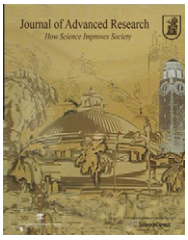
Journal of Advanced Research (2011) 2, 185–189

Cairo University

Journal of Advanced Research



SHORT COMMUNICATION

Reproductive outcome, hormone levels and liver enzymes in agricultural female workers

Khadiga S. Ibrahim *, Nagat M. Amer, Eman M. El Tahlawy, Heba M. Abd Allah

Department of Environmental and Occupational Medicine, National Research Centre, Dokki, Cairo, Egypt

Received 26 August 2010; revised 21 December 2010; accepted 10 January 2011
Available online 9 February 2011

KEYWORDS

Agriculture;
Female;
Estradiol;
Progesterone;
Follicle stimulating hormone;
AST;
ALT

Abstract The study aimed to explore the effects of exposure to pesticides on the reproductive health and liver function of females participating in agricultural work. Blood samples were obtained from the thirty-five females (out of one hundred females of reproductive age) who were willing to donate blood. Fifty females matched for age and socio economic status were recruited as a control group to compare levels of hormones (estradiol, progesterone and follicle stimulating hormone), liver enzymes alanine aminotransferase (ALT), and aspartate aminotransferase (AST). Results showed that 53% of the females examined in this village were illiterate. Agricultural work represented 42% of the occupations encountered by females in the study. Females who helped in farming operations showed a higher incidence of adverse pregnancy outcome such as abortions and stillbirths compared to those who did not share in agricultural work. There was a significant elevation in estradiol and progesterone levels among female agricultural workers and controls. There was also elevation in serum liver enzymes (AST and ALT) in agricultural workers compared to the controls. However, there was a significant decrease in FSH level in females sharing in agricultural activities compared to the controls. It could be concluded that participation of females in agricultural activities with potential exposure to pesticides endangers their reproductive health and liver functions. Rural areas in Egypt require more attention to increase the percentage of literacy among females and raise their health awareness.

* Corresponding author. Tel.: +20 2 33369651; fax: +20 2 33370931.
E-mail address: khadigasalah@yahoo.com (K.S. Ibrahim).

Peer review under responsibility of Cairo University.
doi:10.1016/j.jare.2011.01.004

ELSEVIER Production and hosting by Elsevier

Introduction

The agricultural sector is a very important part of the Egyptian economy. In rural Egypt, one of the main activities of women, besides their household duties, is helping in agricultural work. This is due to change in the economic life of families. Huge families with no chance of increasing cultivated land and labor migration led to increasing the load of agricultural work done by women. Also, in many parts of the world, women constitute a large proportion of farmers [1]. Nowadays, women must be

considered as an important force in agricultural work. They are exposed to a wide variety of health hazards including pesticide exposure.

Pesticides are used in agriculture and public health to control insects, weeds and vectors of disease. Exposure to pesticides can occur directly from occupational and environmental sources and indirectly through diet. There is a growing public concern about the impact of exposure to pesticides on human health. Lack of knowledge, careless attitude and appalling safety practices in handling pesticides pose a serious health risk to our farmers. Some pesticides were classed as reproductive and developmental toxins in the Pan American Pesticide Database classification [2]. Pesticide exposure has been also associated with several disease conditions including hypertension, hepatomegaly, dermatosis, neurological and immunological effects, chromosomal aberrations and elevated cancer risks [3,4].

Pesticide exposure causes leakage of cytosolic enzymes from hepatocytes and other body organs [5]. A high degree of abnormal liver function in agricultural workers may indicate toxic effects of pesticides and the presence of pesticide residues in blood. Altered liver enzyme activities have been reported among occupational workers exposed to Organophosphorus pesticides alone or in combination with Organochlorines [6].

Reproductive effects that have been associated with pesticide exposure in women are decreased fertility, spontaneous abortions, stillbirth, premature birth, low birth weight, developmental abnormalities, ovarian disorders, and disruption of the hormonal function [7–10].

