

Awareness of Reproductive Health Risks, Sex Hormone Levels and Sperm Indices among Farmers Exposed to Pesticides in Akungba Akoko, Nigeria

Evelyn Apiriboh Yeiya  and Mathias Abiodun Emokpae* 

Department of Medical Laboratory Science, School of Basic Medical Sciences, University of Benin

ABSTRACT

Background: The indiscriminate use of pesticides in Nigeria may have harmful effects on reproductive health of farmers.

Objectives: This study assessed the awareness of reproductive health, serum follicle stimulating hormone (FSH), luteinizing hormone (LH), testosterone, estradiol, progesterone and sperm characteristics of male farmers occupationally exposed to pesticides.

Methods: Eighty four male farmers were recruited for the study. Structured questionnaire was used to obtain the socio-demographic data. Blood and semen samples were collected from the subjects in the morning for hormonal assays and semen analysis using enzyme linked immunosorbent assay (ELISA) method and SQA V sperm quality analyzer. Data were analyzed using chi square, Student's-t-test, and Regression analysis.

Results: Serum FSH ($p < 0.01$), LH ($p < 0.005$) and Estradiol ($p < 0.001$) were significantly higher while prolactin ($p < 0.02$) and testosterone ($p < 0.001$) were significantly lower among pesticides exposed farmers than non-exposed subjects. Some 34/84 (40.5%) of the pesticides exposed farmers had serum testosterone levels below the lower limit of the reference range. Those with low testosterone levels ($p < 0.001$), also had FSH ($p < 0.05$), LH ($p < 0.001$) and Estradiol ($p < 0.002$) significantly lower than those with normal testosterone levels. The sperm count among pesticides exposed farmers; total motility and percentage morphology were significantly lower than non-pesticides exposed subjects. Some 14/84 (16.7%) of the pesticides exposed farmers had sperm count below 15 million/mL (oligozoospermia). More than 70% of the farmers were not aware of the reproductive health risks associated with pesticides and only 23.8% of the farmers were using protective devices.

Conclusions: Deliberate efforts to improve awareness, knowledge, personal hygiene, and interventions necessary to lessen both pesticides exposure and health risks by adopting safe practices are suggested.

Key words: Farmers, pesticides, reproductive health, sex hormones, spermatozoa

Received May 25, 2022

Revised July 13, 2022

Accepted July 14, 2022

Highlights:

- Uncontrolled use of pesticides might be harmful for reproductive health.
- Sex hormones and semen quality were evaluated among farmers in Nigeria.
- Over 70% of farmers were ignorant of the risks associated with pesticide exposure.
- About 17% of them have sperm counts below 15 million/mL.

*Corresponding author:

Department of Medical Laboratory Science,
School of Basic Medical Sciences, University
of Benin, Benin City 30000128, Nigeria
Tel: +2348034511182
E-mail: mathias.emokpae@uniben.edu

1. Introduction

The decline in reproductive potentials all over the world especially in the so-called infertility belt of sub Saharan Africa¹⁾ have been linked among other causes to occupational and environmental pollutants.²⁾ Exposure to numerous types of pesticides may occur in occupational settings and the situation is worrisome because of lack of awareness of their reproductive health risks and failure to use adequate personal protective devices among farmers. The use of pesticides is common among farmers to prevent invasion of pests and improve yield by farmers. Despite the reported harmful effects of these pesticides,³⁾

several farmers still continue to apply them every year on their farms. To make matter worse, the use of these pesticides in several developed countries of the world has been prohibited; unfortunately, their use in Nigeria has not abated. Evidence has shown that small scale farmers in Nigeria use large amounts of classes I and II pesticides considered to be extremely hazardous and highly hazardous respectively by the World Health Organization. Some 26 out of 40 (65%) brands sampled in the field belong to the highly hazardous chemicals because they are cheaper than the less hazardous chemical substances.⁴⁾ The four main groups of pesticides are organochlorine, organophosphate, carbamate, and pyrethroid insecticides. It is important

to create the needed awareness among the farmers on the potential health hazards and the use of adequate personal protective devices among occupationally exposed farmers.

The incidence of male infertility is on the increase and the exact causes (even though multifactorial) are not completely known. Optimal levels of follicle stimulation hormone (FSH), luteinizing hormone (LH), estradiol, testosterone, and prolactin are important for spermatogenesis and sperm maturation. Alterations in the levels of these hormones due to the activities of endocrine disrupting chemicals like pesticides might lead to infertility.⁵⁾ Moreover, some of the possible etiological factors are overlooked, for example farmers and occupationally exposed individuals to pesticides are not aware of the health hazard of pesticide to pesticide users. There is need to know if these individuals who are occupationally exposed have endocrine disorders so that appropriate policy or strategies be implemented to avoid or halt the increasing incidence of male infertility. Prevention they say is better than cure. It may be advantageous to provide an excellent set of resources that address the relationship between pesticides and human health in the locality where there is little or no awareness of pesticide-associated hazard. Therefore, the aim of this study was to assess the awareness of reproductive health risks, evaluate sex hormones (follicle stimulating hormone [FSH], luteinizing hormone [LH], testosterone, estradiol and progesterone) levels and sperm indices among male farmers occupationally exposed to pesticides in Akungba-Akoko, Ondo State.

