Pesticides impact on testicular and thyroid functions of farm workers in Gaza Strip

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ABSTRACT

Objectives: To assess the impact of pesticides on testicular and thyroid functions of farm workers in Gaza Strip.

Methods: The study included 96 farm workers exposed to pesticides as well as 96 non-exposed controls from different Governorates of Gaza Strip. Farm workers and controls were age matched. Blood samples were collected from all farm workers and controls to assess testicular function through determination of serum testosterone, luteinizing hormone (LH) and follicle stimulating hormone (FSH) and to assess thyroid function through determination of serum thyroid stimulating hormone (TSH), triiodothyronine (T3) and thyroxine (T4).

Results: Serum testosterone was significantly decreased in farm workers compared to controls whereas LH and FSH were increased in farm workers with significant change for LH. Serum TSH of farm workers was significantly higher than that of controls whereas T3 and T4 were significantly lower in farm workers. When related to age, significant decrease in testosterone, T3 and T4 as well as significant increase in LH, FSH and TSH were found only in farm workers of age group 31 - 45 years compared to their counterparts of controls. Regarding work duration, the longer the work duration of pesticides use, the higher percentage of decrease in testosterone and the higher percentage of increase in LH and TSH levels were observed.

Conclusion: The results of the present study confirm that pesticides exposure affects farm workers testicular and thyroid functions through alterations with significant values in testosterone, LH, FSH, TSH, T3 and T4.

KEY WORDS: Pesticides, Testicular function, Thyroid function, Farm workers, Gaza Strip

Introduction

Agriculture is a basic source of income and subsistence in Gaza strip where about 2 million people lived and work in an area of 365 Km2 [1]. Due to increased demand to improve income and to feed the teeming population, farmers resort to the extensive use of pesticides to increase yield. More than 544.4 metric tons of pesticides are used annually in Gaza Strip [2]. Farm workers may be occupationally exposed to pesticides through direct contact with thsese chemicals, contact with pesticide residue on treated crops or equipment, drift, and entering treated fields before it is safe [3]. Pesticides from any of these contacts can enter human body through mouth, skin or inhalation [4].

Pesticides can cause immediate and delayed advers health effects but the severity depends on the extent of exposure [5]. In this context, work duration and age of farm workers may be related to the degree of illness in response to pesticides exposure [6]. Approximately 25 million pesticide poisoning cases occur annually among agricultural workers in developing countries where protective measures are poorly followed [7,8]. In Gaza Strip, several cases of death were reported among farm workers as a result of pesticides poisoning [9].

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Pesticides have been associated with endocrine-disrupting activity and their potential to modify the male hormone profile was studied [10,11]. The hormonal changes may result from destructive and degenerative changes caused by pesticides in many organs including testis and thyroid gland [12,13]. Most studies in the literature reported lower serum testosterone, T3 and T4 levels whereas serum LH, FSH and TSH levels were shown to be higher in pesticides-exposed workers compared their counterparts of controls [14-17].

Desptite overuse and/or misuse of pesticides in agricultural sector and their health and environmental problems in Gaza Strip, few studies investigated the health impact of pesticides on farm workers who are frequently exposed to these highly toxic compounds [6,18]. To our best knowledge, the present study is the first to assess the effect of pesticides on testicular and thyroid functions of farm workers in Gaza Strip.

Materials and Methods

Study population

The study population comprised male farm workers using pesticides in Gaza Strip as well as non-exposed male controls from different Governorates of Gaza Strip: North, Gaza, Mid-Zone, Khan Yunis and Rafah Governorates. The sample size included 96 farm workers and 96 controls aged between 20 - 60 years. Farm workers and controls were age matched.

Ethical consideration

The study was conducted in accordance with the Declaration of Helsinki and was approved by the Local Ethics Research Committee. All subjects provided written informed consent prior to the study.

Blood sampling and processing

Venous blood samples (about 5 ml) were taken by venipuncture from each subject into vacationer tubes from the exposed farm workers as well as from controls. Samples were left without anticoagulant to allow blood to clot. Serum samples were obtained by centrifugation at room temperature by Rotina 46 Hettich centrifuge, Japan at 4000 rpm/10 minutes. Then, serum samples were used for hormonal analysis.

