EXPOSURE TO PESTICIDES AS A RISK FACTOR FOR PARKINSON'S DISEASE

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ABSTRACT

Background: Parkinson's disease (PD) is an idiopathic chronic neurodegenerative disorder. Pesticides and correlated lifestyle factors (e.g., exposure to ground-water and farming) are reported risk factors for Parkinson's disease (PD).

Objective: The aim of the current study was to investigate if pesticides exposure has a significant association of Parkinson's disease.

Materials and Methods: The research design of this study was a case control study carried out in Aswan University Hospital in the period from May 1st 2016 to 30th April 2017. This study was done on 50 Parkinson's patients exposed to pesticides (case group) and 50 age and sex- matched subjects with non Parkinson's and non occupational pesticides exposure (control group). Associations of direct pesticide application, ground-water consumption, and farming residences/occupations with PD were obtained. Pseudocholinesterase enzyme level was measured among cases and control groups.

Results: Data showed that cases were consisted of 31 male and 19 female; average age (±SD) was 51.9 (±8.1) years old. The results showed that the mean serum cholinesterase enzyme level in the case group (3305.4 ± 1894.2 U/L) was lower than those of the control group (5430 ± 1477.5 U/L). No significant association was observed between the level of pseudocholinesterase enzyme and age, sex distribution of the case group. Duration of pesticides exposure in the case group was significantly associated with PChE levels. Uses of pesticides safety measures by the case group was significantly associated with PChE levels.

Conclusion: This study described an association between Long- term exposure to cholinesterase inhibiting agricultural pesticides and PD, especially in areas with high pesticides use.

INTRODUCTION

Parkinson's disease (PD) is an idiopathic disease of the nervous system characterized by progressive depletion of dopaminergic neurons in the substantia nigra that manifests clinically as resting tremor, rigidity, loss of postural reflexes and bradykinesia. Currently, diagnosis of PD requires the presence of at least two of the cardinal symptoms as Parkinson's disease is a clinical diagnosis **(Health NIo., 2014)**. The cause of PD is unknown, but there are many predisposing factors like aging, environmental factors, dietary factors, oxidative stress, and genetic factors that contribute to the disease **(Goldman., 2014).** Age is the strongest risk factor for PD and incidence in men increases with age **(Driver et al., 2009).** Epidemiological studies have demonstrated an increase prevalence of Parkinson's disease (PD) in human populations exposed to pesticides specially organophosphorous (OP) compounds **(Rhodes et al., 2013 and Fitzmaurice et al., 2014).**

Pesticide is any substance or mixture of substances intended for preventing, destroying, repelling or mitigating any**.** Pesticides are toxic and designed to repel or kill unwanted organisms, and when applied to the land they may be washed into surface waters and kill or, at least adversely influence, the life of aquatic organisms **(Grube et al., 2011).**

The activity of cholinesterase enzymes in the blood can be measured and used as a biomarker for the effect of organophosphates. Pseudocholinesterase **(PChE)** is characteristically used as an indicator for chronic exposure **(Brown et al., 2006).**

Aim of the work

1. To investigate if pesticides exposure has a significant association of Parkinson's disease. 2- To find the relationship between frequency of pesticide exposure, type of pesticides and the progress of the disease. 3- To investigate if the area of pesticides exposure is endemic of Parkinson's disease.

PATIENTS AND METHODS

A- Patients:

The research design of this study was a case control study carried out in Aswan University Hospital in one year from May 1st 2016 to 30th April 2017. Target populations were divided into two groups; case group (n=50) and cross matched control group (n=50). Inclusion criteria for the case group were Parkinson's patients, were exposed to pesticides in the field, both male and female, aged 30 to 60 years. Inclusion criteria for the control group were non Parkinson's, were had no contact with pesticide application, both male and female, aged 30 to 60 years. Those with a history of systemic disease, liver failure, renal failure and cardiovascular disease, were excluded from the cases and control groups. Prior to initiation of the study; every subject was informed about the aim of the study and gave a written consent. Also the ethical rules of Aswan University, Faculty of Medicine were followed.