II. Materials and Methods

1. Study design

This is a case-control study conducted to investigate the levels of sex hormones and sperm indices among farmers occupationally exposed to pesticides and compared with non-occupationally exposed counterparts in a rural community. A total of 84 adult farmers frequently using pesticides and residing communities in Akungba Akoko were recruited for this study. The active ingredients of the pesticides used by the participants are glyphosate, paraquat, oxyfluorfen, atrazine, cypermethrin, fipronil, deltamethrin, methoxychlor, lindane and Dichlorodiphenyltrichloroethane (DDT).

2. Inclusion and exclusion criteria

Adult farmers between aged 30 to 65 years who are pesticides users and are living in Akungba Akoko area were used for

this study. Control subjects were adults who are non-occupationally exposed to pesticides and are also residing in Akungba Akoko town. Farmers with history of sickle cell anaemia, HIV positive or any other chronic diseases were excluded from the study.

3. Sample size determination

Sample size was determined using the sample size determination for health studies; $n = Z^2 P(1-P)/d^2$ ⁶⁾ and prevalence of 8.3% health hazard among pesticides exposed farmers in three rural communities in South West Nigeria.⁷⁾

Total of 90 male farmers who use pesticides in their farm were recruited for the study. However, 84 males were eventually used because six farmers dropped out of the study during data and specimen collection. Fifty male subjects in the same environment were recruited as controls.

4. Ethical approval

Ethical approval was sought and obtained from the Health Research Ethics Committee of the Federal Medical Centre (FMC) Owo, Ondo State via letter with reference FMC/OW/380/VOL.CI/168 dated 3rd November 2020.

5. Informed consent

After educating each participant on the importance and value of the research, questionnaire was filled by the participant and informed consent was sought and obtained from subjects before sample collection.

6. Sample collection and analyses

About 5 mL of blood was collected from the participants for the assay for fertility hormone profile by venepuncture into properly labeled plain sterile bottle. Samples were allowed to clot and properly retract within 2 hrs of collection. The specimens were centrifuged at 1,000 g for 10 mins to obtain the serum. The serum was then aliquoted into a properly labeled, plain clean tube and stored at -20°C appropriately prior to analysis. Semen specimens were collected directly into wide mouthed containers without the use of condom or lubricant. Semen was collected after 3 to 5 days of sexual abstinence and analysis was done using the SQAV sperm quality analyzer (Medical Electronic Systems, Caesarea, Israel). The blood samples were analyzed using 2nd generation Autoplex ELISA and CLIA Analyser (Monobind Inc, Lake Forest, CA, USA).

7. Statistical analysis

The data were analyzed using statistical software SPSS version 20.0. Continuous data was analyzed using chi-square and Student's-t-test was used to analyze discrete variables after

confirmation of normality by software SPSS. A p-value ≤ 0.05 was considered statistical significant.

Table 1. Comparison of sex hormone levels among pesticides exposed and non-exposed male farmers

Variables (reference range)	Pesticides exposed farmers n=84 (min~max)	Non-pesticides exposed farmers n=50 (min~max)	p-value
Age (years)	42.95±2.51 (30~65)	42.12±2.05 (30~64)	0.841
FSH (2.0~12.0 mIU/mL)	10.13±2.43 (0.72~94.55)	3.29±0.16 (5.0~7.9)	0.01
LH (0.5~10.5 mIU/mL)	22.66±4.80 (1.45~200)	8.16±0.98 (7.5~9.0)	0.005
Prolactin (1.2~19.5 ng/mL)	6.27±1.03 (0.2~28.5)	8.97±1.02 (1.3~19.4)	0.02
Testosterone (2.5~10.0 ng/mL)	3.99±0.61 (0.1~11.8)	6.10±0.81 (2.8~10.1)	0.001
Progesterone (2.0~25 ng/mL)	0.68±0.20 (0.01~7.76)	0.69±0.31 (1.2~9.12)	1.0
Estradiol (44.0~196 pg/mL)	31.92±2.84 (0.1~71.05)	19.58±1.16 (10.0~35.0)	0.001

FSH: follicle stimulating hormone, LH: luteinizing hormone.

Table 2. Comparison of sex hormone levels between exposed male farmers with low serum testosterone and exposed farmers with normal testosterone levels

Variables	Low testosterone levels (n=34)	Normal testosterone levels (n=50)	p-value
Testosterone (2.5~10.0 ng/mL)	0.61±0.14	6.79±0.62	0.001
FSH (2.0~12.0 mIU/mL)	6.46±1.19	9.28±1.91	0.05
LH (0.5~10.5 mIU/mL)	5.13±0.78	10.47±2.13	0.001
Prolactin (1.2~19.5 ng/mL)	7.51±1.98	5.89±1.12	0.5
Progesterone (2.0~25 ng/mL)	0.42±0.20	0.52±0.13	0.7
Estradiol (44.0~196 pg/mL)	22.8±4.66	38.43±3.01	0.002

FSH: follicle stimulating hormone, LH: luteinizing hormone.

