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# The Effect of Smoking on Fertility Hormones in Male Adult Smokers in South-South Nigeria

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***Authors' contributions***

*This work was carried out in collaboration between all authors. Authors UAE and BIE initiated and designed the research. Authors IIKAP and BIE did the analysis and interpretation of data. Authors BIE and AUO wrote initial draft manuscript while authors UAE and EOE critically reviewed the manuscript. All authors read and approved the final manuscript.*

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## ABSTRACT

**Aims:** To investigate the relationship between tobacco smoking and serum concentrations of male reproductive hormones-luteinizing hormone (LH), follicle stimulating hormone (FSH), testosterone and prolactin.
**Study Design:** The design of the study was cross sectional.
**Place and Duration of Study:** the Department of Chemical Pathology, University of Calabar Teaching Hospital between October 2012 and October 2013.
**Methodology:** 140 male tobacco smokers and 61 male non-smokers aged between 19 and 45

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years were recruited for this study. Serum testosterone, prolactin, FSH and LH was determined using Enzyme linked immunosorbent assay. Body mass index was measured and smoking pack years calculated.

**Results:** The mean values for testosterone, prolactin, FSH and LH was 8.5±3.43 ng/ml; 8.9±4.65 ng/ml; 7.97±9.06 mIU/ml and 17.2±9.35 ng/ml respectively for the smokers and 12.3±4.01 ng/ml; 9.2±5.97 ng/ml; 4.3±2.57 mIU/ml and 10.8±5.18 ng/ml respectively for the non-smokers. The mean testosterone level was significantly lower ($P$<.0001) in the smokers compared to the controls while LH and FSH values were significantly higher ($P$<.0001) in the smokers compared to controls. There was however no significant difference ($P$ = .699) in the mean levels of prolactin.

**Conclusion:** The risk of infertility associated with smoking may be attributed to lower levels of testosterone rather than hyperprolactinaemia. This decrease in testosterone levels may translate to a decrease in fertility as testosterone is the principal reproductive hormone in males.

*Keywords: Smoking; testosterone; luteinizing hormone; follicle stimulating hormone; prolactin; infertility.*

## 1. INTRODUCTION

Tobacco smoking is a major public health problem that is associated with high morbidity and mortality. Each year tobacco is responsible for the deaths of about 6 million people worldwide [1]. It is estimated that by the decade 2020 – 2030, tobacco will kill 10 million people yearly, with 70% of these deaths occurring in developing countries [2], if the current trend of deaths attributed to tobacco are not reversed.

Shockingly, in spite of the high death-toll attributed to tobacco and the damaging effects this cankerworm presents, its consumption is increasing by 3.4% yearly in developing countries [3]. This upsurge has been blamed on ignorance as well as enticing adverts tobacco manufacturers put up [4]. However, youths unrelenting desire to experiment, peer pressure, pleasure and addictive effects tobacco presents, are pressing factors accounting for the persistent rise in tobacco consumption, cigarettes being the most patronized [5]. Cigarette smoking is five times higher among men than women although this gender gap declines with the younger age groups [3]. The prevalence of smoking among male adults in Nigeria is 9% [6].

Smoke from cigarettes and other tobacco products contain more than 4000 toxic chemicals that are harmful to different tissues and organs of the body [7]. Some of these chemicals are carcinogenic, antigenic, cytotoxic or pharmacologically active with adverse effects on vital body systems [8]. Some dangers associated with tobacco smoking include heart attack, stroke, emphysema, chronic pulmonary disease, cancers to mention but a few [9].

In males, cigarette smoking is associated with reduced libido, premature ejaculation, erectile dysfunction and impotence [10]. Destruction of sperm cells, decreased sperm motility, and relative infertility are also consequences of tobacco use, smoking being the most predisposing risk factor [11].

It is believed also that smoking affects some male reproductive hormones such as luteinizing hormone (LH), follicle stimulating hormone (FSH), prolactin and testosterone. Controversial however, is the actual effect of smoking on these hormones. While some authors report that smoking increases serum testosterone levels [12]; others have reported that testosterone levels are unaffected [13]; while another group have reported decreased serum testosterone levels in smokers [14]. Bakheet and Amarshad [15] and Mitra et al. [16] have reported increased serum levels of LH and FSH in the studies on smokers while Pasqualotto et al. [17] reported no significant differences in levels of FSH, LH and total testosterone in smokers.

This research work therefore was designed to investigate the relationship between tobacco smoking and serum concentrations of male reproductive hormones - luteinizing hormone (LH), follicle stimulating hormone (FSH), testosterone and prolactin.

## 2. MATERIALS AND METHODS

### 2.1 Subject Selection

One hundred and forty (140) apparently healthy regular male tobacco smokers and 61 apparently healthy non-smokers aged between 19 and 45 years were recruited for this study. They were all

of Nigerian origin. The consecutive sampling method was used. The purpose and nature of the research was explained to the participants and they gave their consent. A standard questionnaire was administered to them to obtain information from the subjects about their age, family history, dietary and physical lifestyle.

