

# Effect of Hormonal Contraceptives on the Total Antioxidants Status of Women from Isolo, Lagos State, Nigeria

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## Abstract

The use of hormonal contraceptives has been implicated in the depletion of serum antioxidants and resultant promotion of oxidative stress which is associated with various disorders including cardiovascular disease and cancer. This study investigated serum total antioxidant status (TAS) in women taking hormonal contraceptives and compared their results with non-contraceptive users (age- and sex-matched). Sixty women aged 30 - 45 years, were enrolled for the study which included forty-five users of hormonal contraceptives from the Planned Parenthood Federation of Nigeria, Isolo, Lagos state and fifteen age-matched, apparently healthy, non-contraceptive users from the same geographical location were selected as controls. The *in vitro* determination of the serum total antioxidant status (TAS) was performed using Biorex enzymatic kit. Data obtained were statistically analyzed using student's t-test and  $P < 0.05$  was considered significant. The serum levels of TAS in the users of hormonal contraceptives were significantly lower than non-users ( $P < 0.05$ ). The study concluded that women on hormonal contraceptives especially those taking either combined oral or combined injectable contraceptives were at risk of developing disorders associated with reduced levels of serum antioxidants.

## Keywords

Hormonal Contraceptives, Oxidative Stress, Antioxidant Status

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## 1. Introduction

Hormonal contraceptives are synthetic biochemical substances that act on the endocrine system and permit sex-

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ual union without resultant pregnancy.

Hormonal contraceptives are used by millions of women worldwide. Although other methods of contraception exist, the use of oral and injectable contraceptives is the most popular. In the United States, 18% of women who adopted contraceptive methods to prevent conception relied upon hormonal contraceptives [1].

There are two main classes of hormonal contraceptives and these include combined contraceptives which contain both an oestrogen and a progestin, most oral contraceptives fall under this category and progestogen-only contraceptives which contain only progesterone or a synthetic analogue (progestin).

In Africa, approximately 30% of women use birth control and more than this proportion would have used, if it were readily available. In Sub-Saharan Africa, the use of contraceptives among women, increased from about 5% in 1991 to about 30% in 2006 [2].

According to Nigeria Demographic and Health Survey (NHDS), the prevalence rate of hormonal contraceptives use among Nigerian women between the ages 15 - 49 was 13% in 2003, 15% in 2008 and 18% in 2012. Further analysis of the total contraceptive rate in Nigeria revealed wide state variations, ranging from 0.3% in Jigawa to 41.6% in Lagos state as well as zonal variations ranging from 2.7% in the northwest to 28.5% in the southwest [3].

Recently, the possibility of alterations in various metabolic processes and antioxidant status, by hormonal contraceptives, has received much attention but unfortunately, there has been conflicting reports in this regard. Thibodeau *et al.* (2002) opined that this divergence in reports could be attributed to the chemical heterogeneity of the oestrogen family and their varying concentration [4].

Generally, stress can be described as inability to cope with increased demands. Oxidative stress occurs when an individual's antioxidant defense mechanism has been overwhelmed by destructive reactive oxygen species. Oxidative stress has been implicated in the pathogenesis of many diseases including cardiovascular disease, cancer, diabetes complications, macular degeneration and arthritis.

The antioxidant effect of oestrogen was observed in most of the *in vivo* studies performed on rats and women receiving hormone-replacement therapy [5]-[8]. The antioxidant activity of oestrogen has been attributed to prevention of expression and function of NADP<sup>+</sup>/NADPH oxidase, increase in the expression and activation level of endothelial isoform of the nitric oxide synthase (eNOS) and stimulation of the expression and activation of manganese superoxide dismutase [9]-[11]. Contrarily, Bhat *et al.* (2003) and Gordon *et al.* (2005) reported the direct pro-oxidant effect of oestrogen in experimental model rats [12] [13]. Prokai-Tatrai *et al.* (2005) attributed the pro-oxidant effects of oestrogens to the metabolic conversion of oestrogens to catecholestrogens by cytochrome p450. Catecholestrogens are easily auto-oxidized to ortho-quinone by-products which are powerful oxidizing agents capable of generating reactive oxygen species [14].

Despite the divergent views about the relationship between the use of hormonal contraceptives in women and oxidative stress, there is paucity of information about this association in Nigeria. Lands *et al.* (2000) and Maxwell *et al.* (2006) recommended the study of total antioxidant status rather than monitoring the response to a single antioxidant, as this gives a representation of mixed antioxidant response [15] [16]. This study therefore aimed to determine the effect of hormonal contraceptives on the serum total antioxidants status of women who enrolled for the use of hormonal contraceptives at Planned Parenthood Federation of Nigeria, Isolo, Lagos State.

