Respiratory, hepatic, renal, and hematological disorders among adolescent females environmentally exposed to pesticides, Menoufia governorate, Egypt

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Abstract
Adolescent females are often environmentally exposed to pesticides by living near agricultural fields, by using pesticides at home, or by having contact with contaminated clothes and pesticide application work tools. This study assessed respiratory, hepatic, renal, and hematological health disorders that might arise due to environmental exposure to pesticides among adolescent females. A cross-sectional study was conducted with 100 adolescent females environmentally exposed to pesticides that had one or more of their family members working as seasonal pesticide applicators and 50 nonexposed (control) adolescent females from Menoufia governorate, Egypt. The studied period of pesticide application season of the cotton crop was from May 1 to September 1, 2017. Participants completed a self-administered questionnaire about pesticide exposure and respiratory, hepatic, renal, and hematological disorders. In addition, serum acetylcholinesterase (AChE), spirometry, complete blood count, and liver and kidney function tests were measured pre and post-pesticide application season. The control adolescent females had a higher AChE activity, a lower prevalence of respiratory symptoms, and higher means of spirometric measurements than the exposed group. During the pre- and postseason, the exposed group presented a prevalence of (6%, 24%) for cough, (4%, 11%) for rhinitis, and (6%, 26%) for dyspnea during the pre and postseason, respectively. In addition, there was a decrease in means of spirometric measurements (FEV1, FEV1/FVC, FEF25–75%, and PEF) in the postseason compared to preseason among the exposed group. Also, there were significant associations between (AChE) activity and both the prevalence of respiratory manifestations and spirometric measurements among the exposed females. On the other hand, there was a statistically significant increase in red blood corpuscle (RBC) and lymphocyte counts, and a statistically significantly lower mean hemoglobin level among the exposed group (postseason) than each of their pre-season values and the control group (P < 0.05). AChE level, total protein, albumin, and albumin/globulin (A/G) ratio levels were statistically significantly lower, while SGPT, SGOT and globulin, blood urea, and serum creatinine mean levels were statistically significantly higher among the exposed group (postseason) than either of their preseason or the control group (P < 0.05). There was a positive correlation between the AChE level and all studied CBC parameters for the exposed group reaching a statistically significant level with basophils (P < 0.05). Also, there was a negative correlation between the AChE level and each of SGPT, SGOT, ALP, globulin, blood urea, and serum creatinine for the exposed group reaching a statistically significant level with each of SGPT and SGOT (P < 0.05). At the same time, a nonsignificant positive correlation was found between AChE level and each of total protein, albumin, and A/G ratio (P > 0.05). So, environmental exposure to organophosphorus pesticides has a detrimental impact on respiratory, hepatic, renal, and hematological systems of adolescent females living in rural districts at the Menoufia governorate. Educational and training intervention programs on pesticide handling and safety precautions are recommended for protecting both pesticide workers and their family members who might be exposed.

Keywords Environmental pesticide exposure · Adolescent females · Respiratory · Hepatic · Renal and Hematological Disorders · AChE
Introduction

Pesticides are toxic chemicals that are widely used throughout the world in agriculture on crops as well as for domestic purposes for mosquito and cockroach control operations (Rani et al. 2017). They are semi-volatile, even nonvolatile substances, and surface deposition occurs rapidly after use. These substances enter the body through the skin, the digestive, and the respiratory tracts (Baldi et al. 2012). Environmental pollution results from pesticide use as more than 98% of applied insecticides and 95% of herbicides affect other destinations than their required target species (Miller 2004).

Children and adolescents constitute a high-risk vulnerable group on exposure to pesticides (than adults) due to the expected occurrence of significant anatomical, maturational, and physiological changes as they are in the developmental stage of body systems (Abdel-Rasoul et al. 2008). This is evidenced by the health effects of pesticides in adults, which come from studies of occupationally exposed adult males. Scanty information is known concerning pesticide-related health effects in adolescent females, and there may be reproductive toxicity due to sex-specific risk differences (Rohlman et al. 2007).

