) The other two aliquots were stored at -8 C°. The following assays were performed for all subjects. Hepatitis C antibody: enzyme-linked immunosorbant assay (ELISA) by 3rd generation kit from Abbott Laboratories (Wiesbaden, Germany). Polymerase chin reaction (PCR) using a quantitative real time HCV RNA (Rotor Gene 6000) according to the method of (Abdel Hamid et al., 2010), using nested primers from the highly conserved 50-untranslated region (50-UTR) of the HCV genome. HCV RNA by conventional PCR, this procedure is done only for ELISA positive HBV core antibody (HBcAb). Positive test result indicates previous or ongoing infection with HBV or long lasting immunity. The kit used in this procedure is Corzyme enzyme which is a competitive immunoassay (Abbott Laboratories, Wiesbaden, Germany). HBV surface antigen (HBsAg), a positive test result indicates current active or recent

infection with HBV. The kit used in this procedure is Auszyme, which is a 3rd generation enzyme immunoassay (EIA) (Abbott Laboratories, Wiesbaden, Germany). AFP: this test was performed for the cases only, using the IMx Microparticle Enzyme Immunoassay (MEIA) system for quantitative determination of AFP (Abbott Laboratories, Abbott Park, Illinois, USA).

Statistical analysis

The collected data were organized, tabulated and statistically analyzed using SPSS software computer package version 16 (SPSS Inc. USA). For quantitative data, all the values were expressed as mean ± standard deviation (SD). For comparison between the two groups, the students (t) test was used. For qualitative data, number and percent distribution were calculated and Chi square test (X^2), was used for comparison between two groups. The value of $P< 0.05$ is considered significant.

RESULTS

1- Socio-demographic data (Table 1).

As regarding the demographic data of the studied cases, 80 were males (80.0%) and 20. were females (20%) in study group, 46 males (92%) and 4 females (8.0%) in control group. There was no significant difference in sex distribution between the study and control groups (P=0.099).

The mean ages of the studied groups were (40.10 ± 11 y) in study group and (30.05±10 y) in control group. There was no significant difference in age distribution between the studied groups (P=0.320).

Regarding residence distribution in the study group, urban were 5 cases (5.0%) and 95 cases (95.0%) were rural while in control group 40 cases (80.0%) urban and 10 cases (20.0%) from rural area, which is statistically significant (P= 0.004).

Education levels in the study group as regarded learning degree; 20 cases (20.0%) were illiterate, 41 cases (41.0%) read and write, 32 cases (32.0%) had a secondary technical certificate and 7 cases (7.0%) had received a higher education while in control group 10 cases (20.0%) were illiterate, 10 cases (20.0%) read and write, 22 cases (44.0%) had a secondary technical certificate and 8 cases (16.0%) had received a higher education. There was a significant difference regarding levels of education between the study and control groups (P=0.005).

With regard to the smoking index among the study group; the number of non-smokers were 9 cases (9.0%), mild in 19 cases (19.0%), moderate in 21 cases (21.0%) and heavy smokers in 51 cases (51.0%) while smoking index in control group, number of non-smokers were 5

cases (10.0%), mild in 10 cases (20.0%), moderate in 15 cases (30.0%) and heavy smokers in 10 cases (20.0%). There was a significant difference as regarding smoking index between the study and control groups (P=0.002).

The prevalence of alcohol intake, were 10 cases (10.0%) in study group and 4 cases (8.0%) in the control group. There was no significant difference as regarding alcohol consumption between both groups (P=0.420).

In the study group, past history of bilharziasis was 80 cases (80.0%), oral antibilharzial therapy was 90 cases (90.0%), blood transfusions was 10 cases (10.0%) and having a positive family history of cancer represented (2.0%) while in control group, past history of bilharziasis was 42 cases (84.0%), oral anti bilharzial therapy was 45 cases (90.0%), blood transfusions was 3 cases (6.0%) and having a positive family history of cancer represented (4.0%). There was no significant difference in past history between the study groups (P=0.410).

Agricultural activities in the study group, working or helping was 95 cases (95.0%), exposures was in 90 cases (90.0%) and crops grown in 100 cases (100.0%) while in control group working or helping was in 2 cases (4.0%), exposures in 1 case (2.0%) and crops grown in 20 cases (40.0%). There was a significant difference as regarding agricultural activities between the study groups (P=0.002).

The number of cases wearing protective clothes in the study group were 24 (24.0%) and 2 cases (4.0%) in the control group, which is statistically insignificant (P = 0.200).

2- Clinical data (Table 2).