Table 3. Comparison of sperm indices among pesticides exposed farmers and non-pesticides exposed farmers

Variables	Pesticides exposed farmers (n=84)	Non-pesticides exposed farmers (n=50)	p-value
Sperm count ($\times 10^6$ cells/mL)	57.7±9.33	98.21±9.8	0.001
Total motility (%)	36.5±0.5	68.2±1.28	0.001
Percentage morphology (%)	2.72±0.02	4.68±0.04	0.001
Semen volume (mL)	3.2±0.05	3.2±0.01	0.9

Table 4. Comparison of sperm indices of pesticides exposed male farmers with sperm count $<15 \times 10^6$ /mL and those with $>15 \times 10^6$ /mL

Parameters	Exposed farmers with sperm count $<15 \times 10^6$ /mL	Exposed farmers with sperm count $>15 \times 10^6$ /mL	p-value
Number of subjects	14 (16.7%)	70 (83.3%)	0.001
Sperm count ($\times 10^6$ cells/mL)	9.75±1.01	67.32±9.01	0.001
Total motility (%)	33.2±0.8	37.3±0.6	0.05
Percentage morphology (%)	2.42±0.02	2.81±0.01	0.001
Semen volume (mL)	3.20±0.1	3.2±0.01	1.0

III. Results

The results of the investigation are presented in Tables 1~8. Table 1 shows the comparison of sex hormone levels among pesticides exposed and non-exposed male farmers. The mean age of pesticides exposed farmers (42.95 ± 2.51) was significantly higher ($p < 0.001$) than the controls (34.12 ± 2.05). Serum FSH ($p < 0.01$), LH ($p < 0.005$) and Estradiol ($p < 0.001$) were significantly higher while prolactin ($p < 0.02$) and testosterone ($p < 0.001$) were significantly lower among pesticides exposed farmers than non-exposed subjects.

Table 2 indicates the comparison of sex hormone levels among exposed subjects with serum testosterone levels below the lower limit of the reference range and those within the reference range (that is, between lower and upper limits of the reference range). The data show that some 34/84 (40.5%) of the pesticides exposed farmers had serum testosterone levels below the lower limit of the reference range. Those with low testosterone levels ($p < 0.001$), FSH ($p < 0.05$), LH ($p < 0.001$) and Estradiol ($p < 0.002$) were significantly lower among subjects with low testosterone levels than those with normal testosterone levels.

The sperm count among pesticides exposed farmers, total motility and percentage morphology were significantly lower than non-pesticides exposed subjects (Table 3).

Table 4 indicates that some 14/84 (16.7%) of the pesticides exposed farmers had sperm count below 15 million/mL (oligozoospermia). The mean sperm count ($p < 0.001$), total motility ($p < 0.05$) and percentage morphology ($p < 0.001$) were significantly lower among exposed farmers with oligozoospermia than exposed farmers with sperm count greater 15 million/mL (normozoospermia).

Table 5 shows that liquid formulation type of pesticides is the commonly used (77.4%) and emulsifiable concentrates were the less commonly used (3.6%). Aerial sprayer (48.8%) and Knapsack sprayers are the most equipment used for applying pesticides. The predominant side effects experienced by subjects were skin irritation (40.5%) and eye irritation (27.3%) while throat irritation (3.6%) was the least. The preventive measures commonly observed by farmers include wearing of overall (made of cotton materials) (57.1%), and farm boots (44.0%).

Table 6 shows that farmers' knowledge of the effects of pesticides on male reproductive system. More than 70% of the farmers do not know that pesticides are potential risk factors for infertility. The results show that 67/84 (79.8%) of the

respondents were aware of at least one type of personal protective equipment (PPE). The awareness of the different types of PPEs by respondents was significant ($p < 0.001$) (Table 7). Only 20/84 (23.8%) of farmers were using PPE while 43/84 (51.2%)

Table 5. Pesticide usage among farmers occupationally exposed to pesticides

Variable	Frequency (N=84)	Percentage (%)
Duration of use		
Less than a year	10	11.9
1~5 years	27	32.8
6~10 years	17	20.2
11~15 years	16	19.0
Over 15 years	14	16.7
Most common route of exposure		
Oral exposure	14	16.7
Ocular exposure	11	13.1
Dermal exposure	40	47.6
Inhalation exposure	19	22.6
Form (s) of pesticide		
Liquid formulation	65	77.4
Emulsifiable concentrate	03	3.6
Gaseous concentrate	08	9.5
Powder formulation	08	9.5
Equipment used for applying pesticide		
Knapsack sprayer	29	34.5
Hand flit gun	04	4.7
Dust blower	05	6.0
Aerosol dispenser	05	6.0
Aerial sprayer	41	48.8
Side effects experienced		
Irritation of the nose	19	22.6
Irritation of the skin	34	40.5
Irritation of the eyes	23	27.3
Irritation of the throat	05	6.0
Others	03	3.6
Preventive measures applied		
Wearing of overall	48	57.1
Wearing of face and nose mask	25	29.8
Wearing of farm boot	37	44.0
Other forms	06	7.1
Educational status		
Primary school	16	19.1
Secondary school	17	20.2
Tertiary education	10	11.9
No formal education	41	48.8

Table 6. Farmers' knowledge of the effects of pesticides on male reproductive system

Variable	Frequency (N=140)	Percentage (%)
Exposure to pesticides can result to impaired fertility in men		
Yes	21	25.0
No	13	15.5
I don't know	50	59.5
Exposure to pesticides can result to declining sperm count in men		
Yes	13	15.5
No	13	15.5
I don't know	58	69.0
Exposure to pesticides can result to declining sperm quality in men		
Yes	24	17.1
No	28	20.0
I don't know	88	62.9
Exposure to pesticides can result to reduction of fertilization ability in men		
Yes	14	16.7
No	17	20.2
I don't know	53	63.1
Exposure to pesticides can result to impairment of motility in men		
Yes	17	20.2
No	13	15.5
I don't know	54	64.3
Exposure to pesticides can result to undescended testes in men		
Yes	20	23.8
No	09	10.7
I don't know	55	65.5
Exposure to pesticides can result to production of abnormal sperm in men		
Yes	18	21.4
No	11	13.1
I don't know	55	65.5