B- Methods:

All participants in this study were subjected to the following:

i) History taking:

a) Full detailed history was taken from each participant. Questions such as name, age, residence, occupation, history of any other medical problems as diabetes, hypertension and history of cardiac disease, renal or hepatic problem.

b) History of pesticides exposure (pesticides questionnaire) including type of pesticides used, amount, duration of usage, whether protective gear, such as a mask, rubber gloves, or rubber boots, was used during application, whether they lived on or next to a farm, whether they drank well-water.

ii) Neurological examination:

a) Any signs such as; tremors, rigidity of arms or legs, bradykinesia, ataxia of gait, loss of postural reflexes or dysarthria were noted.

b) Modified Hoehn and Yahr Staging were applied on all participants. It was used to describe the symptom progression of Parkinson disease. The scale was originally described in 1967 and included stages 1 through 5. It has since been modified with the addition of stages 1.5 and 2.5 to account for the intermediate course of Parkinson disease **(Hoehn and Yahr., 1967).**

iii) Serum pseudocholinesterase enzyme level measurement:

Three ml of blood was collected from all included participants by vein puncture on a plan vacotainers tubes. Then samples centrifuged at 3000 rpm for 20 min to obtain serum. Serum samples stored at - 20℃ until analysis **(Mason and Lane., 2000).**

. The level of butyrylcholinesterase enzyme was determined in serum by a colorimetric technique on the basis of Ellman method using colorimetric kinetic buturyl cholinesterase kit. Normal enzyme level according to the kit was equal to 3500-8500 U/L. The principle of the method is that measurement of the rate of production of thiocholine as the substrate acetylcholine is hydrolysed by cholinesterase present in the sample. The reaction between thiocholine and 5-dithio-bis-2-nitrobenzoic acid (DTNB) gave yellow compound of 5-thio-2- nitrobenzoic acid and the rate of color production was measured at 405 nm by spectrophotometer. The change of color is proportional to the enzyme activity **(Ellman et al., 1961)**

$$\text{Butyrylthiocholine} + H_2O \xrightarrow{Cholinesterase} \text{Thiocholine} + \text{butyrate}$$

$$\text{Thiocholine} + \text{DTNB} \longrightarrow \text{5 thio-2- nitrobenzoic acid}$$

C- ***Material*** **:**

Colorimetric kinetic butyryl cholinesterase kit from sky medical company

D- Instruments:

EMPEROR_200 TOUCH spectrophotometer

Statistical analysis

Categorical variables were described by number and percent (N, %), where continuous variables described by mean and standard deviation (Mean, SD). P value < 0.05 is considered statistically significant. Chi-square test was used in analysis of the categorical variables. Independent T-test was

used to determine differences in mean among the case and control groups. The statistical analysis performed using SPSS 20.0 software.

RESULTS

The study was a case control study and conducted on 50 cases (19 females and 31 males) and 50 cross matched controls (24 females and 26 males) to correlate the level of pseudocholinesterase enzyme as an indicator for pesticides exposure as a risk factor for Parkinson's disease. Their ages ranged from 30-60 years.

Table (1) respresented age and sex distribution of the case group and revealed that age of the cases ranged from 30 to 60 years with mean age 51.9 years. About two thirds of cases were above 50 years, while only 8% of the cases ranged from 30-40 yaers old. 62% of the case group were males and 38 % were females.

Table (2) showed the residence of the case and control groups. It revealed that 76% of the case group lived on or near a farm compared to 60% of the control group, 20% of the case group and 30% of the control lived near a fertilizer factory, while 2% of the case group and10% of the control drank ground water.

Figure (1) showed duration of pesticides exposure of the case group and revealed that 64 % of the cases exposed to pesticides for more than one years, while only 36% of the cases exposed for less than one year, with range of years of exposure was 0.5-2.5 years and mean of years was 1.6 years.

Figure (2) showed sources of environmental exposure to pesticides in the case group. It revealed that half of the cases sprayed pesticides by hands, and 10% of the cases sprayed them by tractor, 28% of the cases put pesticides in irrigation water , and 12% of the cases put pest strips or traps.

Table (3) showed pesticides safety measures used by the case group. It revealed that 48% of the cases did not use any protective measures, while 18% of the cases wear mask, 8% of them wear boots, 6% of them wear gloves, 16% of them washed hands after spraying and 4% of cases changed cloths after spraying.

Table (4) respresented staging of parkinson's disease patients according to Modified Hohen and Yahr stage. It revealed that 34% of patients were stage 1, 32% of patients were stage 1.5, 20% of patients were stage 2, 6% of patients were stage 2.5, and another 6% were stage 3, 2% of them were stage 4, while no cases were diagnosed as stage 0 or stage 5.

Table (5) showed the blood level of pseudocholinesterase enzyme in the case and the control groups and revealed that 86% of the cases had abnormal enzyme level and 14% of them had norrmal level, while all the control group had normal enzyme level (chi-square, $p < 0.01$).

Figure (3) showed the mean (±SD) of pseudocholinesterase enzyme level between case and control groups. It was 3305.4 (± 1894.2) U/L in the case group compared to 5430 (± 1477.5) U/L in the control group.