The responsibility of environmental factors explained the relationship between the presence of allergic asthma and pesticide exposure. A lower potentiated vagally induced bronchoconstriction threshold level and increased formation of proinflammatory cytokines in allergen sensitized guinea pigs were initiated by organophosphorus insecticides (Proskocil et al. 2010).

A higher prevalence of upper respiratory tract infections and “influenza-like” symptoms were observed in workers occupationally exposed to organophosphates (OPs) and was associated with a decrease in serum and red blood corpuscle cholinesterase activity (Kamanyire and Karalliedde 2004). Also, pesticide production workers and farmers exposed to organophosphorus (OP) and carbamates (CM) are reported to have significantly decreased pulmonary functions, increased wheezing, and increased risk for asthma compared to controls. Moreover, workers employed in the manufacture of chlorfenvinphos (an organophosphorous compound) showed decreased lung functions and weakened respiratory muscles than controls (Mamane et al. 2015).

The liver represents a major center in the detoxification process as it faces the challenge of maximum exposure to xenobiotics and their metabolic by-products. The overall balance between the degree of oxidative stress and the antioxidant capability determines the susceptibility of liver tissues to this stress resulting from exposure to pesticides (Khan et al. 2005).

Acute renal failure and multiple organ dysfunction syndromes, suggesting that high intratubular OP concentrations and hypovolemia might be responsible for acute kidney injury (AKI) following exposure to OP, which is currently defined by either change in serum creatinine or urine output. The persistent decline of renal function without recovery can lead to end-stage renal disease and increase the short-term and long-term risk of death (Lee et al. 2015).

Many steps in heme biosynthesis are inhibited by pesticide residues. Another possible mechanism is the binding of organophosphate pesticides on iron, followed by a lack of incorporation of iron in hemoglobin (Abu Mourad 2005). This effect may increase to reach aplastic anemia (Adad et al. 2015).

According to the Egyptian culture, no females are allowed to work as pesticide applicators, hence their exposure to pesticides could be exclusively environmental either by living nearby agriculture fields, domestic use of home pesticides or handling clothes of their family members (brothers and/or fathers) that are contaminated with pesticide residues.

To our knowledge, no studies have been carried out examining the effects of exposure to pesticides among environmentally exposed adolescent females in Egypt. This study aimed to compare respiratory, hepatic, renal, and hematologic parameters between adolescent girls exposed and non-exposed to pesticides.

Subjects and methods

Study design

This was a cross-sectional comparative study with pre-post exposure comparison in the exposed group.

Place and duration of the study

The study was conducted at three randomly chosen districts (Shebin El-Kom, El-Bagour, and Menouf) out of the ten districts in Menoufia governorate, Egypt. The studied period of pesticide application season of the cotton crop was from May 1st to the end of September.

Study sample

As the total number of seasonal and private pesticide applicators is approximately 2000 subjects (according to statistics of the Agriculture Directorate-Menoufia governorate), and the prevalence of health disorders due to exposure to pesticides at this age group is 66% (Kalkbrenner et al. 2014). So, at 95% confidence interval and 80% power, the sample size is calculated by using Epi Info™ 7 technique to be 100 female adolescents (aged from 9 to 18 years, after
application of exclusion criteria) who had one or more of their family members working as seasonal pesticide applicators in cotton fields and/or working privately with their backpack sprayers applying pesticides to other crops throughout the year. The pesticide-exposed female adolescents’ homes were located less than 1000 m from the agricultural fields. In many studies, the buffer radiuses around a residence defining the zone of influence for agricultural pesticide exposure varied considerably but were all less than 1000 m (Teyssère et al. 2020).

The pesticide exposure in the exposed group was a combination of para-occupational, environmental, and domestic exposures (Silvério et al. 2017).

The control group included 50 adolescent females (after application of exclusion criteria) that were matched with the exposed group regarding age, residence, socioeconomic standard, educational level, and their family members were never involved in pesticide application. Their homes were located more than 1000 m away from the agricultural fields.

All participants in both groups were never been married. Chosen adolescent females having a history of chronic medical disorders (i.e., diabetes, hypertension, chest, liver, kidney, or blood disease) were excluded from the study.