Table 7. Awareness of types of personal protective devices

Variables	N (%)	X ² ; P
At least one	67 (79.8)	0.001
Googles/eye shield	1 (1.2)	
Hand gloves	2 (2.4)	
Sturdy footwears (boots)	37 (44)	
Aprons	0 (0)	
Masks	25 (29.8)	
Earplugs	0 (0)	

There were multiple responses by participants.

do not use PPE and 21/84 (25%) did not respond to the question. There was an association between non-use of PPE and awareness of reproductive health hazards among farmers, with farmers who do not use PPE were three times more likely to be

unaware of health hazards of pesticides exposure (OR 3.42; CI 1.81~10.31). The use of PPE was significantly lower ($p < 0.005$) when compared with those who do not use PPE. The duration on the job correlated negatively with awareness of health hazards of pesticides exposure. The probability of farmers being aware of hazards decreases with duration on the job. Those who had spent 6~10 years were two times likely to be unaware of health hazards compare to those who had spent <5 years, while those who had spent more than ten years were three times likely to be unaware of health hazards compared to those who had spent <5 years on the job (OR 3.4; CI 1.82~6.81) (Table 8).

Table 8. Factors associated with the use of personal protective equipment among farmers

Variables	N (%)	P, 95% C.I
Using PPE	20 (23.8)	1.00
Not using PPE	43 (51.2)	0.005 3.42; 1.81~10.31
No response	21 (25)	

Duration on the job	Use	Non-use	P, 95% C.I
Less than 5 years	10	27	0.001 1.00
6~10 years	06	11	1.81; 1.02~2.71
Greater than 10 years	04	26	3.4; 1.82~6.81

PPE: personal protective equipment.

IV. Discussion

In most developing countries like Nigeria, the indiscriminate and non-selective use of pesticides can lead to the infiltration of the chemicals into different tissues of non-target organisms including the farmers themselves thereby resulting in impaired reproductive health. This is particularly important because most farmers are illiterate and may not be aware of health hazards associated with such practices. Adequate knowledge of health hazards and the use of safety measures by farmers are important to preventing and/or reducing a lot of health risks associated with pesticides exposure.⁸⁻¹¹ Occupational health is tailored toward the promotion and maintenance of the highest degree of physical, mental, and social well-being of workers in their work environment.^{2,12} Several studies have shown a decline in human semen quality and increased risks of male and female subfertility.¹³⁻¹⁶ The predominant routes by which pesticides gain entrance into the human body are dermal via contact with skin, inhalation, oral via ingestion in food, and ocular through contact with eyes. The exposure to pesticides mainly occurs during the mixing and loading of the spraying equipment and the process of spraying without the use of appropriate personal protective devices as well as improper handling.^{17,18} This study compares the sex hormones and semen characteristics between farmers who are exposed and subjects who are not exposed to pesticides as well as the awareness of health hazards and use of PPE among farmers in Akungba-Akoko, Ondo State, with the aim of evaluating the burden of pesticide-induced reproductive toxicity. The four main groups of pesticides commonly used by study participants are organochlorine, organophosphate, carbamate, and pyrethroid insecticides. The active ingredients of the pesticides used by the participants are glyphosate, paraquat, oxyfluorfen, atrazine,

cypermethrin, fipronil, deltamethrin, methoxychlor, lindane and Dichlorodiphenyltrichloroethane (DDT). Most of the exposed farmers use large amounts of these classes I and II pesticides because they are cheaper to buy than the less hazardous products. Previous study has shown that about of 65% of pesticides used in Nigeria contain dangerous substances that have been banned or tightly regulated in most advanced countries of the world.⁴

In this study serum FSH, LH and estradiol were significantly higher while prolactin and testosterone were significantly lower among pesticides exposed farmers than non-exposed subjects. The significantly lower level of serum testosterone can lead to low sexual desire and erectile dysfunction. Also the chemical compositions of pesticides can severely damage a man's testicles, sperm cells, or mature sperm. Such damages could lead to deterioration in sperm count, reduction in their morphology and motility or function. This observation aligned partly to that of Abdallah et al.,¹⁸ who reported a significantly higher level of FSH among occupationally exposed farmers compared to non-exposed control subjects, but without significant changes in the levels of LH and testosterone. The authors attributed the insignificant changes in LH and testosterone to the work habits of the study participants in which the farmers only spray for 141.5 ± 80.6 days per year. They also suggested that the resting days could allow for the excretion of the high levels of pesticides from the body and to the recovery of their AChE and BuChE (cholinesterase enzymes) levels to do their physiological functions since organophosphate pesticides are non-persistent pesticides, and do not accumulate in the body over a long period.¹⁸ Significantly higher levels of FSH and LH but lower testosterone were reported among exposed subjects to organophosphate pesticides in China.¹⁹ Among adult males, organophosphate and Carbamates metabolites significantly lower