Figure (4) showed the relationship beween blood level of pseudocholinesterase enzyme and age distribution of the case group. It revealed that blood enzyme level was abnormal in 7% of the cases of age group 30-40 compared to normal level in 14.3%, abnormal in 23.3% of the cases of age group >40-50 compared to 14.3% normal level, and abnormal in 69.8% of the cases of age group >50-60 compared to normal level in 71.4%.

Table (6) showed the relationship beween blood level of pseudocholinesterase enzyme and sex distribution of the case group. It revealed that abnormal level of the enzyme was more in males (62.8%) compared to females (37.2%), but there was no significant difference between them (chi-square, $p = 0.775$).

Figure (5) showed the relationship beween blood level of pseudocholinesterase enzyme and residence distribution of the case group. It revealed that blood level of the enzyme was abnormal in 76.7% of the cases who lived on or near a farm compared to normal enzyme level in 71.4%, abnormal level in 20.9% of the cases who lived near a fertilizer factory compared to normal level in 14.3%, while the enzyme level was abnormal in 2.3% of the cases who drank ground water and normal in 14.3% of them.

Figure (6): showed the relationship between blood level of pseudocholinesterase enzyme and mean (±SD) of duration of disease in years among the case group. It revealed that enzyme level was abnormal in the mean of 1.35 (±0.53) years while normal in the mean of 1.11 (±0.64) years.

Table (7) showed the relationship beween blood level of pseudocholinesterase enzyme and Modified Hoehn and Yahr Stage of the case group. It revealed that enzyme level was abnormal in 28% of stage 1 patients compared to normal level in 6%, abnormal level in 28% of stage 1.5 patients compared to 4 % normal level, abnormal level in 18% stage 2 patients compared to 2% normal level, abnormal enzyme level in 4% of stage 2.5 patients and normal level in 2%, abnormal level in 6% of stage 3 patients and abnormal level in 2% of stage 4 patients, while there were no patients on stage 0 nor stage 5 (chi-square, p =0.858).

Table (8) showed the relationship beween blood level of pseudocholinesterase enzyme and duration of pesticides exposure among the case group. It revealed that blood enzyme level decreased with increase in years of exposure to pesticides as 25% of cases who exposed for less than one year showed abnormal enzyme level compared to 100% with normal level, this percent increased to 74.4% in cases who exposed for 1 year and more (chi-square, $p < 0.01$).

Table (9) showed the relationship beween blood level of pseudocholinesterase enzyme and route of pesticides exposure in the cases group. It revealed that the enzyme level was abnormal in 51.2% of cases who sprayed pesticides by hands compared to normal level in 42.9%, abnormal level in 7% of cases who sprayed them by tractor and normal level in 28%, abnormal enzyme level in 30% of cases who sprayed pesticides by tractor compared to normal level in 14%, and abnormal enzyme level in 11.6% of cases who put pest strips or traps and normal level in 14% of the cases (chi-square, $p = 0.324$).

Table (10) showed the relationship between blood level of pseudocholinesterase enzyme and pesticides safety measures used by the case group. It revealed that 46% of cases who didn't use such measures reported abnormal enzyme level.

Table (11) showed the relationship between blood level of pseudocholinesterase enzyme and types of pesticides safety measures used by the case group. It revealed that enzyme level was abnormal in 46% of the cases who didn't use any safety measures while normal level in 2% of them. 10% of the cases who wear mask showed abnormal enzyme level while 8% of the showed normal level. 8% of the cases who wear boots showed abnormal enzyme level, 6% of the cases who wear gloves showed abnormal enzyme level. 12% of the cases who washed hands after spraying showed abnormal enzyme level, while 4% of them showed normal level and 4% of the cases who changed cloths after spraying showed abnormal enzyme level %) (chi-square, $p<0.05$).

Table 1: Age and sex distribution of the case group

Age group	Cases	
	No.	**%**
30-40	4	8.0
>40-50	11	22.0
>50-60	35	70.0
Total	50	100.0
Mean+SD	51.9±8.1	
Range	30-60	
Sex	**Cases**	
	No	**%**
Male	31	62.0
Female	19	38.0
Total	50	100.0

Table 2: Comparison between cases and control group as regards residence

Residential character	Cases		Control	
	No.	**%**	**No.**	**%**
Live on or near a farm	38	76.0	30	60.0
Live near fertilizer factory	10	20.0	15	30.0
Drinking ground water	2	4.0	5	10.0
Total	50	100.0	50	100.0

