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Biochemical Changes Associated with Long Term Exposure to Pesticide among Farmers in the Gaza Strip

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Abstract

The study characterized the biochemical changes associated with long term exposure to pesticides. Practical parameters of pesticides were collected using 500 questionnaires. Farmers having 10 years working period were invited to a private clinic for blood sampling and enzyme analysis. All participants were male farmers of different age groups, and education levels. Occupational parameters indicated that majority of farmers used manual methods for pesticide works. About 130 pesticides are currently used in Gaza. Toxicological symptoms indicated that dizziness, headache, and nausea were dominant among farmers, whereas vomiting abdominal colic and tearing were less dominant. Acetyl Cholinesterase (ACHE) cumulatively inhibited among farmers after work whereas Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST) and Alkaline Phosphatase (ALP) activities were above range after long term exposure. It can be concluded that long term exposure to pesticides may damage liver and kidney cells resulting in hepatic-toxicity and/or nephrotoxicity.

Keywords

Long Term Exposure, Toxicology of Pesticides, ALT, AST, ALP, ACHE Activities

1. Introduction

The Gaza Strip is a semi-arid region with an annual rainfall ranged from 180 - 450 mm. The population in Gaza is about 1,750,000 who live and work in an area of 365 km^2. Agriculture in the Gaza Strip is highly intensive and relies on frequent application of pesticides, which results in contamination of food samples and agricultural commodities [1]. Health hazards associated with pesticide application have been reported, for instance, cancer

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cases [2], risks to agricultural workers [3] and health disabilities [4]. Eco-toxicity of pesticides has been reported to cyanobacteria [5]-[8], to fish [9] [10] and D magna [11]. Occupational exposure to pesticides has been reported in many countries for instance Egypt [12], Barazil [13], UK [14], Bangladesh [15], South Korea [16] and other countries. These reports dealt with knowledge, practices and attitudes of farmers but lacked investigation of biochemical changes associated with long term exposure to pesticides.

Moreover, long term exposure to pesticides may occur via indirect way such as ingestion of contaminated food with pesticides residues [17], drinking of contaminated milk [18] [19], contaminated fish [20] contaminated water [21] [22] and contaminated soil [23]-[25]. It is necessary to understand the effects of long term exposure to pesticides to be able to minimize and/or control the possible associated health hazards. Accordingly, this study was initiated to: 1) characterize the current occupational parameters of pesticide works; 2) determine toxicity symptoms under field conditions; and 3) characterize the biochemical changes associated with long term exposure to pesticides among farmers.

2. Materials and Methods

2.1. Data Collection

About 500 questionnaires were used to collect the occupational data from the field via direct contact, face to face interviews. The data collection included demographic parameters, Knowledge of pesticides hazards, occupational parameters, and toxicity symptoms

2.2 Biochemical Investigation

Blood sampling and analysis for enzyme activities

Farmers having long term exposure (10 years or more) to pesticides were invited to a private health clinic for voluntarily blood sampling (10 ml). The blood samples were collected in heparin containing tubes and analyzed in the same day for ACHE, ALP, AST, ALT activities and urea, uric acid, and total protein concentrations.

Acetylcholine esterase activity (ACHE) was measured by a spectrophotometer according to the method developed previously by Ellman *et al.* [26] using acetyl thiocholine iodide as a substrate. The yellow color produced by the reaction was determined at 420 nm.

The activity of ALP was determined according to Bessey *et al.* [27] whereas AST and ALT activities were measured by the procedure of Reitman and Frankel [28] using a commercially available kit from Bio-Merieux.

The total protein content was determined by the method of Lowry *et al.* [29] using bovine serum albumin as the standard.

Determination of urea, creatinine and uric acid uses kit techniques.

2.3. Previous Health Records

Previous health records of the farmers having long term exposure to pesticides were collected from the health departments and personal health files. Each farmer working on pesticide spry processes should have an official medical investigation including AST, ALP, AST, ACHE, and kidney function test. The data of each farmer were saved in the particular file. This medical examination test is an obligatory for officially employed works.