Hormonal analysis

Serum testosterone was determined according to the method of Tietz using enzyme-linked immunosorbent assay (ELISA) TECO kit [19]. Serum LH and FSH were measured according to Lenton et al. and Vitt et al. methods respectively using ELISA TECO kits [20,21]. Serum TSH was determined according to the method of Uotila et al. using ELISA TECO kit [22]. Serum T3 and T4 were measured according to Schuurs and Van Weemen method using ELISA ALPCO kits [23].

Statistical Methods

Data were computer analyzed using SPSS / PC (Statistical Package for the Social Science Inc. Chicago, Illinois USA, version 21.0) statistical package. The independent sample t-test procedure was used to compare means of quantitative variables by the separated cases into two qualitative groups such as the relationship between farm workers and controls testosterone. The one-way ANOVA test was applied for analysis of variance. The results were accepted as statistical significant when the P value was less than 5% ($P < 0.05$). The percentage difference was calculated according to the formula: Percentage difference equals the absolute value of the change in value, divided by the average of the 2 numbers, all multiplied by 100. Percent difference = (| (V1 - V2) | / ((V1 + V2)/2)) * 100. Excel program 2007 was used for chart graphs plotting.

Results

Effect of pesticides on serum testosterone, LH and FSH

Table 1 and figure 1 illustrate the effect of pesticides exposure on serum testosterone, LH and FSH levels of farm workers in Gaza Strip.

Figure 1. Serum testosterone, luteinizing hormone (LH) and follicle stimulating hormone (FSH) levels of controls and farm workers in Gaza Strip.

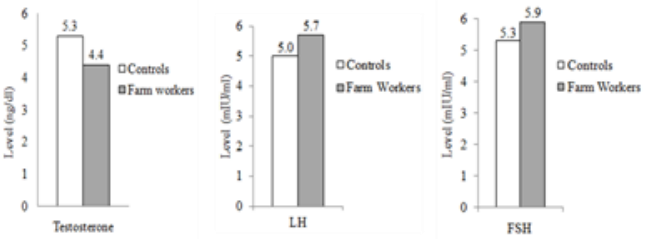
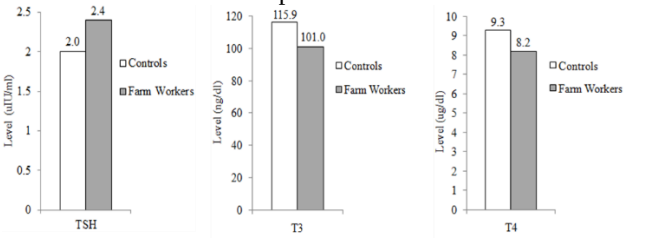


Figure 2. Serum thyroid stimulating hormone (TSH), triiodothyronine (T3) and thyroxine (T4) levels of controls and farm workers in Gaza Strip.



The mean level of testosterone was significantly decreased in farm workers compared to controls. Conversely, the mean levels of LH and FSH were increased in farm workers than in controls with significant change for LH. The most affected farm workers were from Rafah Governorate.

Table 1. Serum testosterone, leuteinizing and follicle stimulating hormones levels of controls and farm workers in different Governorates of Gaza Strip.

Governorate	Group	Testosterone (ng/dl)	LH (mIU/ml)	FSH (mIU/ml)
North	Control	5.7 ± 1.0	5.0 ± 0.10	5.2 ± 1.8
	Farm workers	4.7 ± 1.5	5.8 ± 2.1	5.4 ± 1.0
	% difference	-19.2	14.8	3.8
	P value	< 0.05	N.S.	N.S.
Gaza	Control	5.1 ± 0.7	5.3 ± 0.7	4.8 ± 1.8
	Farm workers	4.7 ± 1.8	5.5 ± 1.9	5.5 ± 0.9
	% difference	-8.2	3.7	13.6
	P value	N.S.	N.S.	N.S.
Mid-Zone	Control	4.9 ± 0.7	5.0 ± 0.5	5.3 ± 0.7
	Farm workers	4.3 ± 1.4	6.0 ± 1.8	5.9 ± 1.8
	% difference	-13.0	18.2	10.7
	P value	N.S.	< 0.05	N.S.
Khan Yunis	Control	4.8 ± 0.7	4.9 ± 1.2	5.3 ± 1.3
	Farm workers	5.1 ± 1.4	5.9 ± 1.8	6.3 ± 2.0
	% difference	6.1	18.5	17.2
	P value	N.S.	< 0.05	< 0.05
Rafah	Control	5.3 ± 1.1	5.4 ± 1.5	5.2 ± 1.9
	Farm workers	4.3 ± 1.2	5.7 ± 1.8	6.8 ± 2.2
	% difference	-20.8	5.4	26.7
	P value	< 0.05	N.S.	< 0.05
Gaza Strip (total)	ANOVA	1.206	0.142	3.832
	P value	N.S.	N.S.	< 0.05
	Control	5.3 ± 1.4	5.0 ± 1.0	5.3 ± 1.1
	Farm workers	4.4 ± 1.3	5.7 ± 1.8	5.9 ± 2.0
	% difference	-18.6	13.1	10.7
	P value	< 0.05	< 0.05	N.S