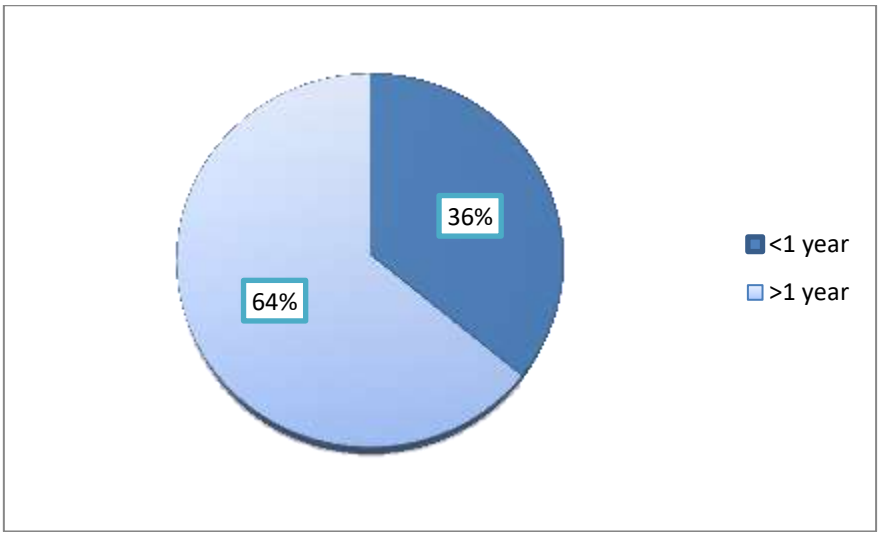

Fig 1: Duration of pesticides exposure in years among the case group.

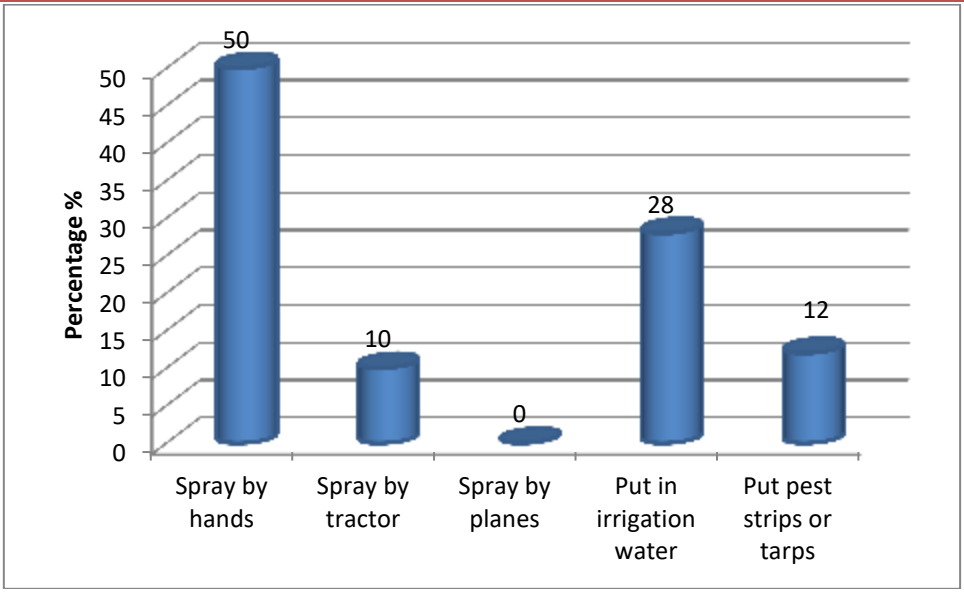

Fig 2: Sources of environmental exposure to pesticides of the case group.

Table 3: Pesticides safety measures used by the case group

Pesticides safety measures	No.	%
Wear mask	9	18.0
Wear boots	4	8.0
Wear gloves	3	6.0
Wash hands after spraying	8	16.0
Change cloths after spraying	2	4.0
None of them	24	48.0
Total	50	100.0

Table 4: Staging of Parkinson's disease patients on Modified Hohen and Yahr.