the serum level of LH and total testosterone,²⁰⁾ while in Djutitsa (West Cameroon) a significantly lower levels of serum total testosterone and androstenedione were reported among farmers exposed to agro pesticides.²¹⁾ Some authors have shown that exposure to endosulfan (END) and atrazine (ATZ) during the embryonic life of *Caiman latirostris* altered histomorphology of the testis and the balance between proliferation and apoptosis of hatchlings' testicular cells. In adult male exposed to END, a significantly lower level of testosterone was reported.²²⁾ Several authors have associated organophosphate pesticides with impair functions of cholinesterase enzymes, decrease in insulin secretion, abnormal cellular metabolism of proteins, carbohydrates and fats, genotoxicity, impair mitochondrial function, increased cellular oxidative stress and disruption of endocrine systems.^{2,23,24)} The control of weeds, pests and moulds in the rain forest regions may be more than in savannah regions of the world, therefore the possibility of spraying for fewer days of the year may not occur. It should be noted that pesticides may be metabolized, excreted, bioaccumulated in body fat of animals and human.^{25,26)} Similarly, significant differences were reported in the levels of FSH and testosterone in the growing and non-growing periods among exposed farmers in Myanmar.²⁷⁾ Our observation is consistent with that of Pérez-Herrera et al.,²⁸⁾ who reported elevated serum LH, FSH and low testosterone among organophosphate pesticides exposed farmers. Some authors reported that other contributory factors to semen health and hormonal imbalance among pesticides exposed farmers include lifestyle behaviours, education, and use of PPE.²⁷⁾ There are several factors leading to a preponderance of adverse health impacts associated with pesticide use in developing countries such as Nigeria, despite relatively lower volume used compared with developed countries.²⁹⁾ Some authors have reported that deadliest pesticides are used in Nigeria since these groups are cheaper and affordable to farmers.^{4,29)} The potential of a chemical released into the environment to cause harm is measured largely in terms of its toxicity and persistence. Pesticides are classified by the World Health Organization (WHO) as extremely hazardous (Class Ia), highly hazardous (Class Ib), moderately hazardous (Class II), slightly hazardous (Class III) and unlikely to be hazardous under short-term use (Class U).²⁹⁾ It is well documented that small-scale farmers in developing countries use large amounts of pesticides belonging to classes Ia, Ib, and II due to their relatively cheaper price than the less hazardous, newer ones.^{4,29-31)} Invariably, newer safer formulations tend to be more expensive because they are protected by

foreign patents, and local firms are not permitted to formulate them without paying heavy charges which eventually drive up market prices.³²⁾ Such cheaper chemicals could be stored easily in fatty tissues and build up in food chains.³³⁾ In 2001, under the auspices of the United Nations Environment Programme, nine highly persistent pesticides (viz aldrin, chlordane, DDT, dieldrin, endrin, heptachlor, mirex, toxaphene, and hexachlorobenzene) were officially proscribed for use in agriculture. Unfortunately, several of these are still openly sold in Nigeria. Some are smuggled in or even donated by some "caring" donor countries.³⁰⁾ Other factors responsible for poor control of pesticides distribution and used are poor legislation and lack of enforcement of available legislation, correct, effective, and safe applications of pesticides, lack of adequate information, knowledge, and awareness of the inherent dangers of pesticides and inadequacies in medical recognition and responses to pesticide poisoning.^{34,35)} Conversely, some authors have reported significantly higher testosterone level³⁶⁾ or no significant difference in testosterone level³⁷⁾ in experimental animal model and humans exposed to pesticides. This may be attributed to the agrochemicals use, severity and/or length of exposure, agricultural practices and the use of personal protective equipment.³⁷⁾

The data show that some 40.5% of the pesticides exposed farmers had serum testosterone levels below the lower limit of the reference range. In this group of subjects, serum FSH, LH and estradiol were significantly lower among those with low testosterone levels than those with normal testosterone levels. This aligned with previous studies which stated that most subjects with low testosterone also had low LH and FSH levels.¹⁸⁾ Few cases of isolated FSH deficiency may exist in which LH and testosterone levels are within reference ranges but the sperm count may be low. Similarly, subjects with low FSH, LH, and testosterone levels also present with high prolactin, all of which may resolve with normalization of prolactin levels.³⁸⁾ Also, Erhunmwunse et al.,³⁰⁾ reported a significantly lower concentration of testosterone ($p < 0.001$) among pesticides exposed farmers than non-exposed control subjects. Total serum testosterone and estradiol levels were reported to be significantly lower in subjects exposed to organophosphate pesticides.^{19,39)} It was demonstrated in animal model that, organophosphate pesticides exposure changes the metabolism of testosterone and estradiol.^{40,41)} Gomina et al.,¹⁶⁾ recently reported significantly lower testosterone level among farmers in Benin Republic. The prevalence of abnormal levels of LH, FSH and testosterone in farmers were 13.7%, 7.3% and 18.9% respective.¹⁶⁾

Organophosphate impairs the reproductive functions mainly through decreasing brain acetylcholinesterase (AChE) activity and also impacting the gonads. The decreased level of AChE may result in elevated level of acetylcholine, gamma-aminobutyric acid (GABA), epinephrine, norepinephrine, 5-hydroxytryptamine and dopamine concentration.⁴²⁾ Increase level of GABA then prevents the release of gonadotropin releasing hormone (GnRH) in the median eminence, which is responsible for the release of gonadotropins (LH and FSH) from the anterior pituitary. The gonadotropins are involved in steroidogenesis and gametogenesis.⁴³⁾ Pesticides can also increase dopamine concentration which has down-regulatory effect on GnRH secretion thereby suppressing the reproductive functions.^{44,45)} Organophosphate and carbamates could change pituitary adrenal axes.⁴⁶⁾