LH: Luteinizing hormone, FSH: Follicle stimulating hormone. All values are expressed as mean ± SD. P = Probability, P < 0.05: Significant, P > 0.05: Not significant (N.S).

Effect of pesticides on serum TSH, T3 and T4

Table 2 and figure 2 revealed that the mean level of serum TSH in pesticides-exposed farm workers was significantly higher than that of controls. In contrast, the mean levels of serum T3 and T4 were significantly lower in farm workers with respect to controls. Farm workers from the North Governorate were the most affected.

Effect of pesticides on serum testosterone, LH and FSH of farm workers with regards to their age.

Serum testosterone, LH and FSH levels of pesticides-exposed farm workers in Gaza Strip with regards to their age are presented in table 3. Significant decrease in testosterone level and significant increase in LH and FSH levels were found in farm workers of age group 31 - 45 years compared to their counterparts of controls. On the other hand, there were no significant change in testosterone, LH and FSH levels in farm worker's categories of less than 30 years and more than 45 years.

Table 2. Serum thyroid stimulating hormone, triiodothyronine and thyroxine levels of controls and farm workers in different Governorates of Gaza Strip.

Governorate	Group	TSH (µIU/ml)	T3 (ng/dl)	T4 (µg/dl)
North	Control	1.9 ± 1.1	126.1 ± 26.0	9.1 ± 1.5
	Farm workers	2.3 ± 1.0	97.0 ± 25.8	8.3 ± 1.7
	% difference	19.0	-26.1	-9.2
	P value	N.S.	< 0.001	N.S.
Gaza	Control	1.9 ± 0.8	110.8 ± 19.0	9.1 ± 0.8
	Farm workers	2.0 ± 1.5	99.7 ± 24.0	8.4 ± 1.6
	% difference	5.1	-10.5	-8.0
	P value	N.S.	N.S.	N.S.
Mid-Zone	Control	1.8 ± 1.0	120.7 ± 35.2	9.4 ± 1.2
	Farm workers	1.7 ± 1.3	118.6 ± 22.1	8.2 ± 1.7
	% difference	-5.7	-1.8	-13.6
	P value	N.S.	N.S.	< 0.05
Khan Yunis	Control	1.7 ± 0.9	115.9 ± 22.2	9.4 ± 1.2
	Farm workers	2.1 ± 1.3	105.4 ± 28.8	8.2 ± 1.7
	% difference	21.1	-9.5	-13.6
	P value	N.S.	N.S.	< 0.05
Rafah	Control	2.7 ± 1.1	98.6 ± 21.4	8.8 ± 1.4
	Farm workers	2.5 ± 1.2	102.2 ± 31.7	8.0 ± 1.8
	% difference	-7.7	3.6	-9.5
	P value	N.S.	N.S.	N.S.
Gaza Strip (total)	ANOVA	0.782	1.764	1.014
	P value	N.S.	N.S.	N.S.
	Control	2.0 ± 0.9	115.9 ± 26.1	9.3 ± 1.3
	Farm workers	2.4 ± 1.1	101.0 ± 27.3	8.2 ± 1.7
	% difference	18.2	-13.7	-12.6
	P value	< 0.05	< 0.05	< 0.05

TSH: Thyroid stimulating hormone, T3: Triiodothyronine, T4: Thyroxine. All values are expressed as mean ± SD. P = Probability, P < 0.05: Significant P > 0.05: Not significant (N.S).

Effect of pesticides on serum TSH, T3 and T4 of farm workers with regards to their age.

Table 4 points out the effect of pesticides on serum TSH, T3 and T4 of farm workers in Gaza Strip with regards to their age. There was an increase in TSH level and significant decreases in T3 and T4 levels in farm workers group aged 31 - 45 years compared to their counterparts of controls. However, no significant change in TSH, T3 and T4 levels was recorded in farm workers groups of less than 30 years and more than 45 years.