2.4. Statistical Analysis

The collected data were analyzed using an Excel program. Occupational exposure to pesticides were categorized into three modes as follows: mode 1, (M1) contained farmers working in pesticide application for 1 - 5 years; mode 2, M2, (6 - 10 years) and mode 3, M3, (>10 years).

The range of enzyme activities were assigned, average and standard deviation were calculated. T-test were used to detect significant differences.

3. Results

3.1. Demographic Data

The participants of the study are male Palestinian farmers from Gaza belonged to different age groups: group 1, (20 - 30) 130 farmers, group 2 (31 - 40) 185 farmers, and group 3 (41 - 60) 164 farmers. The education levels were below general secondary school (65%), General secondary schools (25%), and meddle education and above (10%).

3.2. Farmers and Pesticide Information

Distribution of farmers using different pesticides type in the Gaza Strip is shown in **Table 1**. It can be seen that farmers using insecticides are majority among all (n = 221, 44.47%), followed by those using herbicides, fungicides and nematicides. It can be seen that the majority of farmers (n = 164) are located in the north zone whereas the minority (n = 57) are located in Rafah.

The scientific name, frequency of application and lethal does (LD_{50}) of pesticides used by farmers are shown in **Table 2**. It is obvious that Chlorpyrifos, Fenamiphos and Imidacloprid have the highest frequency among other insecticides. Oxadiazon, Prometryn and Paraquat are the most frequent herbicides. Mancozeb, Triadimenol and Penconazole are most frequent fungicides. Methyl bromide, DBCP and Metham sodium are the most frequent nematicides used by farmers.

Table 1. Distribution of farmers using pesticides in different locations in Gaza Strip.

Type of pesticide	Farmers locations				Total	
	Rafah	KH. Y	Gaza	North	Number	%
Insecticides	25	71	54	71	221	44.47
Herbicides	10	37	31	40	118	23.73
Nematicides	12	14	23	21	70	14.1
Fungicides	10	20	26	32	88	17.7
Total	57	142	134	164	497	100

Table 2. Scientific name, LD_{50}, and frequency of application.

Insecticide	LD_{50}	Frequency	Fungicides	Frequency	LD_{50}
Chlorpyrifos[1]	135 - 165	156	Mancozeb	113	>5000
Fenamiphos[1]	6 - 10	153	Triadimenol	100	700
Dimethoate[1]	387	67	Penconazole	96	2125
Imidacloprid	>5000	71	Propamocarb	34	2000 - 2009
Carbosulfan[2]	250	61	Propineb	26	5000
Cadusafos[1]	37.1	59	Cymoxanil	62	
Aldicarb[2]	0.93	57	Chlorothalonil	25	5000
Cypermithrin[4]	105.8	37	Iprodione	12	2000
Chlorfluazuron[5]	>1000	67	Bupirimate	12	4000
Metham sodium[(N)]	1800	29	**Herbicides**	**Frequency**	**LD50**
Abamectin[3]	25	29	Oxadiazon	73	5000
Lufenuron[5]	>2000	26	Prometryn	53	2000
Methyl bromide[s,(N)]	3.03	25*	Paraquat	33	127
Fenpropathrin[4]	70.7	23	Diquat	32	408
Cypermethrin[4]	250	23	Glyphosate	32	5600
Methamidophos[1]	16.6	50	2, 4-D	21	
DBCP[s]	NA	13	Metribuzin	20	2000
Endosulfan[5]	70	16	Pendimethalin	20	1050 - 1250
Bromopropylate[5]	>5000	8	Cycloxydin	20	5000
Chlorfenapyr	441	8	Imazapic	20	5000
Methomoyl[2]	34	18			
Oxydemeton methyl[1]	50	19			
Fenazaquin	134	14			

1 = Organo-Phosphorus compounds; 2 = Oxim carbamate compounds; 3 = Bio-pesticides; 4 = Pyrothriods; 5 = Organo-Chlorine compounds; 6 = Thiazoles; 7 = Thiocarbamate; S = suspended, * = by inhalation, N = Nematicides. LD_{50} values obtained from Tomlin [30].