The sperm count among pesticides exposed farmers, total motility and percentage morphology were significantly lower than non-pesticides exposed subjects. Some 16.7% of the pesticides exposed farmers had sperm count below 15 million/mL (oligozoospermia) and poor sperm indices than those with sperm count greater 15 million/mL (normozoospermia). This observation is consistent with previous study elsewhere.²⁷⁾ The 71% oligozoospermic subjects observed by the authors were higher than (16%) observed in the present study. Lwin et al.,¹⁵⁾ stated that some 71% of the farmers had oligozoospermia during growing season than 46% in non-growing season. They attributed the differences to non-exposure during non-growing season. These findings may indicate that occupational exposure to pesticides and pesticide residues adversely impacts semen quality. Some authors have reported that neonicotinoid pesticides including IMI and ACE affect the reproductive organs of mammals leading to inhibition of testicular development, damage to spermatogenesis, poor sperm quality.⁴⁷⁻⁴⁹⁾ Organophosphate pesticides exposure can lead to male infertility. It is also genotoxic to animal sperm because of its phosphorylating potential. It combined with DNA and protamines to change the chromatin structure that will make DNA to be easily susceptible to denaturation by oxidizing agents *in situ*.⁵⁰⁻⁵³⁾

Majority of farmers 79.8% were aware of at least one type of personal protective equipment (PPE), but only 23.8% of them were using PPE while 51.2% do not use any form of PPE and 25% did not respond to the question. There was an association between non-use of PPE and awareness of reproductive health hazards among farmers, with farmers who do not use PPE were three times more likely to be unaware of health

hazards of pesticides exposure (OR 3.42; CI 1.81~10.31). This is consistent with the study in Myanmar.²⁷⁾ The farmers in this study did not use PPE, even though majority were aware of at least one form of PPE, probably due to the tropical climate, the inconvenience of wearing it for long working periods, and the expense and limited availability of certain items of PPE. There appears to be dearth of information regarding the health risks associated with non-use of PPE. Information of health risks arising from the use of pesticides without adequate PPE and other precautionary measures is urgently required to halt the damaging effects of pesticides. Simple PPE like protective clothes or aprons, goggles, face masks, ear plugs could be provided for the farmers at subsidized rates if not completely free. Also, education, training, and educational activities on pesticide safety should be regularly organized for the farmers. Health education should be provided to avoid the overuse of pesticides and non-adherence to the recommended protocols. The use of biopesticides and the harmful effects of pesticides, especially organophosphate and carbamate on health and the environment should be regularly broadcasted on radio and television. The careful and responsible use of pesticides among the farmers in order to avoid environment pollution has been advocated.²⁷⁾

It would be better that pesticide measurements were made in environmental media such air, water, and soil concurrently. However, the classification of occupational exposure was done using questionnaires that asked about exposure experience of using pesticides on farms over the previous one to two years, and we don't think it changes the results we've made thus far.

V. Conclusions

The data from this study show that some 40.5% of the pesticides exposed farmers had serum testosterone levels below the lower limit of the reference range. Those with low testosterone levels had significantly lower levels of FSH, LH, and Estradiol than those with normal testosterone levels. The sperm quality among pesticides exposed farmers; sperm count, total motility and percentage morphology were significantly lower than non-pesticides exposed subjects. Some 16.7% of the pesticides exposed farmers were oligozoospermia. There was poor adherence to precautionary protocol and use of PPE among farmers. The preventive measures commonly observed by farmers include wearing of overall and farm boots. The risks from occupational exposure to harmful pesticides should be effectively

communicated to farmers. This will make them to be better informed, adhere to safety guidelines for prevention of health hazards associated with pesticides use. Deliberate efforts to improve the awareness, knowledge, personal hygiene, and interventions necessary to reduce both pesticide exposure and health risks, adopting safe practices are suggested.

Acknowledgments

We appreciate the contributions of all the Medical Laboratory Scientists and the research assistants toward the completion of this study.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