Women's health is an area that is gaining attention with the realization that men's and women's bodies react differently to environmental agents. The number of women in the workforce is increasing worldwide and a considerable proportion of them are of reproductive age. Therefore attention is required to note any reproductive dysfunction due to occupational exposure. Such exposures may affect the female endocrine system and thus play an important role in the increasing infertility problem.

Material and methods

This is a cross section comparative study; location of the study is a village in Kafer El sheikh which is north east of Lower Egypt about three hours from Cairo. The study was conducted during harvest time. This village consists of 100 families living in two small satellites (one composed of 60 families and the other of 40 families). Sample: all families in the village were surveyed and from each family one female in reproductive age was randomly selected to participate. Data collection: a special questionnaire was constructed to cover the following points: socio-demographic data, agricultural activities, exposure to pesticides, menarche history, and outcome of pregnancy (abortion, stillbirth, preterm labour, low birth weight or congenital anomalies), dysfunctional uterine bleeding, and tumors of the uterus or ovaries. Exposed females named a lot of pesticides that they use and mentioned that they frequently use them in the form of mixtures. This is due to variation in agricultural crops. Exposure was considered chronic because the females included in the study are always engaged in pesticide application. The females were considered exposed if they shared in preparing, mixing or spraying pesticides on a regular basis. The exposed females did not report any co-existing exposure. They did not use any protective measures during mixing or spraying. Fifty females matched for age and socio economic status were recruited as a control group to compare levels of hormones (estradiol, progesterone and follicle stimulating hormone), liver enzymes alanine aminotransferase (ALT) and aspartate aminotransferase (AST). The control group was chosen from a neighboring village whose main occupation was fishing not related to any agricultural activities. All the studied populations were non-smokers and non-alcohol drinkers receiving no medications on a regular basis.

Approval consent was obtained from all participants. Under complete aseptic conditions, a blood sample of 5 cm was taken by venipuncture from each subject. Samples were centrifuged for separation of serum to be used for analysis of the following:

- Estimation of serum liver enzymes (ALT and AST) according to the method of Reitman and Frankel [11].
- Determination of hormones (estradiol, progesterone and follicle stimulating hormone) by immunologic methods (Elisa technique) using commercial kits purchased from DRG diagnostic Germany [12–14].

To overcome variation in hormone levels in different phases of the menstrual cycle, samples were taken from both groups during the follicular phase of the menstrual cycle (starting from the first day of menstruation to mid cycle). Also, pregnant females were not included in the study to exclude high progesterone level during pregnancy.

Statistical analysis was performed using the SPSS package system version 16.

Results

Table 1 shows that more than half of the females in the village were illiterate. University graduates represented only 2% of the studied females. Agricultural work represented 42% of occupations encountered in the study. Females who helped in preparing pesticides represented 61.2%. Females who shared in spraying pesticides represented 14.9%. Duration of work exceeded 10 years in 55.25% of the studied females as shown in Table 2. All studied populations were non-smokers,

Table 1 Basic socio-demographic characteristics of the females in the studied village.

Basic socio-demographic characteristics	No.	%
Education		
Illiterate	53	53
Can read and write	6	6
Primary	12	12
Preparatory	2	2
Secondary or diploma	23	23
Two years after secondary school	2	2
University graduate	2	2
Total	100	100
Occupation		
Agricultural worker	42	42
Others	58	58
Total	100	100

Table 2 Agricultural activities conducted by the studied group.

		No.	%
Helping in farming operations	No	33	33
	Yes	67	67
	Total	100	100
Preparation of pesticides for spraying	Help or do it by herself	41	61.2
	No	26	38.8
	Total	67	100
Helping in spraying pesticides	No	10	14.9
	Yes	57	85.1
	Total	67	100
Duration of exposure	Less than 10 years	30	44.8
	10 years and more	37	55.2

non-alcohol drinkers, apparently in good health and taking no medication on a regular basis.

