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Organophosphate Pesticide Exposure during Pregnancy and Adverse Perinatal Outcome

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Abstract

Objective: Little is known about potential adverse health effects of in utero exposure to organophosphate (OP) pesticides. The aim of this study was to assess the effect of organophosphate pesticide exposure during pregnancy and adverse perinatal outcome.

Subject and Methods: This prospective study was conducted during the period from March 2013 to March 2105 and included two groups of pregnant women, 40 exposed women and 100 unexposed women as a control group. Both groups were matched for age, socioeconomic class educational level and body mass index. Serum acetyl cholinesterase (AChE) was measured in all participants at 20-22 weeks' gestation. All women were followed up till delivery. Perinatal outcome was assessed in terms of gestational age at delivery, birth weight, head circumference and body length of the newborn.

Results: Exposed participants exhibited significantly shortened gestational age, low birth weight and smaller head circumference than controls. There was a positive correlation between reduced level of AChE and gestational age and birth weight.

Conclusions: Our results confirmed the association between organophosphate pesticide exposure during pregnancy and adverse perinatal outcome in terms of reduced gestational age, low birth weight and small head circumference.

Keywords: Perinatal outcomes; Birth weight; Acetyl cholinesterase; Organophosphate pesticide

Introduction

Organophosphorous (OPs) compounds are one of the most important classes of pesticides and the most commonly used insecticides worldwide. There are more than 100 different OPs that are widely used as insecticides and to a lesser extent as herbicides [1]. They are widely used in agriculture, horticulture and veterinary medicine. They are frequently used around households for public hygiene and used in tropical countries to control disease vectors [2].

The cotton crop is the primary agricultural product in Egypt where organophosphorous pesticides are used with large quantities relative to other crops [3].

Potential health hazards associated with exposure to pesticides during pregnancy have become a major public health concern due to the widespread use of pesticides and the high sensitivity of the foetus and the pregnant mother to toxic exposures [4].

Prenatal exposure to OP pesticides is associated with a variety of harmful outcomes including increased risk of spontaneous miscarriages, low birth weight and head circumference, preterm delivery, delayed neurodevelopment, poor attention in early infancy, rapid weight gain in the first 6 months, elevated body mass index later in infancy, obesity, type 2 diabetes later in life and delayed age at menarche [5-7].

The aim of this study was to assess the effect of organophosphate pesticide exposure during pregnancy on the perinatal outcome.

Subject and Methods

This prospective observational study was carried out in the period between March 2013 to March 2015 at the department of Obstetrics and Gynaecology in collaboration with Family Medicine department, Faculty of Medicine, Menoufia University, Egypt.

The study was approved by the Ethical Committee of the Faculty of Medicine, Menoufia University and an informed consent was obtained from all participants after simple and clear explanation of the research objectives.

The consent form was developed according to the standard in Quality Improvement System in Ministry of Health in Egypt which was introduced in all family health centers and units. The study included two groups:

Group 1 (exposed group):

A group of 40 pregnant women at 20-22 weeks' gestation recruited from Manshiet Sultan family health center, Menouf district, Menoufia Governorate which is a rural area with women being working in agriculture or living within 20 meters of fields (i.e. using of organophosphorus during the period of the study was confined to certain area by the regulation in the governorate).

Group 2 (non-exposed or control group):

A group of 100 pregnant women at 20-22 weeks' gestation recruited from the outpatient clinic of Obstetrics and Gynaecology, Menoufia University hospital in Shebin Elkom city (the capital of the governorate) to ensure that women with low or no possibility of exposure to organophosphate pesticides.

Both groups were selected according to strict inclusion and exclusion criteria.

Inclusion criteria: Participants age at 18-35 years (to avoid the possibility of the effect of advancing age on pregnancy) and pregnant in the second trimester because the highest concentration of Acetyl cholinesterase (AChE) is found at approximately 20-22 weeks of gestation.

Exclusion criteria: Women with history of chronic medical disorder (diabetes mellitus, hypertension, asthma, thyroid disease, liver or kidney diseases etc.) obstetric history show past or recent history of a pregnancy complication (gestational diabetes, preeclampsia, obstetric haemorrhage etc.).

Multiple pregnancy and pervious history of infant with congenital malformation to exclude other factors that may affect pregnancy outcome, factors hindering the follow up (as travelling or participation in other study), women from areas allowed to use organophosphrus for cotton crop and uncooperative participants.

Both groups were matched for age, socioeconomic status, educational level and body mass index and followed up till delivery. After delivery their neonates were included in study.