**Study methods**

Each participant completed the following at two-time points, before the application season (preseason in the first week of May) and after the application season ended (postseason during the first week of September):

I: A self-administered predesigned questionnaire which included.

a. Personal data as age, residence, level of education, the distance of the house from fields, and past medical history of diseases

b. Pesticide exposure history as applying pesticides at home, use of empty pesticide containers, handling contaminated clothes of their relatives, existing in fields within 3 days after pesticide spraying

c. The occupational history of their pesticide applicators’ relatives: working days and duration of work

d. Respiratory symptoms as rhinitis, cough, expectoration dyspnea, wheezes, and chest pain. The respiratory symptoms were reported in the first week of May (pre-exposure) and during the first week of September (postexposure)

II: Spirometric measurements.

Spirometric tests were done using the MEE Spiro PFT Touch, Germany. Participants performed up to three maneuvers according to the American Thoracic Society guidelines for pulmonary function tests. Percent predicted values were calculated as a percent of the participant measured value to a predicted value of that participant. The predicted values were those of Knudson’s method (Quadrelli et al. 1999). Percent predicted forced expiratory volume in the first second (FEV1%) and percent predicted forced vital capacity (FVC%) are the primary ventilatory parameters reported herein. The restriction was defined as total lung capacity below the 5th percentile and normal FEV1/FVC ratio (the American Thoracic Society guidelines for restriction (Pellegrino et al. 2005).

III: Liver function tests.

Serum glutamic oxaloacetic transaminase (SGOT), glutamic pyruvic transaminase (SGPT), total proteins, serum albumin, and globulin were measured. Blood samples were analyzed by Beckman AU480 automated chemistry analyzer, USA.

IV: Kidney function tests: e.g., serum urea and creatinine were estimated (Gowda et al. 2010).

V: Complete blood count (CBC): EDTA samples were analyzed within 24 h by Siemens ADVIA 2120i Hematology Analyzer, Germany.

VI: Serum AChE assessment.

Five milliliters of blood were drawn from all participants and serum AChE was determined according to Weber in Pohanka (2012) using standard kits (test-combination Boehringer Mannheim GmbH Diagnostics). Serum AChE was selected because it is a better short-term indicator of cholinesterase inhibition than RBC AChE due to its more rapid response to exposure; used as an indicator of recent, acute exposure to cholinesterase inhibiting pesticides. Also, because the primary pesticide being applied is chlorpyrifos, which has a preferentially inhibiting effect on serum AChE rather than RBC AChE (Abdel-Rasoul et al. 2008).

**Data management**

Data were analyzed using IBM SPSS version 22 (SPSS Inc., Chicago, IL, USA). Chi-squared test ($\chi^2$) was used to examine the relation between qualitative variables; the comparison between two groups was conducted using the student $t$-test and paired $t$-test for the same group on two occasions (preseason and postseason). The Pearson’s correlation test and $t$-test for correlation coefficient ($r$) were used to examine the association between two quantitative variables. $P$-values less than 0.05 were considered statistically significant.
**Results**

There is a nonsignificant difference between exposed and control groups regarding sociodemographic data (age, income, and education level) and BMI ($P > 0.05$) as shown in Table 1.

Figures 1 and 2 show a statistically significant decrease in AChE level and higher prevalence of cough, wheezes, dyspnea, and asthma among the exposed group (postseason) than each of the preseason and the control group ($P < 0.05$).

Table 2 shows that the prevalence of respiratory manifestations (cough, wheezes, dyspnea, and asthma) among the exposed group was significantly increased with the decrease in AChE level ($P < 0.05$).

There are statistically significantly lower mean values of spirometric measurements (FEV1%, FEV1/FVC%, FEF25–75%, and PEF%) among the exposed group (postseason) than each of preseason and the control group ($P < 0.05$) as shown in Table 3.