All chemicals listed above are synthesized and formulated in many chemical companies around the world (e.g. Bayer, Monsanto, Sigma, Makhteshim, Agan, Syngenta, Simonis, Tapazol, Sumotomo, Laid Chemicals, Niho Nohyaku, Dow Agrosciences).

3.3. Occupational Parameters

3.3.1. Exposure Time

It can be seen that large fraction of farmers (n = 310, 62.37%) did not use full protective clothes during pesticides application. Low fraction (n = 175, 35%) partially used protective clothes. Moreover, majority of farmers (n = 275, 55%) use their own hands to prepare pesticide solution and other related activities. In addition about 55% (n = 273) of farmers revealed body contamination with pesticide solution or its drift during application. Moreover, many farmers (n = 87, 18%) indicated that they changed application mode during the same day, resulting in increasing the exposure time and the contaminated area of the body. Furthermore, 55% of farmers revealed that they did not know the hazards of pesticide accordingly they did not use safety measures during work and claimed that skin, hand, face contamination are usually occurred during spray process. About 35%, (n = 175) of farmers have concerns about pesticides but they did not believe that pesticide can cause serious health damage to human life. About 17% (n = 84) eat or drink during work period. Moreover, 43% (n = 213) believed that pesticides are not harmful to human body accordingly they did not use protective clothes. Furthermore, about 22% (n = 109) believed that pesticides are safe for human life because they are specific chemicals for pests. Low fraction of farmers (n = 44, 9%) revealed that they used pesticide containers for domestic purposes. So far about 67% (n = 332) believed that pesticides are toxic to the human beings if they were taken orally (ingestion), whereas 77% (n = 381) believed that pesticides are not harmful to the human body through skin contamination.

Distributions of farmers according to their exposure time are shown in **Table 3**. Three modes of occupational exposure are presented. Mode 1 represents farmers exposed to a period of 1 - 5 years working with pesticides (n = 190, 38.2%) distributed in all locations with a majority in the northern Gaza Strip (52 farmers). Mode 2 represents farmers exposed for 6 - 10 years working with pesticides (n = 187, 37.6%), whereas Mode 3 represents farmers exposed for more than ten years (n = 120, 24.1.2%).

3.3.2. Working Parameters with Pesticides

Methods of pesticide works such as solution preparation, application and disposal methods are shown in **Table 4**. The majority of pesticide works were done manually by farmers whereas little was done mechanically.

Table 3. Distribution of farmers according to the exposure time in all locations.

Exposure time (year)	Farmers using pesticides (locations)				Total	
	Rafah	KH. Y	Gaza	North	Number	%
Mode 1 (1 - 5 y)	22	45	54	69	190	38.2
Mode 2 (6 - 10 y)	20	55	43	59	187	37.6
Mode 3 (>10)	15	37	33	35	120	24.1
Total	57	142	134	164	497	100

Table 4. Occupational parameters of pesticides.

Location	Pesticide application		Preparation of spray solution		Disposable method	
	Manual	Mechanical	Manual	Mechanical	Manual	Mechanical
Rafah	19	10	27	4	22	8
KH. Y	87	55	107	25	122	5
Gaza	46	49	65	30	81	7
North	78	51	97	14	102	7
Total	230 (58.2%)	165 (41.8%)	296 (80.2%)	73 (19.8%)	327 (92.4%)	27 (7.6%)

P-value between manual and mechanical pesticides application is 0.07, whereas p-value between manual and mechanical preparation of spray solution 0.019 and p-value between manual and mechanical disposable method is 0.02, indicating significant differences.