Table 3. Effect of pesticides on serum testosterone, leuteinizing and follicle stimulating hormones levels of farm workers in Gaza Strip with regards to their age.

Age (year)	Group	Testosterone (ng/dl)	LH (mIU/ml)	FSH (mIU/ml)
Less than 30	Control	5.1 ± 0.9	4.9 ± 1.0	5.3 ± 0.9
	Farm workers	4.9 ± 1.7	5.4 ± 1.8	5.5 ± 2.1
	% difference	-4.0	9.7	3.7
	P value	N.S.	N.S.	N.S.
31 - 45 year	Control	5.3 ± 0.9	5.0 ± 1.1	5.1 ± 1.1
	Farm workers	4.6 ± 1.4	6.1 ± 2.0	6.0 ± 2.2
	% difference	-14.1	19.8	16.2
	P value	P < 0.05	P < 0.05	P < 0.05
More than 45	Control	5.1 ± 0.6	5.4 ± 0.8	6.3 ± 1.5
	Farm workers	4.5 ± 1.5	5.6 ± 1.6	6.0 ± 1.4
	% difference	-12.5	3.6	-4.9
	P value	N.S.	N.S.	N.S.
	ANOVA	0.083	1.691	0.616
	P value	N.S.	N.S.	N.S.

LH: Luteinizing hormone, FSH: Follicle stimulating hormone. All values are expressed as mean ± SD. P = Pobability, P < 0.05: Significant, P > 0.05 Not significant (N.S).

Table 4. Effect of pesticides on serum thyroid stimulating hormone, triiodothyronine and thyroxine levels of farm workers in Gaza Strip with regards to their age.

Age (year)	Group	TSH (µIU/ml)	T3 (ng/dl)	T4 (µg/dl)
Less than 30	Control	2.0 ± 1.0	113.0 ± 26.6	8.9 ± 1.2
	Farm workers	2.1 ± 1.3	102.5 ± 25.8	8.4 ± 1.6
	% difference	4.9	-9.7	-5.8
	P value	N.S.	N.S.	N.S.
31 - 45	Control	1.8 ± 1.0	121.4 ± 26.4	9.8 ± 1.2
	Farm workers	2.1 ± 1.2	101.6 ± 25.4	8.3 ± 1.6
	% difference	15.4	-17.8	-16.6
	P value	N.S.	P < 0.05	P < 0.05
More than 45	Control	2.3 ± 1.4	106.0 ± 26.3	8.4 ± 1.1
	Farm workers	2.2 ± 1.1	112.3 ± 26.6	8.3 ± 1.9
	% difference	-4.4	5.8	-1.2
	P value	N.S.	N.S.	N.S.
	ANOVA	0.122	1.209	0.053
	P value	N.S	N.S	N.S

TSH: Thyroid stimulating hormone, T3: Triiodothyronine, T4: Thyroxine. All values are expressed as mean ± SD. P = Probability, P < 0.05: Significant, P > 0.05 Not significant (N.S).

Effect of pesticides on serum testosterone, LH and TSH of farm workers in relation to work duration.

As indicted in table 5, testosterone levels were decreased at all work duration intervals compared to controls with significant decrease during work durations of 7 - 14 and > 14 years.

On the other hand, LH and TSH levels were increased at all work duration intervals with significant increase during work duration of > 14 years. In general, the longer the work duration of pesticides use, the higher percentage of decrease in testosterone and the higher percentage of increase in LH and TSH levels were observed.

Table 5. Serum testosterone, leuteinizing and thyroid stimulating hormones levels of farm workers in relation to work duration of pesticides use in Gaza Strip.

Work duration (year)	Group	Testosterone (ng/dl)	LH (mIU/ml)	TSH (µIU/ml)
Less than 7	Control	5.3 ± 0.9	5.0 ± 1.1	1.9 ± 1.0
	Farm workers	4.9 ± 1.0	5.3 ± 1.5	2.0 ± 0.7
	% difference	-7.8	5.8	5.1
	P value	N.S.	N.S.	N.S.
7 - 14	Control	5.2 ± 0.9	5.1 ± 1.1	1.9 ± 1.0
	Farm workers	4.3 ± 1.2	5.8 ± 2.2	2.1 ± 1.1
	% difference	-18.9	12.8	10.0
	P value	P < 0.05	N.S.	N.S.
More than 14	Control	5.3 ± 0.9	5.0 ± 1.1	2.0 ± 1.1
	Farm workers	4.0 ± 1.0	6.0 ± 1.8	2.8 ± 1.2
	% difference	-28.0	18.2	33.3
	P value	P < 0.05	P < 0.05	P < 0.05
	ANOVA	16.973	3.785	6.428
	P value	P < 0.05	P < 0.05	P < 0.05

LH: Luteinizing hormone, TSH: Thyroid stimulating hormone. All values are expressed as mean ± SD. P = Probability, P < 0.05: Significant, P > 0.05 Not significant (N.S).