**Table 1** Sociodemographic and anthropometric data of exposed and control groups

| Sociodemographic and anthropometric data | Studied groups | Test of significance | $P$ value |
|-----------------------------------------|----------------|----------------------|-----------|
|                                         | Exposed ($n = 100$) | Controls ($n = 50$) |
| Age (years)                             |                |                      |           |
| Mean ± SD                               | 14.25 ± 1.88   | 13.80 ± 2.09         | $t$-test = 1.29 | 0.191 |
| Range                                   | 9–18           | 10–18                |           |
| Education                               |                |                      |           |
| Basic education                         | 60             | 29                   | $\chi^2$ test = 0.06 | 0.812 |
| Secondary                               | 40             | 21                   |           |
| SEL*                                    |                |                      |           |
| Low (< 5)                               | 59             | 24                   | 48.0      |
| Moderate (5–8)                          | 24             | 18                   | 36.0      | $\chi^2$ test = 2.46 | 0.293 |
| High (9–12)                             | 17             | 8                    | 16.0      |
| BMI (kg/m$^2$)**                        |                |                      |           |
| Mean ± SD                               | 20.19 ± 2.66   | 19.59 ± 2.57         | $t$-test = 0.83 | 0.413 |
| Range                                   | 13.60–22.50    | 12.80–22.30          |           |

*SEL, socioeconomic level (Ibrahim and Abdel-Ghaffar 1990)

**BMI, body mass index**

**Fig. 1** A significant decrease in acetylcholinesterase (AChE) level in the exposed at postseason than for the control group ($P < 0.05$)
Table 4 and Fig. 3 show that means of AChE, total protein, albumin, and A/G ratio levels were statistically significantly lower, while SGPT, SGOT, globulin, blood urea, and serum creatinine were statistically significantly higher among the exposed group (postseason) than each of the preseason and the control group ($P < 0.05$).

Table 5 shows statistically significantly lower measurements of RBCs, Hb, and lymphocytes among the exposed group (postseason) than each of the preseason measurements and the control group ($P < 0.05$).

Table 6 shows that there was a statistically significant positive correlation between AChE level and spirometric measurements for the exposed group (FVC%, FEV1%, FEV1/FVC%, FEF25–75%, and PEF% ($r = 0.62, 0.41, 0.55, 0.61,$ and 0.43, respectively) ($P < 0.05$). On the opposite side, it shows a statistically significant negative correlation between AChE and SGPT, SGOT, ALP, globulin, blood urea, and serum creatinine for the exposed group reaching a statistically significant level with both SGPT and SGOT ($P < 0.05$). Also, a statistically nonsignificant positive correlation was found between AChE (IU/L) and each of total protein, albumin and A/G ratio ($P > 0.05$). At the same time, there was a positive correlation between AChE level and all studied CBC parameters for the exposed group; only basophils showed a statistically significant correlation ($P < 0.05$).

**Discussion**

This study revealed a statistically significant higher prevalence of health effects in adolescent females environmentally exposed to pesticides compared to the control group. Exposed participants had lower AChE activity levels, impaired ventilatory functions, and more prevalent respiratory manifestations.

The exposed adolescent females reported a statistically significant higher prevalence of respiratory manifestations as...
cough, wheezes, dyspnea, and asthma compared to the control participants and also in postexposure than a pre-exposure season. Moreover, exposed adolescent females positive for these manifestations had significantly lower AChE levels than negative ones. The decrease in serum and red blood corpuscle cholinesterase activity leads to the accumulation of acetylcholine which is the predominant parasympathetic neurotransmitter in the airways and plays a key role in the pathophysiology of obstructive airway diseases, such as asthma, through bronchial smooth muscle contraction and mucus secretion and airway inflammation and remodeling (Kistemaker and Gosens 2015). The previous findings coincided with the study of Ohayo-Mitoko et al. (2000) on agricultural workers and pesticide applicators in Kenya. Also, pesticide use in the kitchen or dining rooms was associated with an increased prevalence of wheezes among children under 18 years of age in the USA (Hoppin et al. 2002).