3.4. Toxicology Symptoms

Toxicity symptoms among farmers observed during work periods or immediately after finishing are shown in **Table 5**. It can be seen that variety of toxicological symptoms were recorded among farmers during work. For instance, dizziness, headache, nausea, diarrhea, vomiting, and abdominal colic were dominant symptoms among farmers during work periods. Loss of appetite and losing conscious have also high percentage in all locations but less pronounced than those mentioned above. Tearing, tremors, convulsions and paralysis were less dominant toxicological symptoms in all locations.

3.5. Biochemical Changes

Effect on ACHE, ALT, AST and ALP Activity

Effects of occupational exposure to pesticides on the activity of ACHE, ALT, AST and ALP in blood serum are shown in **Table 6**.

It can be seen that the activity range of ACHE before exposure to pesticides was 6000 - 18,200 u/l with an average and standard deviation 8867 ± 2584 u/l whereas the activity reduced to a lower range due to long term exposure to pesticides and reached 2000 - 6000 u/l with an average and standard deviation 4343 ± 1325 u/l indicating commutative toxicity.

In addition ALT range before exposure to pesticides was 4 - 35 u/l with an average of 20.9 ± 7 and dramatically increased up due to long term exposure to pesticides and reached to 35 - 567 u/l with an average of 98 ±

Table 5. Toxicity symptoms among farmers.

Toxicity symptoms	Farmer locations							
	Rafah		KH. Y		Gaza		North	
	n	%	n	%	n	%	n	%
Dizziness	22	7.77	105	37.10	66	23.32	90	31.80
Headache	23	8.30	102	36.82	64	23.10	88	31.77
Nausea	23	10.18	78	34.51	51	22.57	74	32.74
Diarrhea	20	9.52	89	42.38	39	18.57	62	29.52
Vomiting	15	7.43	70	34.65	50	24.75	67	33.17
Abdominal colic	17	8.25	77	37.38	47	22.82	65	31.55
Losing appetite	13	8.02	59	36.42	38	23.46	52	32.10
losing conscious	12	8.33	53	36.81	32	22.22	47	32.64
Tearing	6	4.44	47	34.81	42	31.11	40	29.63
Tremors	5	5.15	42	43.30	26	26.80	24	24.74
Convulsions	4	5.48	31	42.47	18	24.66	20	27.40
Paralysis	6	10.71	24	42.86	15	26.79	11	19.64

Table 6. Effects of occupational exposure of pesticides on Liver enzyme activities.

	ACHE		ALT		AST		ALP	
	Range	M ± S	Range	M ± S	Range	M ± S	Range	M ± S
Before	6000 - 18,200	8867 ± 2584	4 - 35	20.9 ± 7	8 - 30	21.99 ± 6.63	122 - 200	164 ± 23
After	2000 - 6000	4343 ± 1325	36 - 567	98 ± 131	31 - 802	209 ± 550	201 - 2195	651 ± 631

M and S are mean and standard deviation respectively.

131. Similarly the activities of AST and ALP followed the same trend.

Effects on cholesterol, total protein, triglyceride, urea, creatinine, and uric acid are shown in **Table 7**. Similar to the liver enzymes (ALT, AST and ALP), concentrations of cholesterol, triglyceride and total protein were in lower ranges before exposure to pesticides and the concentrations increased after long term exposure to pesticides. It can be seen that the concentration range of urea creatinine, uric acid and total protein were in the following range before exposure to pesticides: 15 - 45, 0.6 - 1.4, and 2.6-6 mg/dl respectively. The concentrations increased dramatically and reached several times higher than the range before long term exposure to pesticides.

3.6. Farmers Frequent Visits to Hospitals or Private Visits

Farmer visits to hospitals and private clinics are shown in **Table 8**. It can be seen that there are dramatic increase in hospital visits due to pesticide works. The number of visits increased by nearly three to four folds to liver and kidney clinical tests whereas the general visit to the hospital increased by nearly four folds.