## 2. Materials and Methods

### 2.1. Subjects

A total of sixty eligible volunteers within the age range of 30 - 45 years were recruited for this study which included 45 women using hormonal contraceptives at the Planned Parenthood Federation of Nigeria, Isolo, Lagos State. These participants were divided into 18 subjects on combined oral contraceptives and 27 subjects on injectable contraceptives. 15 apparently healthy age and sex-matched subjects who had never used contraceptives were selected as controls. All the subjects were selected from the same geographical location. Exclusion criteria for participating in the study were; intake of antioxidant-vitamin supplements, smokers, alcohol users, those who have diabetes, cardiovascular diseases. The study was approved by Babcock University Ethical Committee.

### 2.2. Sample Collection and Analysis

Blood sample (5 ml) was aseptically collected by venipuncture from each subject using sterile disposable needles and syringes. The blood samples were dispensed into plain containers and were allowed to retract, to obtain sera

for the determination of total antioxidant status. Biorex enzymatic kit was used for the *in vitro* colorimetric determination of serum total antioxidant status.

### 2.3. Statistical Analysis

Statistical analysis was done using the statistical package for social sciences (SPSS) version 17.0. Results were expressed in mean  $\pm$  s.d. Student's t-test was used to compare the means between the test and control subjects where  $P < 0.05$  was considered significant.

## 3. Results

Comparison of the serum levels of Total antioxidant status (TAS) in hormonal contraceptive users and control subjects is presented in **Table 1**. There was a significant decrease in the serum levels of TAS of hormonal contraceptive users when compared with the control subjects.

**Table 1.** Comparison of the serum levels of total antioxidant status (TAS) in hormonal contraceptive users and control subjects.

	Hormonal contraceptives (n = 45)	Control subjects (n = 15)	P-value
TAS (mmol/L) mean $\pm$ s.d	1.0 $\pm$ 0.60	1.56 $\pm$ 0.96	0.000*

\*Significant at  $P < 0.05$ .

**Table 2** shows the comparison of serum levels of TAS in both oral contraceptive users and control subjects. A significant decrease was observed in the serum levels of TAS of oral contraceptive users when compared with the control subjects.

**Table 2.** Comparison of serum levels of TAS in both oral contraceptive users and control subjects.

	Oral contraceptives (n = 18)	Control subjects (n = 15)	P-value
TAS (mmol/L) mean $\pm$ s.d	1.17 $\pm$ 0.74	1.56 $\pm$ 0.96	0.020*

\*Significant at  $P < 0.05$ .

Comparison of serum TAS for both injectable users and control subjects is shown in **Table 3**. There was a significant decrease in the serum TAS of injectable contraceptive users when compared with the control subjects.

**Table 3.** Comparison of serum levels of TAS in both oral contraceptive users and control subjects.

	Injectable contraceptives (n = 27)	Control subjects (n = 15)	P-value
TAS (mmol/L) mean $\pm$ s.d	0.94 $\pm$ 0.64	1.56 $\pm$ 0.96	0.000*

\*Significant at  $P < 0.05$ .

## 4. Discussion

The results of the present study revealed that there was significantly lower levels of serum TAS in users of both oral and injectable hormonal contraceptives when compared with non-contraceptive users. This is in agreement with the study of Palan *et al.* (2010) who reported that hormonal contraceptives deplete antioxidant vitamins and trace elements, as measured by the activity of coenzyme Q<sub>10</sub>, vitamin E and total antioxidant activity [17]. Akinloye *et al.*, 2011 attributed decrease in the serum levels of antioxidant trace elements more specifically to increased use of oral contraceptives [18].

Some other studies however, have reported the antioxidant function of oestrogen which may exert protective

effect on the cardiovascular system [19] [20]. Thibodeau *et al.* (2002) and Pincemail *et al.* (2007) attributed these conflicting reports to the heterogeneity of the synthetic hormonal contents of these contraceptives [4] [21].

According to Wassman *et al.* (2005), the antioxidant effects of oestrogens are antagonized by progestins via the activation of NADPH oxidase and the inhibition of the expression and activity of manganese superoxide dismutase (MnSOD) and extracellular SOD [22]. Therefore it implies that the counteractive effect of progestin would result into decrease in the serum total antioxidant status especially in women taking either combined oral or combined injectable contraceptives, as revealed by the findings of the present study.

## 5. Conclusion

The findings of this study revealed a significant decrease in the serum levels of total antioxidant status among hormonal contraceptive users. This suggests that women taking hormonal contraceptives are at high risk of oxidative stress related diseases. Though alterations in various metabolic processes and antioxidant status associated with the use of hormonal contraceptives remain controversial, prospective large scale studies need to be performed in Nigeria to further elucidate this association.

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