Additionally, the exposed adolescent females showed statistically significantly lower spirometric measurements (FEV1%, FEV1/FVC%, FEF25–75%, and PEF%) than the control ones. These findings are consistent with previous studies of spirometry and OP exposure in adults as Calahan et al. (2014) found significantly lower FEV1% and FVC% among applicators compared to non-applicators. Also, these findings are supported by the results of Peiris-John et al. (2005) who found that lowered FVC% and OP exposure were associated in 25 occupationally exposed Sri Lankan farmers and 22 fishermen who lived within a 25 km radius of fields where OPs were sprayed than nonexposed controls. Similarly, Zhu et al. (2015) found that pesticide applicators aged from 15 to 24 years had

### Table 3
Mean ± SD of spirometric measurements for the exposed and control groups

| Spirometric measurements | Studied groups | t-test | P value |
|--------------------------|---------------|-------|--------|
|                          | Exposed (n = 100) | Controls (n = 50) |       |
|                          | Preseason | Postseason | Paired |       |       |
|                          | Mean ± SD | Mean ± SD |       |       |       |
| FVC%                     | 91.73 ± 19.81 | 88.53 ± 22.71 | 1.06 | 0.281 | 93.90 ± 11.07 | 0.72 \( ^a \) 1.51 \( ^b \) | 0.471 \( ^a \) 0.133 \( ^b \) |
| FEV1%                    | 102.44 ± 19.12 | 99.14 ± 17.59 | 1.57 | 0.042 | 104.18 ± 11.54 | 0.59 \( ^a \) 1.66 \( ^b \) | 0.551 \( ^a \) 0.040 \( ^b \) |
| FEV1/FVC%                | 101.27 ± 22.48 | 96.73 ± 25.88 | 1.62 | 0.032 | 103.81 ± 13.09 | 0.74 \( ^a \) 2.65 \( ^b \) | 0.460a 0.009b |
| FEF25–75%                | 99.13 ± 17.64 | 91.17 ± 23.96 | 2.68 | 0.008 | 104.17 ± 19.72 | 1.59 \( ^a \) 3.65 \( ^b \) | 0.112 \( ^a \) 0.003 \( ^b \) |
| PEF%                     | 59.16 ± 18.91 | 55.07 ± 18.23 | 1.89 | 0.020 | 62.05 ± 16.95 | 1.02 \( ^a \) 2.33 \( ^b \) | 0.340 \( ^a \) 0.020 \( ^b \) |

*Comparison between the exposed group (preseason) and the control group*

*Comparison between the exposed group (postseason) and the control group*

### Table 4
Mean ± SD of AChE level, liver and kidney function tests among the exposed and control groups

| Studied parameters | Studied groups | t-test | P value |
|--------------------|---------------|-------|--------|
|                    | Exposed (n = 100) | Controls (n = 50) |       |
|                    | Preseason | Postseason | Paired |       |       |
|                    | Mean ± SD | Mean ± SD |       |       |       |
| AChE (IU/L)        | 299.60 ± 42.87 | 238.49 ± 23.83 | 12.66 | <0.001 | 302.70 ± 36.54 | 0.44 \( ^a \) 7.73 \( ^b \) | 0.660 \( ^a \) <0.001 \( ^b \) |
| SGPT (u/L)         | 22.51 ± 3.29 | 24.65 ± 3.72 | 4.31 | 0.004 | 21.80 ± 5.08 | 1.03 \( ^a \) 4.59 \( ^b \) | 0.303 \( ^a \) 0.007 \( ^b \) |
| SGOT (u/L)         | 26.09 ± 4.12 | 28.22 ± 5.43 | 3.12 | 0.002 | 27.11 ± 8.87 | 0.96 \( ^a \) 2.56 \( ^b \) | 0.333 \( ^a \) 0.010 \( ^b \) |
| ALP (u/L)          | 169.11 ± 49.33 | 171.02 ± 55.41 | 0.26 | 0.790 | 154.91 ± 55.92 | 1.59 \( ^a \) 1.84 \( ^b \) | 0.110 \( ^a \) 0.042 \( ^b \) |
| Total protein (gm/L) | 7.09 ± 1.03 | 6.74 ± 1.13 | 2.29 | 0.022 | 7.13 ± 1.51 | 1.34 \( ^a \) 2.31 \( ^b \) | 0.182 \( ^a \) 0.001 \( ^b \) |
| Albumin (gm/L)     | 3.94 ± 0.59 | 3.59 ± 0.55 | 4.34 | 0.003 | 4.07 ± 0.52 | 1.32 \( ^a \) 5.46 \( ^b \) | 0.191 \( ^a \) <0.001 \( ^b \) |
| Globulin (gm/L)    | 1.93 ± 0.50 | 1.99 ± 0.51 | 0.84 | 0.402 | 1.87 ± 0.57 | 0.66 \( ^a \) 3.33 \( ^b \) | 0.512 \( ^a \) 0.003 \( ^b \) |
| Albumin/globulin (A/G) ratio | 2.16 ± 0.41 | 1.61 ± 0.41 | 1.78 | <0.001 | 2.29 ± 0.89 | 1.23 \( ^a \) 6.41 \( ^b \) | 0.220 \( ^a \) <0.001 \( ^b \) |
| Blood urea (mg/dL) | 24.95 ± 5.78 | 28.27 ± 4.72 | 4.45 | 0.004 | 24.67 ± 6.41 | 0.27 \( ^a \) 4.56 \( ^b \) | 0.780 \( ^a \) 0.002 \( ^b \) |
| S. creatinine (mg/dL) | 0.84 ± 0.12 | 1.02 ± 0.08 | 12.48 | <0.001 | 0.84 ± 0.13 | 0.41 \( ^a \) 2.74 \( ^b \) | 0.682 \( ^a \) 0.006 \( ^b \) |