4. Discussion

It is obvious that farmers have very low information about the toxicity of pesticides to human life as shown by their answers to pesticide knowledge. Lack of knowledge among farmers was most dominant among farmers. This is probably due to the low education level of farmers.

Demographic and Occupational Parameters

It is obvious (**Table 1**) that farmers dealing with insecticides are majority followed by those dealing with herbicides, fungicides and nematicides. This is due to intensive agriculture in the Gaza strip. Insecticides and nematicides (organophosphourus and carbamate compounds) have nearly similar health risks due to similar mode of action, whereas herbicides and fungicides have different health risk due to different mode of action [30]. Moreover, type and frequency of pesticides used in Gaza Strip (**Table 2**) indicated that Chlorpyrifos, Fenamiphos, Dimithoate, Imidacloprid, carbosulfan, cadusafos and aldicarb are most frequent insecticides used by farmers, with extreme toxicity e.g. Aldicarb, Fenamiphos, methyl bromide, and high toxicity Methamidophos [31]. Moreover, it is obvious (**Table 3**) that majority of farmers exposed to short term (Model 1), and medium term (Model 2) whereas minority exposed to long term (Model 3). The explanation of these results is that farmers leave agricultural works and did commercial works with more benefits to them than agricultural works. In addition farmers frequently visited hospitals were advised to change their agricultural jobs.

Moreover, the occupational parameters of pesticides (**Table 4**), clearly indicated that majority of pesticides application such as, spray solution, and disposal methods are done manually. This is in agreement with lack of

Table 7. Effects of occupational exposure of pesticides on cholesterol, triglyceride, total protein, urea, creatinine and uric acid content in blood serum among farmers.

Test	Cholesterol		Total protein		Triglyceride		Urea		Creatinine		Uric acid	
	Range	M ± S	Range	M ± S	Range	M ± S	Range	M ± S	Range	M ± S	Range	M ± S
Before	40 - 200	162.2 ± 24	40 - 160	126 ± 55	6 - 7.1	5.53 ± 1.5	15 - 45	26.37 ± 8.5	0.6 - 1.4	0.79 ± 0.3	2.6 - 6	3.92 ± 1.3
After	201 - 299	252 ± 38	161 - 342	263 ± 83	7.2 - 8.6	7.44 ± 0.5	46 - 227	103.2 ± 50.2	1.41 - 16.2	3.36 ± 2.5	6.1 - 14.5	8.57 ± 1.9

Table 8. Farmers frequent visits to hospital or private clinic before during the work period.

	Liver test		Kidney test		General hospital	
	Before	After	Before	After	Before	After
Rafah	3	8	5	7	8	20
KH. Y	5	29	7	24	15	68
Gaza	10	32	12	28	17	48
North	8	33	10	29	17	79
total	26	102	34	88	57	215

information as shown in the knowledge section above. The manual application of pesticides exposes the farmers to high potential risk. Statistical analysis shows significant differences between manual and mechanical applications of pesticides. Regardless of the statistical variations contamination of farmer skin, face and body during work indicate high potential for toxicity. This is in agreement with the toxicity symptoms (**Table 5**). For instance, high percentage of dizziness, headache, nausea, diarrhea, vomiting and abdominal colic appeared among farmers indicate the exposure to highly toxic insecticides in accordance with the data in **Table 2**. Losing appetite and conscious suggest the exposure to herbicides and fungicides, whereas tearing, tremors convulsions and paralysis suggest the exposure to extremely toxic pesticides such as Aldicarb phenamiphos and methyl bromide (**Table 2**). Variations in the chemical groups, frequency of pesticides applications and occupational parameters suggest the occurrence of different toxic symptoms among framers. The data in **Table 5** indicate cholinergic symptoms among farmers exposed to organophosphourus insecticides in accordance with the data in **Table 2**. Our results agree with Masri *et al.* [32] who revealed that exposure to organophosphourus insecticides resulted in severe dizziness and headaches.