Agricultural workers showed higher levels of progesterone and estradiol compared to the controls and the difference was statistically significant with p values of <0.0001 and <0.001, respectively. However, FSH level was significantly lower in female agricultural workers with p value <0.0001. Liver functions were affected as evidenced by high enzyme levels with significant difference at p values <0.0001 and 0.05 for AST and ALT, respectively, as shown in Table 3.

There was no correlation between the duration of work and the tested parameters.

It is clear from Table 4 that females sharing in agricultural work gave birth to a lower percentage of well born babies (64.2%) compared to working females (84.8%). Females exposed to pesticides reported higher incidences of uterine bleeding but the difference was not statistically significant compared with those not sharing in the agricultural work.

Discussion

Our study revealed a high percentage of illiterate females in the studied village. Illiteracy, especially among females, still constitutes a major problem in rural Egypt. The study pointed to the large number of females engaged in agricultural activities (67%). The questionnaire showed their unawareness of the health hazards of pesticide exposure on their reproductive health. Only a few of them knew the guidelines for the safe usage and storage of pesticides. None of them gave information about the mixtures of pesticides they use. They only reported that they use different types of pesticides and usually apply them in combinations. The most commonly types supplied by the agricultural governmental association were alderin, heptachlor and ozamyl.

Measuring hormone levels in females helping in agricultural activities and exposed to pesticides during their work demonstrated higher estradiol and progesterone and lower FSH levels compared to controls. Moreover the progesterone level (3.283 ng/ml) is higher than the normal range during the follicular phase, which is 0.2–1.4 ng/ml. This high progesterone level could be attributed to a possible disturbance in hormone level

Table 3 Comparison between agricultural female workers and controls concerning hormone levels namely (progesterone, FSH and estradiol) and liver enzymes namely (AST and ALT).

Parameter	Group	No.	Mean	Std. deviation	P value
Progesterone (ng/ml)	Agricultural worker	35	3.283	4.238	<0.0001
	Control	50	.716	.757	
FSH (mIU/ml)	Agricultural worker	35	4.229	1.584	<0.0001
	Control	50	6.024	2.218	
Estradiol (pg/ml)	Agricultural worker	35	55.369	13.815	<0.001
	Control	50	47.284	10.001	
AST	Agricultural worker	35	28.343	5.434	<0.0001
	Control	50	24.520	3.079	
ALT	Agricultural worker	35	24.429	3.363	<0.05
	Control	50	21.680	5.560	

Table 4 Pregnancy outcome in females engaged in agricultural activities.

Outcome of pregnancy	Helping in farming operations						P value
	No		Yes		Total		
	No.	%	No.	%	No.	%	
Well born fetus (no preterm labour, low birth weight or congenital anomalies)	28	84.8	43	64.2	71	71.0	<0.05
Adverse outcome (abortion, Stillbirth, preterm labour, low birth weight or congenital anomalies)	5	15.2	24	5.8	29	29.0	
Total	33	100.0	67	100.0	100	100.0	

The examined females were adjusted for age and socioeconomic status. None of them were smokers or alcohol drinkers. Also none of them was pregnant.

associated with exposure. Those females might be exposed to organophosphorous pesticides (OPs) in the pesticide mixtures they apply. OPs are suspected to alter reproductive function by reducing brain acetylcholinesterase (AChE) activity and secondarily influencing the gonads. Experiments on animals have shown that repeated doses of OP significantly decreased brain AChE activity and significantly increased acetylcholine, gamma-aminobutyric acid, epinephrine, norepinephrine, dopamine, and 5-hydroxyttyptamine concentrations, altering reproductive function by reducing brain acetylcholinesterase activity and monoamine levels, thus impairing hypothalamic and/or pituitary endocrine functions and gonadal processes [15]. We suggest more detailed study of reproductive hormones to clarify the cause for this marked rise of progesterone. The low FSH level is explained by a negative feedback mechanism of the pituitary gland resulting from high estradiol. These findings were in accordance with previous studies that proposed that pesticides induce hormone disruption [16,17]. This alteration of hormone levels may interfere with the menstrual cycle and lead to adverse reproductive health effects [18–20]. It also explains the increased number of females complaining of dysfunctional uterine bleeding in those exposed to pesticides.