Discussion

Farm workers in Gaza Strip are close in touch with various types of pesticides in many ways. These highly toxic compounds have destructive effects on different body organs. Although pesticides were identified as endocrine disruptors, their impact on male hormone profile in humans has not been fully investigated. In the present study, information of pesticides effects on testicular and thyroid functions of farm workers in Gaza Strip were provided.

The mean level of testosterone was significantly decreased in farm workers compared to controls. Conversely, the mean levels of LH and FSH were increased in farm workers than in controls with significant change for LH. These findings are in accordance with most previous studies in different pesticides occupational settings [17,24]. In this context, pesticides exposure was found to be positively associated with LH and FSH levels whereas testosterone showed an

inverse association [10,25]. Meanwhile, a contradictory study reported higher levels of serum testosterone in pesticides sprayers in comparison to their corresponding controls [26]. This inconsistency may be attributed to the types of pesticides and the magnitude of exposure. However, this needs further investigation. Nevertheless, the present results do confirm impairment in testicular function as a result of pesticide exposure.

Lower levels of testosterone detected in our farm workers may be explained by direct interaction of pesticides with Leydig cells of the testis and reducing testosterone production [27]. Suppression of testosterone levels exerts a feedback control at hypothalamus-pituitary axis activating LH and FSH secretion [28]. In addition, pesticides may induce gene expression and biosynthesis of hypothalamic gonadotropin-releasing hormone (GnRH) which in turn stimulates pituitary secretion of LH and FSH [10,29]. However, variation in GnRH secretion regulates the cyclic release of FSH by the anterior pituitary to a lesser extent than LH. The role of GnRH in the feedback of FSH secretion has been also less clearly defined than for LH secretion [30]. This may justify the observed increase of LH and FSH levels with significant change for LH.

Data presented here revealed that serum TSH level was significantly higher in pesticides-exposed farm workers than that of controls whereas serum T3 and T4 levels were significantly lower in farm workers. Similar results were previously documented in male pesticides sprayers and farmers [15,31]. It is worth mentioning that TSH measurement is the first useful test for evaluating thyroid function. Other measurements such as T3 and T4 would complement diagnosing of thyroid disorders. High sensitive measurement of TSH along with T3 and T4 estimation in this study allowed the evaluation of thyroid function in farm workers exposed to pesticides. Therefore, the results of the present study support the hypothesis that pesticides may cause hypothyroidism in farm workers.

As endocrine disruptors, pesticides may affect thyroid function through different mechanisms: 1) inhibition of the thyroid enzyme thyroperoxidase, reducing the ability of follicular cell in producing T4 and then T3 [32], thereby exert a feedback control at hypothalamus-pituitary axis promoting TSH secretion, 2) activation of hepatocyte constitutive and rostane receptor which induces uridine 5'-diphosphate-glucuronosyltransferase and sulfotransferase that increased hepatic metabolism of thyroid hormones and their clearance leading to a compensatory increase in pituitary gland production of TSH [33], 3) interfering with thyroid hormone binding proteins thyroxine-binding globulin and transthyretin [34], 4) elevating concentrations of the thyroid hormone receptor in the hypothalamus [34] and 5) altering binding to thyroid receptor resulting in altering thyroid hormone directed gene transcription [35].

As indicated in the present study, significant changes of hormones levels in response to pesticides exposure were found only in farm workers of age group 31 - 45 years compared to their counterparts of controls. This may reflect their potential engagement activities in pesticides use. However, this requires further investigation. Concerning work duration, the results pointed out that the longer the work duration of pesticides use, the higher percentage of decrease in testosterone and the higher percentage of increase in LH and TSH levels. Total lifetime years of use of pesticides in men was associated with increased TSH accompanied by decrease in T4, with evidence of a linear trend [36]. It is generally accepted that, the risk of illness increases as the concentration (strength) of the pesticide and duration (length) of exposure increase [37].

Conflict of Interest

We declare that we have no conflict of interest.

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