Application of insecticides followed by fungicides or nematicides may expose the farmers to binary or tertiary pesticides mixtures and may enhance the appearance of synergisms. This hypothesis is supported by the frequent visits to hospitals or private clinic after or during the working day **Table 7**. More supports of our results came from previous work [33] that revealed sever inhibition of ACHE on pesticide sprayers after an intensive working day.

So far, Chlorpyrifos, fenamiphos, imidacloprid, and methyl bromide, (highly toxic) are the most frequent insecticides whereas prometryn, paraquat, diquat, glyphosate, 2, 4-D and metribuzin are the most frequent herbicides. The frequent fungicides are pencanazole, triadimenol, and mancozeb. The high frequency of pesticide application suggests possible formation of binary or tertiary mixtures and exposure of farmers in all locations to adverse health effects. This hypothesis is in accordance with the results in **Table 3**. The numbers of tremors, convulsions cases among farmers indicate synergistic effects of pesticides mixtures. Synergistic effects of pesticide mixtures were recently reported in chicken and rabbits [34]. Further support to our hypothesis comes from Ibrahim *et al.* [35] who revealed adverse health effects among female farmers exposed to pesticide mixtures during application. The data in **Table 6** clearly show the reduced activity of ACHE due to long term exposure to pesticides. This indicates commutative inhibition of ACHE due to long term exposure. It is obvious that ACHE activity before exposure was in the normal range and reduced after long term exposure to insecticides. In the way around, ALT, AST and ALP activities (**Table 6**) are increased due to long term exposure to pesticides.

It has been shown that long term exposure to pesticides created several symptoms such as hypertension, and neurological and immunological effects [36]. So far, exposure time is a key factor for pesticides accumulation, movement, biomagnifications and/or metabolic reactions in the biosystems. Long term exposure, skin, face body contamination and drift ingestion during work suggest the possible accumulation of organo-chlorine pesticide, fast metabolic reactions for organophosphorous (e.g. Chlorpyfos) or carbamate (e.g. Carbaryl) and production of more toxic fragments than the parent compounds, resulting in toxicological symptoms as seen in **Table 5**.

In addition, frequent contamination of human body may result in different metabolic reactions and create hepatic damage or oxidation stress. This argument is supported by the data in **Table 6** which shows changes in ALT, AST and ALP due to long term exposure to pesticides. For example, many of the applied insecticides and nematicides (**Table 2**) can be metabolized to a more toxic compound due to formation of an oxon radical. This indicates the possible enhancement of oxidative stress among exposed farmers. This is in agreement with the results presented in **Table 6**, which shows hyperactivity of ALT, AST and ALP in farmers exposed to long periods during work. Additional supports to our results can be obtained from, Remor *et al.* [37], who revealed that metabolic products undergone subsequent reactions leading to oxidative stress among farmers.

The occupational parameters (**Table 4**) clearly demonstrate the high percentage of manual work related to pesticides such as disposal methods (92.4%). This enlarges the daily exposure time of farmers and thus greater toxic potential. Moreover, the possible combinations of pesticides exposed the farmers to a potential toxicity mixture that may enhance enzyme inductions or increase the toxicological symptoms (**Table 5**), inhibit ACHE activity or elevate liver enzyme activities (**Table 6**). Our results agree with Yassin *et al.* [38] and Safi *et al.* [3] who demonstrated that common self-reported toxicity symptoms among farm workers. More support to our results comes from the research by Ibrahim *et al.* [35] who found different toxicological symptoms among agricultural female workers, and 11% and 12% acute poisoning among farmers and manual workers of pesticides, respectively. The presented results in **Table 6**, clearly shows the highest activities of ALT, AST or ALP due to long term exposure to pesticides. It can be hypothesized that the elevated levels of these enzymes are due to direct or indirect detoxification and/or elimination reactions in the human body. Our hypothesis is supported by Aly and El-Gendy [39] and Igwenyi *et al.* [40] who revealed the elevated levels of AST due to detoxification reactions and formation of a defensive mechanism to antagonize the effects of pesticides. Moreover, it can be suggested that the hyperactivity of ALP, AST and/or ALP may indicate serious damage to some or all organs producing these enzymes such as the liver and kidney. This suggestion is supported by the results of Ambali *et al.* [41] who revealed damages of cell membrane associated with elevated levels of liver enzymes.