References

1. Okonofua FE. Infertility in sub-Saharan Africa. In: Okonofua FE, Odunsi K. editors. *Contemporary Obstetrics and Gynaecology for Developing Countries*, 1st ed. Benin City: Women's Health and Action Research Centre; 2003. p.128-155.
2. Fucic A, Duca RC, Galea KS, Maric T, Garcia K, Bloom MS, et al. Reproductive health risks associated with occupational and environmental exposure to pesticides. *Int J Environ Res Public Health*. 2021; 18(12): 6576.
3. Sharma A, Sharma P, Sharma P, Joshi SC. A review on organochlorine pesticides and reproductive toxicity in males. *Int J Pharm Sci Res*. 2015; 6(8): 3123-3138.
4. Alliance for Action on Pesticides in Nigeria. Nigerian Farmers Using Large Amount of Toxic Pesticides Banned in EU. Available: <https://www.premiumtimesng.com/news/headlines/497623-nigerian-farmers-using-large-amount-of-toxic-pesticides-banned-in-eu-report.html> [accessed 1 July 2021].
5. Uadia PO, Emokpae AM. Male infertility in Nigeria: a neglected reproductive health issue requiring attention. *J Basic Clin Reprod Sci*. 2015; 4(2): 45-53.
6. Lwanga SK, Lemeshow S. *Sample Size Determination in Health Studies: A Practical Manual*, 1st ed. Geneva: World Health Organization; 1991.
7. Desalu O, Busari O, Adeoti A. Respiratory symptoms among crop farmers exposed to agricultural pesticide in three rural communities in South Western Nigeria: a preliminary study. *Ann Med Health Sci Res*. 2014; 4(4): 662-666.
8. Cremonese C, Piccoli C, Pasqualotto F, Clapauch R, Koifman RJ, Koifman S, et al. Occupational exposure to pesticides, reproductive hormone levels and sperm quality in young Brazilian men. *Reprod Toxicol*. 2017; 67: 174-185.
9. Dziejirska E, Radwan M, Wielgomas B, Klimowska A, Radwan P, Kałużny P, et al. Human semen quality, sperm DNA damage, and the level of urinary concentrations of 1N and TCPY, the biomarkers of nonpersistent insecticides. *Am J Mens Health*. 2019; 13(1): 1557988318816598.
10. Hu Y, Zhang Y, Vinturache A, Wang Y, Shi R, Chen L, et al. Effects of environmental pyrethroids exposure on semen quality in reproductive-age men in Shanghai, China. *Chemosphere*. 2020; 245: 125580.
11. Césaire Momo Tetsatsi A, Alumeti Munyali D, Romeo Bonsou Fozin G, Ngadjui E, Wankeu-Nya M, Watcho P. Semen quality among men attending urology services in the Dschang Health District, west Cameroon: a retrospective study on 379 cases. *Int J Reprod Biomed*. 2020; 18(2): 121-128.
12. Berni I, Menouni A, Ghazi El I, Radu-Corneliu D, Marie-Paule K, Godderis L, et al. Understanding farmers' safety behavior regarding pesticide use in Morocco. *Sustain Prod Consum*. 2021; 25: 471-483.
13. Neghab M, Momenbella-Fard M, Naziaghdam R, Salahshour N, Kazemi M, Alipour H. The effects of exposure to pesticides on the fecundity status of farm workers resident in a rural region of Fars province, southern Iran. *Asian Pac J Trop Biomed*. 2014; 4(4): 324-328.
14. Nabi G, Amin M, Rauf T, Khan KM, Khan AA. Link between chronic pesticides exposure and reproductive problems in male farmers. *J Biol Life Sci*. 2014; 5(2): 65-76.
15. Lwin TZ, Than AA, Min AZ, Robson MG, Siriwong W. Effects of pesticide exposure on reproductivity of male groundnut farmers in Kyauk Kan village, Nyaung-U, Mandalay region, Myanmar. *Risk Manag Healthc Policy*. 2018; 11: 235-241.
16. Gomina M, Kakpo AK, Houndetoungan DG, Salifou T, Awede B, Amoussou-Guenou MK. Male reproductive hormonal profile of cotton farmers exposed to synthetic pesticides in the North-East of Benin. *Asian J Biochem*. 2020; 15(1): 7-11.
17. 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): 1739-1744.
18. Abdallah MS, Saad-Hussein A, Shahy EM, Seleem M, Abdel-Aleem AM. Effects of occupational exposure to pesticides on male sex hormones. *J Biosci Appl Res*. 2017; 3(3): 70-79.
19. Padungtod C, Lasley BL, Christiani DC, Ryan LM, Xu X. Reproductive hormone profile among pesticide factory workers. *J Occup Environ Med*. 1998; 40(12): 1038-1047.
20. Meeker JD, Ryan L, Barr DB, Hauser R. Exposure to nonpersistent insecticides and male reproductive hormones. *Epidemiology*. 2006; 17(1): 61-68.
21. Manfo FP, Moundipa PF, Déchaud H, Tchana AN, Nantia EA, Zobot MT, et al. Effect of agropesticides use on male reproductive function: a study on farmers in Djutitsa (Cameroon). *Environ Toxicol*. 2012; 27(7): 423-432.
22. Rey F, González M, Zayas MA, Stoker C, Durando M, Luque EH, et al. Prenatal exposure to pesticides disrupts testicular histology and alters testosterone levels in male Caiman latirostris. *Gen Comp Endocrinol*. 2009; 162(3): 286-292.