As regarding clinical data, there is no significant difference between cases and control groups as regard cachexia or loss of weight and Itching (P > 0.05). While there is significant difference between studied groups as regard ascites, jaundice, edema of lower limbs and Glasgow coma score (P > 0.05).

3- Investigation findings of HCC in the studied groups (Table 3).

Findings of investigation done; abdominal US is positive in 90 cases (90.0%), CT is positive in 95 cases (95.0%), MRI is positive in 98 cases (98.0%) and AFT is high in 76 cases (76.0%) while investigation finding in the control group; is positive in one case (2.0%), in abdominal US, CT and MRI but no cases with AFT which is statistically significant (P > 0.05).

There is slightly above the critical level (P = 0.052) as regarding histopathology between the study groups.

As regarding hepatitis C virus (HCV) in the study group; (HCV-Ab) was positive in 80 cases (80.0%) and polymerase chain reaction (PCR) was positive in 75 cases (75.0%) and in hepatitis B virus (HBV); HBsAg was positive in 40 cases (40.0%) and HBs-Ab was positive in 10 cases (10.0%) while hepatitis C virus (HCV) in control group; the (HCV-Ab) was positive in 20 cases (40.0%) and polymerase chain reaction (PCR) was positive in 3 cases (6.0%) and in hepatitis B virus (HBV); HBsAg and HBsAb were positive in 2 cases (4.0%). There was extremely significant difference between studied groups ($P > 0.001$).

4- Results of pesticide exposure assessment in the study cases (Table 4).

Regarding the pesticide exposure finding in the study group: (2,4,5-trichlorophenoxyacetic acid) was positive in 70 cases (70.0%) and (N- glycerine isopropyl ammonium) was positive in 80 cases (80.0%) while in control group (2,4,5-trichlorophenoxyacetic acid) was positive in two cases (4.0%) and (N- glycerine isopropyl ammonium) was positive in three cases (6.0%). There was an extremely significant difference between studied groups ($P > 0.005$).

Table (1) : Comparison of socio-demographic data between cases and controls (n=150).

Studied Parameters		Study group (n=100)	Control group (n=50)	*P value*
Sex n. (%)	**Male**	80 (80.0%)	46 (92%)	0.099 (NS)
	Female	20. (20%)	4 (8.0%)	
Age (mean±SD) in years.		(40.10±11)	(30.05±10)	0.32
Region of current residence n. (%)	**Urban**	5 (5.0%)	40 (80.0%)	*0.004
	Rural	95 (95.0%)	10 (20.0%)	
Levels of Education n. (%)	**Illiterate**	20 (40.0%)	10 (20.0%)	*0.005
	Read write	41 (41.0%)	10 (20.0%)	
	Secondary education	32 (32.0%)	22 (44.0%)	
	High education	7 (7.0%)	8 (16.0%	
Smoking index n. (%)	**Non**	9 (9.0%)	5 (10.0%)	*0.002
	Mild	19 (19.0%)	10 (20.0%)	
	Moderate	21 (21.0%)	15 (30.0%)	
	Severe	51 (51.0%)	10 (20.0%)	
Alcohol intake n. (%)		10 (10.0%)	4 (8.0%)	0.420
Past History n. (%)	**Bilharziasis**	80 (80.0%)	42 (84.0%)	0.410
	OAT	90 (90.0%)	45 (90.0%)	
	Blood transfusions	10 (10.0%)	3 (6.0%)	
	Family history of cancer	2 (2.0%)	2 (4.0%)	
Agricultural activities n. (%)	**Working or helping**	95 (95.0%)	2 (4.0%)	*0.002
	Exposures	90 (90.0%)	1 (4.0%)	
	Crops grown	100 (100.0%)	20 (40.0%)	
Wearing protective clothes		24 (24.0%)	2 (4.0%)	0.200

n: number, %: percentage, SD: standard deviation, * significant (P< 0.05), OAT: anti-shistosomiasis therapy.

Table (2) : Clinical manifestations of both groups (n = 150).

Studied Parameters		Study group (n=100)	Control group (n=50)	*P value*
Cachexia or loss of weight n. (%)		95 (95.0%)	5 (10.0%)	0.92
Itching n. (%)		80 (80.0%)	1 (2.0%)	0.18
Ascites n. (%)		90 (90.0%)	1 (2.0%)	0.023
Edema lower limbs n. (%)		90 (90.0%)	1 (2.0%)	0.012
Jaundice n. (%)		95 (95.0%)	5 (10.0%)	0.012
Glasgow Coma Scale	**Mild (13 – 15)**	18 (18.0%)	0.001(S)	*0.001
	Moderate (9- 12)	80 (80.0%)	0 (0.0%)	
	Severe (3- 8)	2 (2.0%)	0 (0.0%)	

n: number, %: percentage, * significant (P< 0.05).