Modified Hoehn and Yahr Stage	No.	%
Stage 0	0	0.0
Stage 1	17	34.0
Stage 1.5	16	32.0
Stage 2	10	20.0
Stage 2.5	3	6.0
Stage 3	3	6.0
Stage 4	1	2.0
Stage 5	0	0.0
Total	50	100.0

Table 5: Pseudocholinesterase enzyme level among cases and control group by Chi-square test

Pseudocholinesterase enzyme level	Cases (n=50)		Control (n=50)		P. value
	No.	%	No.	%	
Status					
Normal level	7	14.0	50	100.0	<0.001**
Abnormal level	43	86.0	0	0.0	

** Highly statistically significant difference (p<0.01)

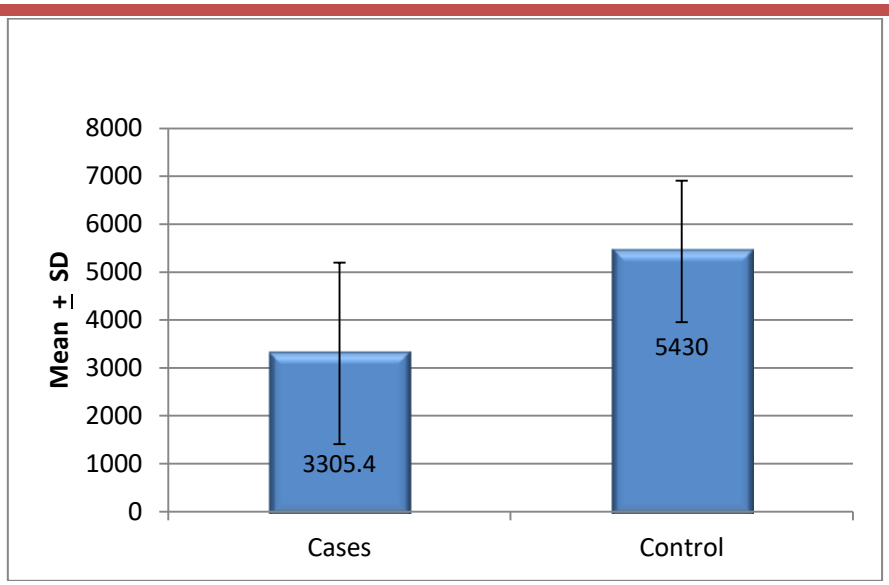

Fig 3: Mean (±SD) of psedocholinesterase enzyme between cases and control groups.

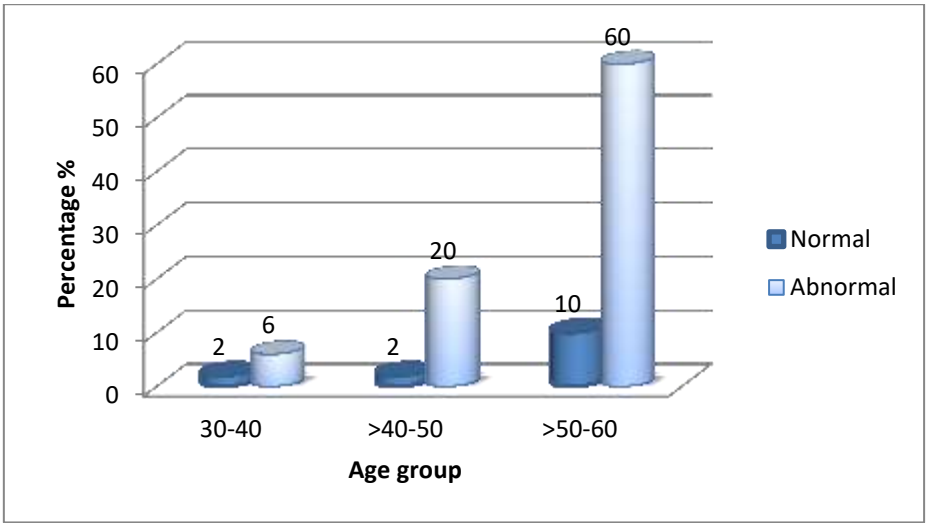

Fig 4: Relationship between pseudocholinesterase enzyme level and age distribution of the case group.

Table 6: Relationship between blood level of pseudocholinesterase enzyme and sex distribution of the case group by Chi-square test

Sex distribution	pseudocholinesterase enzyme level				P. value
	Normal		Abnormal		
	No.	%	No.	%	
Male	4	8.0	27	54.0	0.775 NS
Female	3	6.0	16	32.0	
Total	7	14.0	43	86.0	