After taking written consent from each participant, the participants were subjected to the following:

A-Predesigned questionnaire: For basic evaluation of the participants that administered via face-to-face interview in Arabic language. It included personal history (such as name, age, residence, Socio-economic status), questions about the house condition and use of pesticide, medical history (obstetric history and pregnancy outcome of previous pregnancy), past and family history of chronic disease or history of medication.

B-Clinical examination: To fulfilment of the inclusion criteria and as baseline evaluation.

General and local examination: For chest, heart, abdomen and skin with particular emphasis on height and weight of participants: Using the weight and height measurement scale with the subject standing, erect, bare footed with heels together.

Body Mass Index (BMI) was calculated as weight in kilograms divided by the square of height in meters and its percentile.

(BMI)=Weight (Kg)/ (Height in meter)^2

Normal body weight is defined as BMI ranges from 18.5-25 kg/m^2.

C-Laboratory investigation: Blood sample was taken from the anticubital vein under complete aseptic condition where it was withdrawn (through a plastic disposable syringe) from each women for Acetyl cholinesterase (AChE) measurement. Serum cholinesterase activity was determined using an assay with butyryl-thio-choline as the substrate.

The analyses were carried out within 2 hours of sample separation using Boehringer reagent kits (Boehringer Mannheim GmbH, Mannheim, Germany) on an Olympus AU5400 Automatic Analyzer (Olympus Ltd., Tokyo, Japan) based on Wilson et al. method [8].

D-Perinatal outcome assessment: gestational age at delivery (based on the woman's self-reported date of last menstrual period or first trimester ultrasound) and neonatal examination for birth weight, length, head circumference in relation to the local percentiles.

Low birth weight was defined as <2,500 g. Preterm delivery was defined as birth at less than 37 completed weeks of gestation and small for gestational age was defined as birth weight <10th percentile for gestational age.

Data processing and statistical analysis

Data were transferred to a personal computer, classified, and analyzed with SPSS (version 16) (SPSS Inc. Chicago, USA) for windows and for all the analysis a p value<0.05 was considered statistically significant. Data was shown as mean, standard deviation.

Chi square test was done for qualitative variable analysis. Student t-test is a test of significance used for comparison between two groups having quantitative variables. Analysis of covariance (ANCOVA) was done to adjust the effect of other confounders of pregnancy outcome as age in years and education level.

Results

Table 1 shows socio-demographic characteristics of the studied group. There was insignificant difference between exposed and control groups regarding age (26.3 ± 3.93, 25.6 ± 4.5 respectively).

Education level, Socioeconomic level and Body mass index (29.7 ± 3.2, 30.4 ± 2.9 respectively) (p value>0.05) (Table 1).

Risk factors	Exposed (n=40)	Control (n=100)	X^2	p-value
Age in years	26.3 ± 3.93	25.6 ± 4.5	*0.76	>0.05
Education: n (%)				
Basic	12(30)	17(17)	4.19	>0.05
Secondary (high school)	15(37.5)	34(34)		
Higher	13(32.5)	49(49)		

Socioeconomic level: n (%)				
Low	79(17.5)	32(32)	3.06	>0.05
Middle	20(50)	43(43)		
High	13(32.5)	25(25)		
Body Mass Index kg/m^2	29.7 ± 3.2	30.4 ± 2.9	*2.08	>0.05

Table 1: Socio-demographic characteristics of the studied groups. *Student T test Significance p value<0.05.

Table 2 shows that exposed participant exhibited earlier delivery (37.18 ± 1.44 *vs.* 38.67 ± 1.90, p value<0.001), low birth weight (2733.3 ± 197.87 *vs.* 3100.6 ± 213.15, p value<0.001) and small head circumference (33.18 ± 0.33 *vs.* 35.58 ± 0.19, p value<0.05) with no significant difference regarding the body length of the newborn (33.18 ± 0.33 *vs.* 35.58 ± 0.19, p value>0.05) (Table 2).

Variable	**Group**		**t- test (p-value)**	**ANCOVA (p- value)***
	Control (n=100)	**Exposed (n=40)**		
	Mean ± SD			
Gestational age at delivery (weeks)	38.67 ± 1.90	37.18 ± 1.44	<0.001	1.07(0.000)**
Birth weight (gm)	3100.6 ± 213.15	2733.3 ± 197.87	<0.001	38.90(0.000)
Birth length (cm)	48.60 ± 0.19	48.30 ± 0.37	>0.05	169.28(0.000)
Head circumference (cm)	35.58 ± 0.19	33.18 ± 0.33	<0.05	64017(0.000)

Table 2: Perinatal outcome exposed and control groups with and without adjustment of maternal age, education, Gestational age and gender of the new-born. *Analysis of covariance (ANCOVA), **Adjusted for maternal age and gender of the new-born only.