*Comparison between the exposed group (preseason) and the control group*

*Comparison between the exposed group (postseason) and the control group*
lower spirometric measurements than non-applicators of the same age. However, among 89 greenhouse workers and 25 non-spraying controls in Spain spirometric measurements and exposure to OPs were not associated; OPs exposure was defined as a depression of more than 25% in plasma cholinesterase or 15% depression in AChE levels (Hernandez et al. 2008).

The relationship between the exposure to pesticides and decrement in the different spirometric measurements is confirmed by the presence of a statistically significant positive correlation of AChE levels with values of FVC%, FEV1%, FEV1/FVC%, FEF25–75%, and PEF%. These results are consistent with the study of Chakraborty et al. (2009) who reported that in Indian agricultural workers, the inhibition of AChE more than 50% was associated with increased reporting of respiratory symptoms and reduced lung function (13.6% lower mean FVC and 15.6% lower mean FEV1) than nonagricultural workers.

The statistically significant deterioration in liver function tests was revealed in the present study by the increase in SGOT and SGPT, while the decrease in total protein and albumin levels for the studied adolescent females postexposure and their association with the decreased AChE. These findings agree with other several studies that reported the deterioration of liver enzymes in association with exposure to pesticides (Farahat et al. 2003; Jørs et al. 2006; Mansour and Mossa 2009). Also, Kamel et al. 2003 have been reported altered liver enzyme activities among pesticide workers exposed to OP pesticides alone or in combination with organochlorine or other pesticides. The decrease in the total protein and albumin as a result of decreased synthesis of albumin in the liver, and increase in

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**Table 5** Mean ± SD of CBC parameters among the exposed and control groups

| CBC parameters   | Studied groups | t-test | P value |
|------------------|----------------|--------|---------|
|                  | Preseason      | Postseason | Paired t-test | P value | Mean ± SD | Mean ± SD | Mean ± SD | Mean ± SD |
|                  | Exposed (n = 100) | Controls (n = 50) |                  |         |           |           |           |           |
| RBCs (10⁶/L)    | 4.71 ± 0.37    | 4.19 ± 0.31 | 10.77 | 0.003 | 4.82 ± 0.42 | 1.50b 12.85b | 0.142 < 0.001b |
| Hemoglobin (Hb) (gm/dL) | 12.62 ± 0.98 | 12.32 ± 0.65 | 2.38 | 0.020 | 12.63 ± 1.01 | 1.11b 2.48b | 0.272 0.012b |
| Leucocytes (10³/mm³) | 6.69 ± 2.02 | 6.83 ± 2.01 | 0.49 | 0.623 | 6.48 ± 2.36 | 0.55b 1.75b | 0.580 0.151b |
| Lymphocytes (10³/dL) | 3.58 ± 1.08 | 2.98 ± 0.68 | 4.70 | < 0.001 | 3.63 ± 0.71 | 0.24b 6.67b | 0.81b 0.006b |
| Basophiles (10³/dL) | 78.71 ± 20.62 | 76.33 ± 23.11 | 0.77 | 0.443 | 77.89 ± 23.73 | 0.22b 0.42b | 0.833 0.680b |
| Platelets (10³/mm³) | 249.24 ± 71.61 | 244.57 ± 43.91 | 0.56 | 0.573 | 254.56 ± 63.88 | 0.44b 0.67b | 0.652 0.501b |