NS= No statistically significant difference

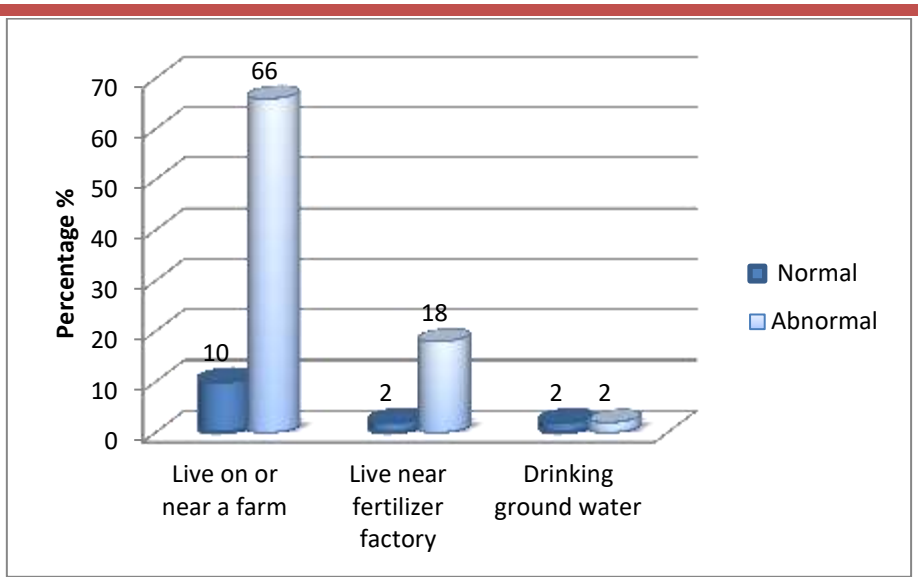

Fig 5: Relationship between blood level of pseudocholinesterase enzyme and residence distribution of the case group.

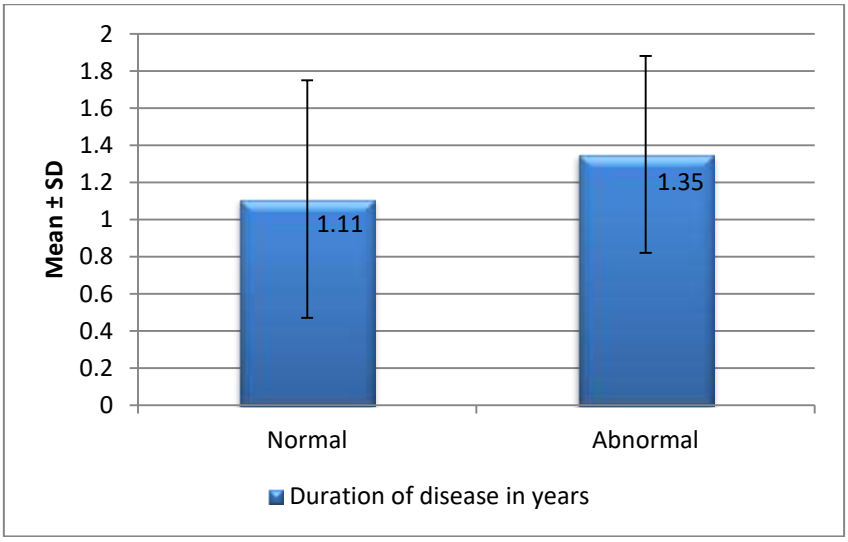

Fig 6: Relationship between blood level of pseudocholinesterase enzyme and mean (±SD) duration of disease in years among studied cases.

Table 7: Relationship between blood level of pseudocholinesterase enzyme and Modified Hoehn and Yahr Stage of Parkinson's patients by Chi-square test

Modified Hoehn and Yahr Stage	pseudocholinesterase enzyme level				P. value
	Normal		Abnormal		
	No.	%	No.	%	
Stage 0	0	0.0	0	0.0	0.858NS
Stage 1	3	6.0	14	28.0	
Stage 1.5	2	4.0	14	28.0	
Stage 2	1	2.0	9	18.0	
Stage 2.5	1	2.0	2	4.0	
Stage 3	0	0.0	3	6.0	
Stage 4	0	0.0	1	2.0	
Stage 5	0	0.0	0	0.0	
Total	7	14.0	43	86.0	

NS= No statistically significant difference

Table 8: Relationship between blood level of pseudocholinesterase enzyme and duration of pesticides exposure in the case group by Chi-square test

Duration of pesticides exposure	pseudocholinesterase enzyme level				P. value
	Normal		Abnormal		
	No.	%	No.	%	
<1 year	7	14.0	11	22.0	<0.000**
>1 year	0	0.0	32	64.0	
Total	7	14.0	43	86.0	

** Highly statistically significant difference (p<0.01)

Table 9: Relationship between blood level of pseudocholinesterase enzyme and route of pesticides exposure among the case group by Chi-square test

Route of pesticides exposure	pseudocholinesterase enzyme level				P. value
	Normal		Abnormal		
	No.	%	No.	%	
Spray by hands	3	6.0	22	44.0	0.324NS
Spray by tractor	2	4.0	3	6.0	
Spray by planes	0	0.0	0	0.0	
Put in irrigation water	1	2.0	13	26.0	
Put pest strips or tarps	1	2.0	5	10.0	
Total	7	14.0	43	86.0	