Figure 1 shows that mean value of serum acetyl cholinesterase among exposed (492.90 ± 34.98 U/ml) was significantly lower than control group (1844.27 ± 53.34 U/ml) (Figure 1).

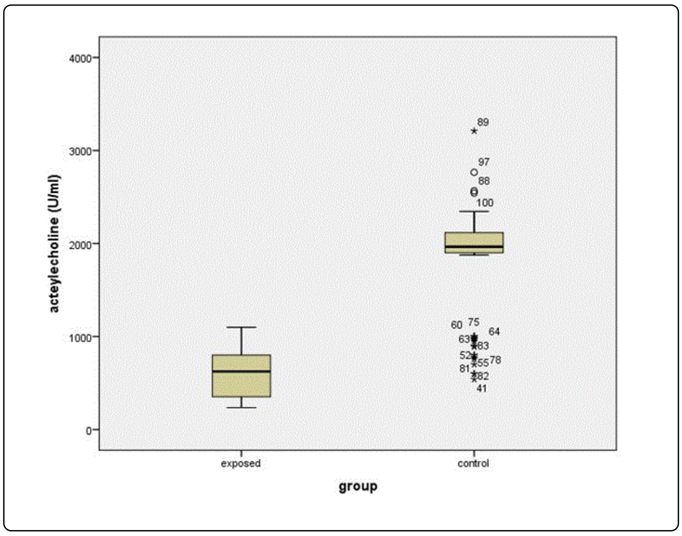

Figure 1: Mean value (SD) of serum acetyl cholinesterase among exposed and control participants.

Table 3 shows a significant correlation between gestational age and birth weight and the serum level of AChE (r=0.34, 0.24 respectively) (Table 3).

Variable	**AChE**	
	r	**p-value**
Gestational age	0.34	0.017
Birth weight	0.24	0.04
Birth length	-0.21	0.462
Head circumference	-0.18	0.573

Table 3: Correlation between the serum level of acetyl cholinesterase (AChE) and perinatal outcome in the exposed group. Critical r^2 tailed at 5%=± 0.05.

Discussion

Organophosphorus (OP) pesticides are used extensively in agriculture throughout the world. It represents more than 80% of total pesticides used in Egypt since 1995 [9].

To date there have been few studies on exposure to pesticides in pregnant women despite reports of widespread exposure, so it is important for evaluating exposure in this susceptible sub-population [10-13].

In our study there was insignificant difference between exposed group and controls regarding socio-demographic characteristics, so any difference between exposed and control group concerning the studied parameters could not be attributed to the effect of any of these confounding factors.

Our results reveals earlier delivery in the exposed group in comparison to controls which is consistent with Eskenazi et al. [10] who studied 448 pregnant women and their infants living in the Salinas Valley, California who came for prenatal care and found that shortened gestational age at delivery (34.7 ± 0.01) and with Wang et al. [14] who studied 187 newborn and their mothers and founded that gestational age at delivery was (39.27 ± 1.32 weeks). In contrast to Willis et al. [15] who reported no association between prenatal organophosphate exposure and gestational age at delivery.

Low birth weight and small head circumference were observed in the exposed group in comparison to the control group with and without adjustment of maternal age, education, gestational age and gender of the new-born. These findings are in agreement with Perera et al. [16] who study effects of trans placental exposure to environmental pollutants including organophosphate pesticide (OP) on birth outcomes in a multi-ethnic population (in 263 pregnant women) and reported that birth weight (g), length and head circumference (cm) was 3382.6 ± 2.45 g, 50.9 ± 2.32 cm 34.1 ± 1.65 cm respectively. Also it was in agreement with Wang et al. [14] who reported that birth weight (g) and length was 49.95 ± 2.16 cm and 39.27 ± 1.32 respectively.

Our results also revealed a significantly lower level of serum AChE in the exposed group (492.90 ± 34.98 IU/L) compared to the control group (1844.27 ± 53.34 IU/L). AChE is used as a biomarker for exposure to OP pesticides [17,18]. This result is in agreement with Eskenazi (10) who found that lower level of AChE in the exposed group (357.12 ± 5.11 IU/L). Previous studies investigated the effect of pesticide exposure on the level of AChE and found AChE significantly lower in the exposed participants than the controls [19-21].

Our study is the first to assess the correlation between gestational age and birth weight and the serum level of AChE.

This study has a number of important limitations. The small sample size means that estimates are likely to be influenced by a few extreme values and cannot be generalized to the larger population of pregnant women in Egypt. In addition to exposure estimates were based on a single blood sample measurement of acetyl cholinesterase which reflects only a recent exposure to organophosphates. Future studies should focus on identifying primary exposure sources to pesticides and health education of the pregnant women.

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