The study supported the possible association between pesticide exposure and adverse pregnancy outcome. Females involved in agricultural work reported a higher percentage of adverse outcomes of pregnancy (abortion, stillbirth and congenital anomalies) compared to females not engaged in agriculture, which agrees with other studies [21–25]. The intricate processes of the menstrual cycle, ovum production, fertilization, implantation, and growth and development of the fetus, may be particularly susceptible to low-dose exposures to endocrine disruptors. This explains the difficulty in studying female reproductive health and fertility.

The study demonstrated elevation of serum liver enzymes (AST and ALT) in agricultural female workers. This was reported in Pakistani tobacco farmers involved in cultivation, pesticides application, and picking and drying of tobacco leaves [26]. A similar increase in AST and ALT levels was reported in agricultural workers in India [27], selected farm workers in Gadap Karachi, Pakistan [28] and in Israel [29]. Ultimately, pesticide exposure may lead to hepatic impairment, which may affect levels of female hormones.

Conclusion

The study highlights the need to evaluate and control the health effects of pesticide exposure in females. A better understanding of potential gender-environment interactions related to pesticide exposure and health effects is needed. Our results support a possible association between adverse pregnancy outcome and pesticide exposure that require further detailed study with increased sample size.

Acknowledgments

This work was an outcome of the project entitled ''Environmental management of water and waste water in Egyptian villages and its impact on health''. Our team would like to thank Dr. Sohair Abou-El Ela, the principal investigator of the project for, her great effort and support throughout the entire work.