NS= No statistically significant difference

Table 10: Relationship between blood level of pseudocholinesterase enzyme and types of pesticides safety measures used by the case group

Use of safety measures	Normal Level		Abnormal Level	
	No.	%	No.	%
Yes	6	12.0	20	40.0
No	1	2.0	23	46.0
Total	7	14.0	43	86.0

Table 11: Relationship between blood level of pseudocholinesterase enzyme and types of pesticides safety measures used by the case group by Chi-square test

Pesticides safety measures	pseudocholinesterase enzyme level				P. value
	Normal		Abnormal		
	No.	%	No.	%	
Wear mask	4	8.0	5	10.0	0.048*
Wear boots	0	0.0	4	8.0	
Wear gloves	0	0.0	3	6.0	
Wash hands after spraying	2	4.0	6	12.0	
Change cloths after spraying	0	0.0	2	4.0	
None of them	1	2.0	23	46.0	
Total	7	14.0	43	86.0	

* Statistically significant difference ($p<0.05$)

DISCUSSION

The present study was conducted to ascertain whether environmental pesticides exposure is associated with increased risk of Parkinson's disease (PD)**.**

As the common organophosphates (OP) agent used by farmers was cholinesterase (ChE) sensitive, the change in ChE activity (RBC or plasma) was measured.

The study showed that the commonest age of the case group with was in the age group more than 50 years (70%).This agreed with studies done in Germany by **Tanner et al., (2011)** and **Beck et al., (2012)** who reported that there was a significant increase in PD risk and history of occupational use of pesticides between the ages of 30 and 70 years, but disagree with a study conducted in Europe by **de Rijk et al., (2000)** who stated that the prevalence of PD has been estimated to be 1.8% in persons ≥ 65 years of age. Although age is unequivocally associated with increasing PD risk, the underlying process of PD is distinct from the natural aging process. This difference is because the age of exposure to pesticides in Egypt is smaller than European countries because they work at an earlier stage.

The study showed that, males were more affected than females as they use pesticides extensively in agriculture and in an unsafe manner and this agreed with **Parrón et al., (2011)** who stated that there was a significant associations between direct pesticide exposure and neurodegenerative disorders including PD were present in both males and females**,** despite a smaller stratum size and lower exposure levels for females. Overall, males represented 62% while females represented 38%.

According to pseudocholinesterase (PChE) enzyme level, 14% of the case group had normal PChE level and 86% of them had abnormal PChE level**,** while all of the control group had normal enzyme level. This agreed also with **Ntow et al., (2009)** who mentioned that prevalence of abnormal PChE levels in the farmer group was 74.3% but all of the non-farmers had normal PChE levels. Similar findings were previously reported in a study performed on 134 farmers and 134 control subjects, conducted by **Singh et al., (2012).** They observed that people exposed to pesticides had considerably abnormal level of PChE compared to control, also agreed with **Pakravan et al., (2015)** who stated that PChE level of farmer groups was low because they these workers are exposed continuously to small doses for prolonged periods of time and they are often simultaneously exposed to a variety of different pesticides as well as mixtures of them. But, there was no concordance between the results of the present study and a study conducted in South Africa by London et al in 1998 **(London et al., 1998),** which were done on 35 farmers,

respectively revealed no significant different in the control groups.

The study found no significant association between PChE enzyme level and the age of the case group. This agreed with **Jahani et al., (2013)** who stated that a significant difference was not observed in the mean cholinesterase enzyme level regarding age in the case group.

The study found that PChE enzyme inhibition was more in males (62.8%) compared to females (37.2%) as males had higher activity than females, and females not directly exposed to pesticides. This agreed with a study performed in Iran, the PChE activity of 35 farmers who were exposed to OP agents was measured and reported that the enzyme inhibition was more prominent in men than in women **(Shokrzadeh et al., 2015),** and also agreed with **Simoniello et al., (2010)** who said that farmer males were more exposed to pesticides and had different enzyme level than females as growing different products and crops is associated with different exposure to organophosphates, and consequently with different PChE activity.

The study found a significant association between PChE enzyme level and the residence. This agreed with **Norkaew et al., (2015**) who described that residential pesticides exposure among people who live in agricultural communities are possibly exposed to pesticides indirectly by their main occupation in the community.