aComparison between the exposed group (preseason) and the control group
bComparison between the exposed group (postseason) and the control group
Table 6 Correlation between AChE level with each of spirometric measurements, liver and kidney function tests, and CBC parameters among the exposed group

| Studied parameters | AChE (IU/L) | r     | P value |
|--------------------|------------|-------|---------|
| 1-Spirometric measurements |           |       |         |
| FVC%               | 0.62       | <0.005 |         |
| FEV1/FVC%          | 0.41       | <0.005 |         |
| FEV25–75%          | 0.55       | <0.005 |         |
| PEF%               | 0.61       | <0.005 |         |
| 2-Liver and kidney functions |           |       |         |
| SGPT (u/L)         | 0.27       | <0.005 |         |
| SGOT (u/L)         | 0.28       | <0.005 |         |
| ALP (u/L)          | 0.16       | 0.100  |         |
| Total protein gm/L | 0.03       | 0.501  |         |
| Albumin (gm/L)     | 0.07       | 0.501  |         |
| Globulin (gm/L)    | 0.25       | 0.012  |         |
| A/G ratio          | 0.17       | 0.501  |         |
| Blood urea (mg/dL) | 0.19       | 0.051  |         |
| Serum creatinine (mg/dL) | 0.05  | 0.502  |         |
| 3-CBC parameters   |           |       |         |
| RBCs (10^6/L)      | 0.17       | 0.502  |         |
| Hemoglobin (gm/dL) | 0.06       | 0.503  |         |
| Leucocytes (10^3/mm^3) | 0.07       | 0.503 |         |
| Lymphocytes (10^3/dL) | 0.13         | 0.203 |         |
| Basophils (10^3/dL) | 0.23       | 0.021  |         |
| Platelets (10^3/mm^3) | 0.16       | 0.100  |         |

r = Pearson’s correlation coefficient

globulin was observed by Barr et al. (2006) in farmworkers exposed to pesticides. Several key biological processes have been reported as involved in OP-induced hepatotoxicities such as disturbances in the antioxidant defense system, oxidative stress, apoptosis, and mitochondrial and microsomal metabolism (Karami-Mohajeri et al. 2017).

The relatively elevated liver enzymes among exposed than controls elicited in the present study may reflect the hepatic effect of long-term exposure to OP pesticides. This assumption was reflected on the chronic hepatocellular biochemical indicators, low protein, and low albumin in the exposed than the control participants and could be documented by the statistically significant correlation between duration of exposure and both ALT and alkaline phosphatase. It may be due to that the effect of chronic exposure to pesticides that could result in acute or subacute liver insult (Deziel et al. 2015).

Liver injury would result in the delay or failure of the detoxification mechanisms with consequent earlier development of cumulative pesticide effects and hence a vicious cycle (Rani et al. 2017). It may be emphasized that hepatic susceptibility to pesticides clinically and biochemically manifested to be mostly related to protein deprivation (Andreotti et al. 2009).

The oxidative damage of liver cells is promoted by exposure to OPs by enhancing the peroxidation of membrane lipid marker changes in the overall histoarchitecture of the liver in response to OPs. This might be a result of toxic effects initiated by the production of reactive oxygen species destroying the various membrane components of the cell (Mansour and Mossa 2009).