Table (3) : Investigation findings of HCC in the studies groups (n = 150).

			Study group (n=100)	Control group (n=50)	*P value*
Abdominal ultrasonography n. (%)			90 (90.0%)	1 (2.0%)	*0.001
Computerized Tomography n. (%)			95 (95.0%)	1 (2.0%)	0.004
Magnetic resonance imaging n. (%)			100 (100.0%)	1 (2.0%)	*0.002
Histopathology n. (%)			20 (20.0%)	--	0.058
Alpha fetoprotein n. (%)			76 (76.0%)	--	*0.001
Viral markers n. (%)	**HCV**	**HCV-Ab**	80 (80.0%)	20 (40.3%)	*0.001
		PCR	75 (75.0%)	3 (6.0%)	
	HBV	**HBsAg**	40 (40.0%)	2 (4.0%)	
		HBsAb	10 (10.0%)	2 (4.0%)	

n: number, %: percentage, * significant (P< 0.05).

Table (4) : Results of pesticide exposure assessment in the studied cases (n = 150).

	Study group (n=100)	Control group (n=50)	*P value*
(2,4,5-trichlorophenoxyacetic acid) n. (%)	70 (70.0%)	2 (4.0%)	*0.001
(N- glycerine isopropyl ammonium) n. (%)	80 (80.0%)	3 (6.0%)	*0.002

n: number, %: percentage, * significant (P< 0.05).

DISCUSSION

In Egypt, rates of HCV and HBV infections vary markedly by geographical location and by age groups and sex (Abdel-Aziz et al., 2000). With a general trend toward higher rates among men and older individuals, in rural communities regions of Delta and Middle Egypt relative to Cairo, Alexandria and Upper Egypt, therefore any studies of the malignant outcomes of HCV and HBV infections should be designed to carefully control these factors (Wichita, 2003).

So, this work was conducted to studied the possible association between some herbicides exposure used in the last decade (2,4,5-trichlorophenoxyacetic acid and N- glycerine isopropyl ammonium) and occurrence of hepatocellular carcinoma in areas of delta in Egypt (Kafr Elshikh, Mansoura and Damietta). The study was conducted from the 1st of January 2014 to 1st of July 2015.

Regarding the demographic data of the studied cases; (80%) were males, in test group while they were (92%) in control group. The majority of male cases are due to the fact that males are more likely to report the use of herbicides in agriculture accepted in the society (Mucci et al., 2001). Male dominance in herbicides was also recorded by (Milena et al., 2015).

Regarding the mean age in years, it was (40.10 ± 11) in the study group and (30.05 ± 10) in control group. These finding signify an alarming trend in the prevalence of herbicides exposure in such age. In a case-control study in Greece, in which herbicides exposure at mean age (40 ± 10%) are significantly associated with an increased risk of HCC (Mucci et al., 2001), whereas a Taiwan study showed that the risk of HCC was inversely related to the number of child bearing period, age and use of oral contraceptives (Yu et al. 2003). Such observations of a relationship between HCC and herbicides exposure are thought to reflect cumulative exposure to herbicides (Mucci et al., 2001).

Observed significant additive risks of HCC from increasing age and from agricultural pesticide exposures among rural males was reported by (Ezzat et al., 2005).

In the present study; there was a significant difference regarding smoking index between the study and control groups. There is strong association between smoking and occurrence of HCC as most of HCC are smokers (91.0%). These results are in agreement with El-Serag and Rudolph (2007), they reported that the risk of HCC increased significantly with an increased duration of smoking (and daily consumption of hard liquor.

The relationship between cigarette smoking and HCC has been examined in more than 50 studies in both low- and high-rate HCC areas. In almost all countries, both a positive association and lack of an association have been reported (El-Serag et al., 2007).

There is no significant difference as regarding alcohol intake between the study and control groups (P=0.420). These results are not agreement with El-Serag and Rudolph (2007) who reported that the risk of HCC increased significantly with daily consumption of more than three standard alcoholic drinks (P = 0.048). These explained by decreased number of alcohol consumption due to religious practices.

Regarding past history of bilharziasis, oral anti bilharzial therapy, blood transfusions and positive family history of cancer, are statistically insignificant.

Working or helping in agricultural activities in the study group, exposures in and crops grown are statistically significant in test group compared to control.

Ezzat et al. (2005) was found that each year of agricultural use of carbamates or organophosphorus compounds was associated additively with excess HCC risks of 5% and 4%, respectively.