References

[1] Rice HR, Baker BA. Workplace hazards to women's reproductive health. Minn Med 2007;90(9):44–7.
[2] Kegley SE, Hill BR, Orme S, Choi AH. PAN pesticide database. 2010; Available from: < http://www.pesticideinfo.org/ > .
[3] Horrigan L, Lawrence RS, Walker P. How sustainable agriculture can address the environmental and human health harms of industrial agriculture. Environ Health Perspect 2002;110(5):445–56.
[4] Raschke AM, Burger AE. Risk assessment as a management tool used to assess the effect of pesticide use in an irrigation system, situated in a semi-desert region. Arch Environ Contam Toxicol 1997;32(1):42–9.
[5] Dewan A, Bhatnagar VK, Mathur ML, Chakma T, Kashyap R, Sadhu HG, et al.. Repeated episodes of endosulfan poisoning. J Toxicol Clin Toxicol 2004;42(4):363–9.
[6] Amr MM. Pesticide monitoring and its health problems in Egypt, a third world country. Toxicol Lett 1999;107(1–3):1–13.
[7] Nurminen T. Maternal pesticide exposure and pregnancy outcome. J Occup Environ Med 1995;37(8):935–40.
[8] Kumar S. Occupational exposure associated with reproductive dysfunction. J Occup Health 2004;46(1):1–19.
[9] Meyer KJ, Reif JS, Veeramachaneni DN, Luben TJ, Mosley BS, Nuckols JR. Agricultural pesticide use and hypospadias in eastern Arkansas. Environ Health Perspect 2006;114(10):1589–95.
[10] Clementi M, Causin R, Marzocchi C, Mantovani A, Tenconi R. A study of the impact of agricultural pesticide use on the prevalence of birth defects in Northeast Italy. Reprod Toxicol 2007;24(1):1–8.
[11] Reitman S, Frankel S. A colorimetric method for the determination of serum glutamic oxalacetic and glutamic pyruvic transaminases. Am J Clin Pathol 1957;28(1):56–63.
[12] Ratcliffe WA, Carter GD, Dowsett M, Hillier SG, Middle JG, Reed MJ. Oestradiol assays: applications and guidelines for the provision of a clinical biochemistry service. Ann Clin Biochem 1988;25(Pt 5):466–83.
[13] Katt JA, Duncan JA, Herbon L, Barkan A, Marshall JC. The frequency of gonadotropin-releasing hormone stimulation determines the number of pituitary gonadotropin-releasing hormone receptors. Endocrinology 1985;116(5):2113–5.
[14] Uotila M, Ruoslahti E, Engvall E. Two-site sandwich enzyme immunoassay with monoclonal antibodies to human alpha-fetoprotein. J Immunol Methods 1981;42(1):11–5.
[15] Recio R, Ocampo Gomez G, Moran Martinez J, Borja Aburto V, Lopez Cervante M, Uribe M, et al.. Pesticide exposure alters follicle-stimulating hormone levels in Mexican agricultural workers. Environ Health Perspect 2005;113(9):1160–3.
[16] Cooper GS, Klebanoff MA, Promislow J, Brock JW, Longnecker MP. Polychlorinated biphenyls and menstrual cycle characteristics. Epidemiology 2005;16(2):191–200.
[17] Bretveld RW, Thomas CM, Scheepers PT, Zielhuis GA, Roeleveld N. Pesticide exposure: the hormonal function of the female reproductive system disrupted? Reprod Biol Endocrinol 2006;4:30.
[18] Farr SL, Cooper GS, Cai J, Savitz DA, Sandler DP. Pesticide use and menstrual cycle characteristics among premenopausal women in the agricultural health study. Am J Epidemiol 2004;160(12):1194–204.
[19] Figà-Talamanca I. Occupational risk factors and reproductive health of women. Occup Med 2006;56(8):521–31.
[20] Mendola P, Messer LC, Rappazzo K. Science linking environmental contaminant exposures with fertility and reproductive health impacts in the adult female. Fertil Steril 2008;89(Suppl. 2):e81–94.
[21] Arbuckle TE, Lin Z, Mery LS. An exploratory analysis of the effect of pesticide exposure on the risk of spontaneous abortion

in an Ontario farm population. Environ Health Perspect 2001;109(8):851–7.
[22] Garcia AM. Pesticide exposure and women's health. Am J Ind Med 2003;44(6):584–94.
[23] Windham GC, Lee D, Mitchell P, Anderson M, Petreas M, Lasley B. Exposure to organochlorine compounds and effects on ovarian function. Epidemiology 2005;16(2):182–90.
[24] Andersen HR, Schmidt IM, Grandjean P, Jensen TK, Budtz-Jørgensen E, Kjærstad MB, et al.. Impaired reproductive development in sons of women occupationally exposed to pesticides during pregnancy. Environ Health Perspect 2008;116(4):566–72.
[25] Shirangi A, Fritschi L, Holman CDJ, Bower C. Birth defects in offspring of female veterinarians. J Occup Environ Med 2009;51(5):525–33.
[26] Khan DA, Bhatti MM, Khan FA, Naqvi ST, Karam A. Adverse effects of pesticides residues on biochemical markers in Pakistani tobacco farmers. Int J Clin Exp Med 2008;1(3):274–82.
[27] Patil JA, Patil AJ, Govindwar SP. Biochemical effects of various pesticides on sprayers of grape gardens. Indian J Clin Biochem 2003;18(2):16–22.
[28] Azmi MA, Naqvi SN, Azmi MA, Aslam M. Effect of pesticide residues on health and different enzyme levels in the blood of farm workers from Gadap (rural area) Karachi-Pakistan. Chemosphere 2006;64(10):1739–44.
[29] Hernandez AF, Amparo Gomez M, Perez V, Garcia Lario JV, Pena G, Gil F, et al.. Influence of exposure to pesticides on serum components and enzyme activities of cytotoxicity among intensive agriculture farmers. Environ Res 2006;102(1):70–6.