The present statistically significant increase in the mean levels of blood urea and serum creatinine among the environmentally pesticide-exposed adolescent females agrees with that obtained by Khan et al. 2005. Quandt et al. 2010 also found that among the 100 rice farmers in their sample, 23 farmers had abnormal levels of blood urea nitrogen (BUN), 22 of which had BUN values exceeding the upper boundary for the normal population. Similarly, Cavari et al. 2013 proposed that OP effects on the renal system could be due to direct parenchymal intoxication, secondary to hemodynamic instability, or seizure-induced rhabdomyolysis (Yardan et al. 2013; Mohamed et al. 2016).

On studying the hematological disorders among adolescent females environmentally exposed to pesticides, a statistically significant decrease in means of RBC, Hb, and lymphocyte measurements was found among the exposed females in the postexposure season than either of the controls or exposed in pre-exposure season. Decreased RBC count and hemoglobin may be attributed either to the fact that OP pesticides affect dietary intake (Leach 2014) or due to the effect of pesticides on the bone marrow (Barr et al. 2006). Another possible mechanism is the binding of organophosphate pesticides on iron, followed by a lack of incorporation of iron in hemoglobin (Abu Mourad 2005). Moreover, Mansour and Mossa 2009 revealed significantly lower values of RBC count, hemoglobin, lymphocyte count, total protein, albumin, and A/G ratio in rat erythrocytes induced by chlorpyrifos compared to the control group.

As mentioned above, the current results showed a statistically significantly lower level of AChE in the exposed adolescent females (238.49 ± 23.83 IU/L) compared to the control ones (303.35 ± 78.54 IU/L). Several studies reported AChE levels showing a consistently significant association between exposure to pesticides and AChE inhibition in farmworkers. All studies stated that AChE was significantly lower in the exposed participants than the controls (Clayton et al. 2003; Abdel-Rasoul et al. 2008; Khan et al. 2010). Jørs et al. 2006 reported a mean ChE activity of 7.11 kU/L for those who have sprayed with OPs compared to a mean ChE of 8.03 kU/L for those who have not and ChE activity of 8.03 kU/L for those who have not sprayed compared to a ChE activity of 7.60 kU/L for those who have sprayed from...
1 to 3 times and a ChE activity of 7.12 kU/L for those who have sprayed >3 times. Moreover, there was a statistically significant negative correlation between levels of AChE and laboratory indices of SGPT ($r = -0.27$) and SGOT ($r = -0.21$) and a statistically significant positive correlation with basophil count ($r = 0.23$), which means that there were significant liver effects in addition to clinical and biochemical changes significantly associated with lower levels of AChE (Jørs et al. 2006).

**Limitations of the study**

Our study had some limitations. First, this survey was designed as a cross-sectional study so we cannot derive any conclusions on the causality of pesticide exposure and respiratory, renal, hepatic, or hematological disorders on adolescent females; therefore, further prospective studies are needed to better clarify the nature of the observed association. Despite these limitations, this study was a reflection of the association between environmental exposures to pesticides in adolescent females with health disorders. The obtained results could be more evidenced by the inclusion of additional studies.

**Conclusions and recommendations**

Pesticides have been linked to numerous adverse health effects that are different in females than in males. Adolescent females living in agricultural areas and from families whose one or more members are pesticides sprayers have statistically significantly lower spirometric measurements and higher prevalence of respiratory manifestations and a statistically significant hepatic, renal, and hematological impact compared to the control group. Since adolescents around the world are exposed to OP pesticides, these studies suggest an urgent need to evaluate this potential problem. Future research should focus on the type of health education training considering the perceived benefits and disadvantages while developing plans to decrease health disorders among adolescent females.

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**Data availability** Available.

**Declarations**

**Ethics approval** The Medical Ethics Committee at the Menoufia Faculty of Medicine approved the study protocol before starting.

**Consent to participate** Written informed consents were signed by all participants’ parents before being enrolled in the study.

**Consent for publication** Not applicable in our IRB (Ethical Committee, Menoufia University, Faculty of Medicine).

**Conflict of interest** The authors declare no competing interests.

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