The study found PChE enzyme level related to years of pesticide exposure. The results of the present study were in concordance with **Jensen et al., (2011)** who demonstrates that the number of years spent spraying with organophosphates / carbamates (OPs/CMs) was a statistically significant risk factor for the farmer's risk of having experienced a moderate case of pesticide poisoning and so affecting the enzyme level.

Routes of pesticides exposure not alter the level of PChE enzyme and this was in concordance with **Caroline et al., (2014**) who reported that there was no modifying effect of different routes of pesticides exposure on the association between pesticides and PD.

The study found a significant association between PChE enzyme level and the use of safety measures during exposure**.** Evaluation of personal protective equipment showed that roughly half of the case group (46%) did not use any of these measures when mixing and spraying pesticides. Items like gloves and boots were rarely used, especially considering the high awareness among the pesticide sprayers about exposure through the skin, also hygiene measures such as changing clothes and washing hands after spraying pesticides were not common practice. Personal protection can be low because the protective equipment is unsuitable, incorrectly fitted, not properly maintained, and improperly used. This finding contrasts to a study conducted in Bolivia by **Jørs et al., (2010)** who documented a low percentage of farmers taking appropriate protective measures**,** but this result disagreed with **Hines et al., (2010**) who stated that wearing gloves can increase exposure under some circumstances, perhaps because fabric (as opposed to chemically impervious) gloves can become impregnated with pesticide and serve as a reservoir of exposure.

CONCLUSION

The results of this study indicate a higher prevalence and greater risk for certain neurodegenerative diseases as PD particularly in areas with high use of pesticides. A screening questionnaire tested in this study can be used as a screening tool for Parkinson's disease and pesticides exposure.

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التعرض للمبيدات الحشرية كعامل خطر لمرض الشلل الرعاش

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مرض الشلل الرعاش (الباركنسون) هو اضطراب عصبى مزمن مجهول السبب، وتعتبر المبيدات الحشرية تم وعوامل أنماط الحياة المختلفة (مثل التعرض للمياه الجوفية والزراعة) من عوامل الخطر لمرض الشلل الرعاش . تم تصميم هذه الدراسة للتحقق من وجود ارتباط محتمل بين التعرض للمبيدات الحشرية ومرض الشلل الرعاش. اجريت هذه الدراسة على ٥٠ شخص مصاب بمرض الشلل الرعاش ، تعرضوا للمبيدات الحشرية (مجموعة المرضى) و٥٠ شخص مطابق فى العمر والجنس لمجموعة المرضى، غير مصاب بمرض الشلل الرعاش، ولم يتعرضوا مهنيا للمبيدات الحشرية (المجموعة الضابطة)، وقد تم تسجيل جميع الحالات الدراسية بالعيادات الخارجية بمستشفي أسوان الجامعي في الفترة من ١ مايو ٢٠١٦ الى ٣٠ أبريل ٢٠١٧ . تم اتخاذ التفاصيل الخاصة بالمبيدات الحشرية المستخدمة ، اذا كانوا يعيشون في مزرعة أو بالقرب منها أو كانوا يشربون من مياه جوفية. تم قياس مستوى انزيم سودوكولينستريز فى مجموعة المرضى والمجموعة الضابطة. أظهرت البيانات أن مجموعة المرضى كانت تتألف من ٣١ ذكرا و ١٩ أنثى؛ متوسط العمر كان ٥١.٩ (± ٨.١) سنة. اظهرت النتائج أن متوسط مستوى انزيم الكولينستريز في مجموعة المرضى ٣٣٠٥.٤ (±١٨٩٤.٢) وحدة/ لتر، كان اقل من متوسط الانزيم فى المجموعة الضابطة ٥٤٣٠ (± ١٤٧٧.٥) وحدة/ لتر (قيمة P < ٠.٠١). لم يلاحظ وجود ارتباط كبير بين مستوى انزيم سودوكولينستريز والعمر، وتوزيع الجنس فى الحالات المدروسة. كان هناك فرق ذو دلالة احصائية في مستوى الانزيم لدى مجموعة المرضى المشاركين فى الدراسة فيما يتعلق بمدة التعرض للمبيدات الحشرية (قيمة P <٠.٠١). كان هناك فرق ذو دلالة احصائية في مستوى الانزيم لدى مجموعة المرضى المشاركين في الدراسة فيما يتعلق باستخدام وسائل الوقاية من المبيدات الحشرية (قيمة P < ٠.٠٥). **الخلاصة:** خلصت هذه الدراسة الى وجود ارتباط بين التعرض الطويل المدى للمبيدات الحشرية المثبطة لانزيم الكولينستريز ومرض الشلل الرعاش، وخاصة في المناطق ذات الاستخدام العالي للمبيدات الحشرية.