Stemhagen et al. (1999) reported an association of agricultural work and HCC in men, in a case-control study from the New Jersey State Cancer Registry. Interestingly, this association was found among farm laborers, but not among farm owners and managers, suggesting that closer contact with agricultural chemicals might have had a causal relationship to liver cancer.

Badawi and Michael (1999) reported a slight elevation in the HCC risk for farming occupations but there was no data available on HCV markers in the study. More specifically, a few studies have described associations of HCC risk with pesticides applied in agricultural work.

Agricultural use of organophosphorus compounds was found to be associated with a five fold increased risk for HCC in males in Vietnam (Cordier et al., 1993). Twenty four percent of them wear protective clothes which is statistically insignificant.

Regarding clinical data, there is no significant difference between cases and control groups as regard cachexia or loss of weight and itching. While there were significant differences between studied groups as regard ascites, jaundice, edema lower limbs and GCS.

Regarding investigation finding in the study group; abdominal US is positive in

(90.0%), CT is positive in (95.0%), MRI is positive in (98.0%) and AFP is high in (76.0%) and investigation finding in the control group; were positive in (2.0%), in abdominal US, CT and MRI but no cases with elevated AFP which is statistically significant (P>0.05). Liver-imaging strategies should incorporate liver lesion characterization as an equally important goal (Karhunen, 2005).

Several imaging modalities are now available for detection and characterization of focal liver lesions. These include (US), computed (CT), (MRI) and positron emission tomography (PET), since technological advances in these modalities and associated contrast media continue to occur, no broad consensus exists over which modality should be used (Noone et al., 1999).

Several studies have consistently shown the superiority of a liver-specific contrast agent-enhanced MRI examination over contrast-enhanced CT or a non-contrast MRI examination (Weinmann et al., 2003).

There is slightly above the critical level (P=0.052) as regarding histopathology between the study and control groups

Regarding hepatitis C virus (HCV) in the study group; (HCV-Ab) is positive in (80.0%) and polymerase chain reaction (PCR) is positive in (75.0%) and HBsAg is positive in (40.0%) and HBsAb is positive in (10.0%) while in control group (HCV-Ab) is positive in (40.0%) and (PCR) is positive in (6.0%) and HBsAg and HBsAb is positive in (4.0%). The similarity of the HCV rates in our controls to those of the Egyptian population (Abdel-Aziz et al., 2000), suggests that these control subjects are representative of the general population with regard to the most important risk factors for HCC.

The decreased number of HBV in the last decade in Egypt may return to the obligatory immunization and these is not in accordance with the studies of Ikeda et al. (1999) who showed that chronic HBV carriers have 5-15-folds increased risk of HCC compared with the general population.

Chronic HCV infection is also one of the major risk factors for the development of HCC. This is inaccordance with the study of El-Serag et al. (2007) in which the markers of HCV infection are found in a variable proportion of HCC patients i.e., 44%–66% in Italy, 27%-58% in France, 60%–75% in Spain, and 80% - 90% in Japan.

In this study we found that, the major risk factors for HCC in Egypt are HCV and HBV infections, but we also observed significant additive risks from increasing

age and from agricultural pesticide exposures among rural males. These results are in accordance with Ezzat et al. (2005).

The burden of HCC is 80.0%. These results are also in accordance with Ezzat et al. (2005) in which the attributable risk of HCV to the burden of HCC is 90.4%.

The results are consistent with the notion that the risk of HCC significantly increases in persons previously infected by HBV and/or HCV. Similar result was observed by El- Serag et al. (2007).

As regarding pesticide exposure finding in the study group; (2,4,5-trichlorophenoxyacetic acid) is positive in (70.0%) and (N-glycerine isopropyl ammonium) is positive in (80.0%) while in control group (2,4,5-trichlorophenoxyacetic acid) is positive in (4.0%) and (N-glycerine isopropyl ammonium) is positive in (6.0%).

Several compounds such as tetrachlorvinphos (2-chloro-1(2,4,5 trichlorophenoxyacetic acid) ethenyl dimethyl ester) and N- glycerine isopropyl ammonium have been tested in experimental systems and found to produce HCC in mice (Robens, 2010) but have not yet been reported as human carcinogens.

In conclusion: the results of the present study revealed a relation between exposure to (2,4,5-trichlorophenoxyacetic acid) and (N-glycerine isopropyl ammonium) and occurrence of HCC.