#### 2.1.1 Inclusion criteria

The smokers had to be male regular smokers i.e. smokers who smoked between 5 – 20 cigarette sticks per day. The controls had never smoked cigarettes in their life.

#### 2.1.2 Exclusion criteria

Smokers who had been diagnosed of any smoking-related disease (such as lung cancer, coronary heart disease, etc), terminal disease or on drugs, were excluded from the study.

#### 2.1.3 Sample size calculation

The number of samples used in this research was determined using the formula below:

$$N = \frac{Z\alpha^2 pq}{d^2}$$

Where

N = desired sample size
Zα = the α level of the coefficient interval at 95% (1.96)
p = proportion of occurrence
q = (1-p) proportion of non-occurrence
d= precision

Substituting the expected occurrence of p= 9% i.e. 0.09 from WHO 2013 [6] we have

$$N = \frac{1.96^2 \times 0.09\ (1 - 0.09)}{(0.05)^2}$$

$$= 125$$

### 2.2 Sample Collection

Blood samples (5ml) were aseptically collected from each subject into a plain sample bottle and allowed to clot at room temperature. The samples were then centrifuged and the sera separated into serum bottles and stored frozen at 4πC until needed.

### 2.3 Estimation of Hormones

Luteinizing hormone, follicle stimulating hormone, testosterone and prolactin were analyzed using Enzyme Linked Immunosorbent Assay kits obtained from DRG International Incorporated, East Mountain Side, USA. The tests were carried out according to the manufacturer's instruction.

### 2.4 Statistical Analysis

This was done using the PAWstatistic 18, a statistical package from SPSS Inc, California, USA. The results were expressed as Mean ± SD. The data was analyzed by Student's t-test. The level of significance was set at 95% confidence interval, where *P*-value less than 0.05 ($P<0.05$) was considered as statistically significant. Correlation was done using Pearson's correlation. Graphs were done using Microsoft excel 2007 version.

## 3. RESULTS AND DISCUSSION

### 3.1 Results

A Comparison of age, body mass index and serum levels of prolactin in male smokers and non-smokers showed no significant differences between the mean values of age ($P = .538$), body mass index ($P = .938$) and prolactin ($P = .699$) of smokers and non smokers. The mean testosterone level was significantly lower ($P = .0001$) in the smokers compared to the controls while LH and FSH values were significantly higher ($P = .0001$) in the smokers compared to controls (Table 1). The subjects were grouped into those that had testosterone levels <3 ng/ml (lower limit of normal) and those with testosterone levels >3 ng/ml. 4.3% of the smokers had testosterone levels below 3ng/ml while none of the controls had testosterone levels below 3ng/ml (Table 2). The smokers smoked a mean of 14.3±5.35 cigarettes per day and had a mean duration of smoking of 6.3±4.47 years. Their mean cigarette smoking pack years was 4.4±3.56 (pack years). There was a positive and significant correlation between FSH and duration of smoking ($r = 0.219$; $P = .009$) in the smokers (Fig. 1).

### 3.2 Discussion

This research work was aimed at establishing the relationship between tobacco smoking and some fertility hormones in male smokers. The mean testosterone levels of the smokers were significantly lower ($P<.0001$) than those of non-smokers. This suggests that testosterone level

decreases with smoking. Similar findings were reported by Funabashi and Kimura [14]. The reason for this may be that nicotine increases the concentration of 6β – hydroxylase, an enzyme responsible for metabolism of plasma testosterone into excretory metabolites which leads to a decrease in circulating testosterone levels.

**Table 1. Comparison of age, body mass index and serum levels of reproductive hormones in male smokers and non-smokers**

| Parameter | Smokers | Non-smokers | Calc t | Crit t | p-value |
|---|---|---|---|---|---|
| Age (years) | 26.7±5.14 | 27.1±4.70 | 0.617 | 1.98 | 0.538 |
| Body mass index (Kg/m$^2$) | 25.4±4.02 | 25.4±4.94 | 0.078 | 1.98 | 0.938 |
| Prolactin (ng/ml) | 8.9±4.65 | 9.2±5.97 | 0.387 | 1.98 | 0.699 |
| FSH (mIU/ml) | 7.97±9.06 | 4.3±2.57 | 4.450 | 1.98 | < .0001 |
| LH (ng/ml) | 17.2±9.35 | 10.8±5.18 | 6.188 | 1.98 | < .0001 |
| Testosterone (ng/ml) | 8.5±3.43 | 12.3±4.01 | 6.860 | 1.98 | < .0001 |
| n | 140 | 61 | | | |