Statistical analysis shows significant differences between the values of ALT, AST and ALP of the farmers before and after long term exposure. Our findings agree with Al-Othman *et al.* [42] who revealed increasing levels of ALP, ALT and AST above the normal range due to long term exposure to pesticides. It was also found that exposure to organophosphourus insecticides increases the activity of, ALP, ALT, and AST enzymes [43]. Our data demonstrated that frequent application of pesticides induced toxicity similar to that of repeated sublethal doses of pesticides, which may cause a tremendous alteration in the levels of liver enzymes [42]. It can be concluded that long-term occupational exposure to pesticides may result in cumulative leakage of enzymes as in the work of Dewan *et al.* [44] which may resulting in severe damage of hepatic cells, hepatocytes and/or other body organs. Consequently accumulation of the enzymes in the blood serum may occur.

The data in **Table 7** present the levels of cholesterol, triglyceride, and total protein content in blood serum among farmers in the Gaza Strip. It is obvious that levels of cholesterol, total protein and triglycerides were in the normal range before exposure to pesticides whereas the levels jumped to a higher level due to long term exposure to pesticides. The explanation of these results is that exposure to organophosphorus pesticides creates toxicity symptoms among farmers such as vomiting and nausea (**Table 5**), this indicates the disturbance of the digestive systems of exposed farmers, leading to a disturbance of carbohydrates and/or protein metabolism. This is in accordance with g Hoppin *et al.* [45], who revealed that exposure to organophosphourus insecticides increased the prevalence of diabetes among farmers.

For the cases of protein content, it is suggested that long term exposures to organophosphourus insecticides disturb protein and lipid metabolism. This suggestion is supported by the toxicology symptoms (**Table 5**) such as loosing appetite and by numerous studies [43] [46]-[47] that reported disturbance of lipid and protein metabolism in animals exposing to organophosphourus insecticides.

The trend of kidney indices (urea, uric acid and creatinine) **Table 7** is similar to above, the concentrations of urea, creatinine and uric acid were in the normal range s before exposure to pesticides and increased several time higher the normal range due to long term exposure to pesticides. This suggests that long term exposure to insecticides of high toxicity may disturb kidney functions resulting in elevated levels of kidney biomarkers in the blood serum. Our suggestion is supported by the data in **Table 8** which showed increased visits to different clinics due to long term exposure to pesticides. More supports come from Sarhan and Al-Sahhaf [48] and Aroonvilairat *et al.* [49], who showed lower levels of serum proteins and increase in creatinine and blood urea and renal damage among farmers exposed to organophosphourus insecticides. Moreover, the increased number of farmer visits to hospital or private clinics indicates the progressive toxicity increase.

5. Conclusions

Long-term exposure to pesticides created severe health problems. Frequent applications of pesticides exposed farmers to the possibility of binary and tertiary mixtures. Toxicity symptoms were found in all locations. Disturbance of digestive systems dominated in most farm locations. Manual application of pesticides was associated with many toxicity symptoms. Levels of ACHE decreased due to long term exposure, whereas levels of ALT, AST and ALP activities increased with exposure time and were the highest for long periods of exposure time. Kidney functions followed the same trend.

Long-term exposure to pesticides created changes in the hepatic biochemical markers, nephro-toxicity and/or cholinergic damage. ALT, ALP, AST, and kidney function indices can be taken as indicators of non-target organisms.

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Conflict of Interest

Author declares that he has no conflict of interest. The study complies with the international ethics issues. Consent form was filled by each farmer participating with the study. Helsinki human right ethics were received before conducting the study.

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