23. Karami-Mohajeri S, Abdollahi M. Toxic influence of organophosphate, carbamate, and organochlorine pesticides on cellular metabolism of lipids, proteins, and carbohydrates: a systematic review. *Hum Exp Toxicol*. 2011; 30(9): 1119-1140.
24. Dewan P, Jain V, Gupta P, Banerjee BD. Organochlorine pesticide residues in maternal blood, cord blood, placenta, and breastmilk and their relation to birth size. *Chemosphere*. 2013; 90(5): 1704-1710.
25. Pirsahab M, Limoe M, Namdari F, Khamutian R. Organochlorine pesticides residue in breast milk: a systematic review. *Med J Islam Repub Iran*. 2015; 29: 228.
26. Nicolopoulou-Stamati P, Maipas S, Kotampasi C, Stamatis P, Hens L. Chemical pesticides and human health: the urgent need for a new concept in agriculture. *Front Public Health*. 2016; 4: 148.
27. Ghafouri-Khosrowshahi A, Ranjbar A, Mousavi L, Nili-Ahmadabadi H, Ghaffari F, Zeinvand-Lorestani H, et al. Chronic exposure to organophosphate pesticides as an important challenge in promoting reproductive health: a comparative study. *J Educ Health Promot*. 2019; 8: 149.
28. Pérez-Herrera N, Polanco-Minaya H, Salazar-Arredondo E, Solís-Heredia MJ, Hernández-Ochoa I, Rojas-García E, et al. PON1Q192R genetic polymorphism modifies organophosphorous pesticide effects on semen quality and DNA integrity in agricultural workers from southern Mexico. *Toxicol Appl Pharmacol*. 2008; 230(2): 261-268.
29. Ojo J. Pesticides use and health in Nigeria. *Ife J Sci*. 2016; 18(4): 981-992.
30. Erhunmwunse NO, Dirisu A, Olomukoro JO. Implications of pesticide usage in Nigeria. *Trop Freshw Biol*. 2012; 21(1): 15-25.
31. Konradsen F, van der Hoek W, Cole DC, Hutchinson G, Daisley H, Singh S, et al. Reducing acute poisoning in developing countries—options for restricting the availability of pesticides. *Toxicology*. 2003; 192(2-3): 249-261.
32. Nnamonu LA, Onekutu A. Green pesticides in Nigeria: an overview. *J Biol Agric Healthc*. 2015; 5(9): 48-62.
33. Moraes R, Molander S. A procedure for ecological tiered assessment of risks (PETAR). *Human and Ecological Risk Assessment*. 2004; 10(2): 349-371.
34. PAN Germany. [Pesticides and Health Hazards. Facts and Figures]. Available: https://www.pan-germany.org/download/Vergift_DE-110612_F.pdf [accessed 12 March 2020]. German.
35. Natural Resources Defense Council. Trouble on the Farm: Growing Up With Pesticides in Agricultural Communities. Chapter 1 Health Hazards of Pesticides. Available: <http://lib.ncfh.org/pdfs/5082.pdf> [accessed 5 June 2020].
36. Sarkar R, Mohanakumar KP, Chowdhury M. Effects of an organophosphate pesticide, quinalphos, on the hypothalamo-pituitary-gonadal axis in adult male rats. *J Reprod Fertil*. 2000; 118(1): 29-38.
37. Recio R, Ocampo-Gómez G, Morán-Martínez J, Borja-Aburto V, López-Cervante M, Uribe M, et al. Pesticide exposure alters follicle-stimulating hormone levels in Mexican agricultural workers. *Environ Health Perspect*. 2005; 113(9): 1160-1163.
38. Jabbour SA. Follicle-Stimulating Hormone Abnormalities. Available: <https://emedicine.medscape.com/article/118810-overview> [accessed 11 June 2020].
39. Straube E, Straube W, Krüger E, Bradatsch M, Jacob-Meisel M, Rose HJ. Disruption of male sex hormones with regard to pesticides: pathophysiological and regulatory aspects. *Toxicol Lett*. 1999; 107(1-3): 225-231.
40. Butler AM, Murray M. Inhibition and inactivation of constitutive cytochromes P450 in rat liver by parathion. *Mol Pharmacol*. 1993; 43(6): 902-908.
41. Murray M, Butler AM. Identification of a reversible component in the in vitro inhibition of rat hepatic cytochrome P450 2B1 by parathion. *J Pharmacol Exp Ther*. 1995; 272(2): 639-644.
42. Hossain F, Ali O, D'Souza UJ, Naing DK. Effects of pesticide use on semen quality among farmers in rural areas of Sabah, Malaysia. *J Occup Health*. 2010; 52(6): 353-360.
43. Terasawa E, Fernandez DL. Neurobiological mechanisms of the onset of puberty in primates. *Endocr Rev*. 2001; 22(1): 111-151.
44. Di Chiara G. Role of dopamine in the behavioural actions of nicotine related to addiction. *Eur J Pharmacol*. 2000; 393(1-3): 295-314.
45. Watkins SS, Koob GF, Markou A. Neural mechanisms underlying nicotine addiction: acute positive reinforcement and withdrawal. *Nicotine Tob Res*. 2000; 2(1): 19-37.
46. Kokka N, Clemons GK, Lomax P. Relationship between the temperature and endocrine changes induced by cholinesterase inhibitors. *Pharmacology*. 1987; 34(2-3): 74-79.
47. Kapoor U, Srivastava MK, Bhardwaj S, Srivastava LP. Effect of imidacloprid on antioxidant enzymes and lipid peroxidation in female rats to derive its No Observed Effect Level (NOEL). *J Toxicol Sci*. 2010; 35(4): 577-581.
48. Kapoor U, Srivastava MK, Srivastava LP. Toxicological impact of technical imidacloprid on ovarian morphology, hormones and antioxidant enzymes in female rats. *Food Chem Toxicol*. 2011; 49(12): 3086-3089.
49. Bal R, Naziroğlu M, Türk G, Yılmaz Ö, Kuloğlu T, Etem E, et al. Insecticide imidacloprid induces morphological and DNA damage through oxidative toxicity on the reproductive organs of developing male rats. *Cell Biochem Funct*. 2012; 30(6): 492-499.
50. Evenson DP, Larson KL, Jost LK. Sperm chromatin structure assay: its clinical use for detecting sperm DNA fragmentation in male infertility and comparisons with other techniques. *J Androl*. 2002; 23(1): 25-43.
51. Sergerie M, Laforest G, Bujan L, Bissonnette F, Bleau G. Sperm DNA fragmentation: threshold value in male fertility. *Hum Reprod*. 2005; 20(12): 3446-3451.
52. Piña-Guzmán B, Solís-Heredia MJ, Quintanilla-Vega B. Diazinon alters sperm chromatin structure in mice by phosphorylating nuclear protamines. *Toxicol Appl Pharmacol*. 2005; 202(2): 189-198.
53. Boe-Hansen GB, Fedder J, Ersbøll AK, Christensen P. The sperm chromatin structure assay as a diagnostic tool in the human fertility clinic. *Hum Reprod*. 2006; 21(6): 1576-1582.

⟨Author information⟩

Evelyn Apiriboh Yeiya (Postgraduate Student),
Mathias Abiodun Emokpae (Professor)