*Mean±SD*

**Table 2. Percentage distribution of testosterone levels in male smokers and non-smokers**

| Testosterone levels | Smokers | Non-smokers |
|---|---|---|
| Testosterone <3 ng/ml | 4.3% (6) | 0% (0) |
| % testosterone >3 ng/ml | 95.7% (134) | 100% (61) |
| Calculated "t" | 2.495 | |
| Critical "t" | 1.98 | |
| p-value | 0.014 | |
| n | 140 | 61 |

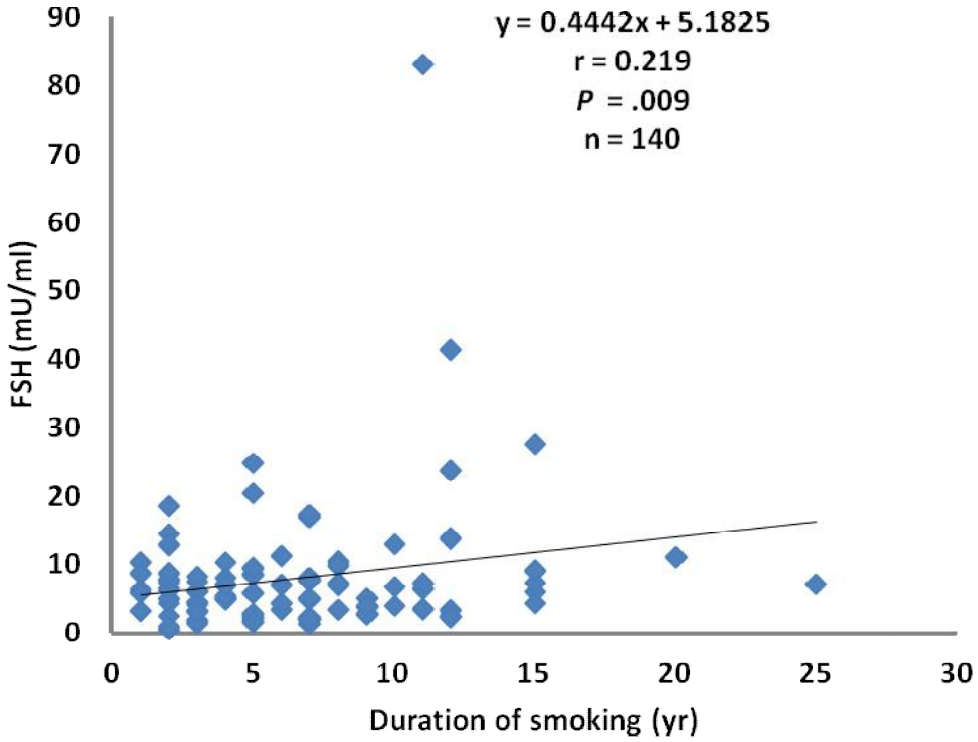


**Fig. 1. Correlation plot of follicle stimulating hormone against duration of smoking in cigarette smokers**

This decrease in testosterone levels may translate to a decrease in fertility as testosterone is the principal reproductive hormone in males. Worrisome also is the fact that low levels of testosterone have also been associated with metabolic syndrome, which in turn, is an emerging risk factor for prostate cancer [18]. In this study, the prevalence of the smokers who had low testosterone levels (below 3 ng/ml) was 4.3% compared to the controls that had 0%.

The increased levels of LH and FSH observed in the smokers in our study are indicators of testicular dysfunction or gonadal failure. Elevated levels of these two hormones in males usually reflect lack of male sex steroid hormone negative feedback. Saadat [19] also reported similar findings in male smokers. Clinically FSH is used as a marker of testicular dysfunction. The positive correlation between FSH and duration of smoking observed in this study is an indicator that longer duration of smoking is associated with greater level of testicular dysfunction. Surprisingly, this association was not observed with smoking pack years which suggests that level of testicular dysfunction in smokers is related with how long a person has been smoking, not how much.

It has been reported in several studies that increased levels of prolactin is associated with cigarette smoking in male smokers [20,21,22,23]. However this was not the case in our study, though there were increases compared to the controls, these were not significant ($p>0.05$). A disruption in the hormonal balance of the sex hormones may lead to a decline in the quality of semen. The quality of semen greatly affects the chances of conception as it is generally considered to be a proxy measure of male fertility.

In this study, there was no significant difference in the mean values of body mass index (BMI) between the smokers and non-smokers. A study by Trichopoulou et al. [24] showed that BMI is higher in non-smokers than in smokers. It has also been reported that smokers weigh less than non-smokers [25]. The absence of any significant differences may be due to moderate smoking by those who do in this study.

## 4. CONCLUSION

The risk of infertility associated with smoking may be attributed to lower levels of testosterone rather than hyperprolactinaemia. This decrease in testosterone levels may translate to a decrease in fertility as testosterone is the principal reproductive hormone in males.

## CONSENT

All authors declare that 'written informed consent was obtained from the patient (or other approved parties) for publication of this case report and accompanying images.

## ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

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## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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