Due to limited literature on the hepatocarcinogenicity of pesticides compounds, it's recommended that;

1. More researches are needed for future testing other pesticides compounds and HCC with consideration other hepatocarcinogenicity,
2. Further studies should be undertaken to assess specific risk factors in more detail, such as aflatoxins and certain lifestyle factors (diet, alcohol and tobacco smoking), as well as some reproductive factors and diabetes as it might be involved in the etiology of HCC to avoid it.

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العلاقة بين إمكانية التعرض المزمن لبعض مبيدات الأعشاب وحدوث أورام سرطانية بالكبد فى منطقة الدلتا بمصر

المشتركون فى البحث

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مبيدات الإعشاب أو المشهور عنها "بقاتلة العشب"، والتي تستخدم في قتل النباتات الغير مرغوب فيها، كما أن انتقاء مبيدات أعشاب لها القدرة على قتل النباتات الغير مرغوب فيها بدون التأثير على النباتات المرغوب فيها أدى إلى استخدام هذه المبيدات في الزراعة بشكل كبير جدا قد يصل إلى ٧٠٪ من المبيدات المستخدمة. وأنة بدراسة العوامل البيئية التي قد تزيد من خطر التعرض لسرطان الكبد نتيجة التعرض لهذه المبيدات. ونظرا لعمل قطاع كبير جدا من المصرين في الزراعة فإن ذلك يؤدى بدورة إلى إمكانية تعرضهم لهذه المبيدات والتي قد تضيف عامل خطورة للإصابة بسرطان الكبد، والذي يعد واحدا من أهم وأكثر السرطانات المشهورة على مستوى العالم، لذا كان الهدف من هذا البحث هو دراسة العلاقة بين إمكانية التعرض لبعض هذه المبيدات العشبية الأكثر انتشارا في مصر في خلال سنة على الأقل وهما (٢ و ٤ و ٥ ثلاثي كلورو-حمض الفينو اكسي اسيتيك) و(ن-جليسرين ايزوبروبيل الامونيوم) وحدوث أورام سرطانية بالكبد في منطقة الدلتا بمصر (كفر الشيخ، المنصورة ودمياط). وقد شملت هذه الدراسة مائه حالة من وحدة أمراض الكبد، الجهاز الهضمي والحميات بمستشفى بدمياط الجديدة،كما تم اختيار خمسون حالة كمجموعة ضابطة. وقد تمت الدراسة في الفترة من أول يناير ٢٠١٤ إلى أول يوليو ٢٠١٥. وبعد وصول المرضى إلى وحدة أمراض الكبد، الجهاز الهضمي والحميات، تم أخذ موافقتهم على إجراء البحث , ثم تم سحب عينة الدم على أنبوبة تحتوى على إيدتا. وتم حفظ العينات في درجة حرارة – ٨ درجة مئوية لحين عمل كلا من التحاليل المعملية للكشف عن هذه المبيدات مستخدمين في ذلك "جهاز الفصل الكروماتوجرافى السائلي عالي الجودة" في وحدة السموم الإكلينيكية و التحاليل المعملية للكشف عن (فيروس (س) و(ب)، دلالات الأورام (البروتين الجنيني ألفا)، كما تم استكمال استبيان لكل الحالات لفحص العوامل الاجتماعية و العوامل الديموجرافية, العادات الشخصية , التاريخ الطبي من حيث (التعرض للإصابة بطفيل البلهارسيا ,والعلاج منه ونقل الدم) ,التاريخ العائلي لحدوث أي أورام سرطانية ,وفترة التعرض لهذه المبيدات بحيث لا تقل عن سنة على الأقل , والعمل أو النشاط الزراعي , كما تم الفحص الاكلينيكى لهم , مع الأخذ في الاعتبار أعراض الاعتلال الكبدي وخصوصا علامات سرطان الكبد ,كما تم تشخيص سرطان الكبد بواسطة (الأشعة التليفزيونية, الأشعة المقطعية، الرنين المغنطيسي إلى جانب اخذ عينة كبدية لتأكيد التشخيص لبعض الحالات) وأسفرت نتائج الدراسة عموما عن وجود علاقة قوية ذات دلالة إحصائية بين التعرض لمركبات (٢ و ٤ و٥ ثلاثي كلورو- حمض الفينو اكسي اسيتيك) حيث كان إيجابي في ٧٠٪ و(ن-جليسرين ايزوبروبيل الامومنيوم) حيث كان إيجابي في ٨٠٪ وحدوث أورام سرطانية بالكبد. وان معظم المرضى حوالي ٩٥٪ من سكان القرى وخصوصا المصابين منهم بفيروس (س) ٨٠٪ وفيروس (ب) ٤٠٪ .