

# Effects of oral contraceptives on total serum proteins, albumin, globulins and cholesterol levels in Ibadan, Nigeria.

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## Summary

Total serum protein, albumin, globulin, albumin/globulin ratio and cholesterol levels were determined in 25 subjects on oral contraceptives and 25 controls. The mean serum total protein, globulin and cholesterol levels were significantly increased in oral contraceptive and their control counterparts. The albumin/globulin ratio in subjects on oral contraceptives users is significantly decreased compared with controls. In view of the findings of this study, it is suggested that the biochemical profile of long term oral contraceptive users be assessed periodically.

**Key words:** Total serum protein, Albumin, Globuline.

## Résumé

Sérum protéine totale, albumine, globuline, le rapport albumine/globuline et le niveau du cholestérol tous étaient déterminés chez 25 clients, en utilisant contraceptifs oraux (vaccin) buccal; et 25 des cas témoins.

La moyenne sérum protéine totale, globuline et le niveau du cholestérol avait été manifestement augmentés sur contraceptifs oraux et chez les cas témoins contre-parties. Le rapport albumine/globuline chez les clients qui utilisent les contraceptifs oraux était en baisse par rapport aux cas témoins.

Prenant les résultats de cette étude en considération nous proposons qui l'on entre prend l'évaluation périodique d'un enregistrement biochimique à long terme des utilisateurs des contraceptifs oraux.

## Introduction

Since the introduction of the oral contraceptive, so called the "Pill", into the market at the middle of the 20<sup>th</sup> century, several millions of women in the reproductive age agroup all over the world have made use of it to prevent unwanted pregnancies and abortions and also to permit improvement in the timing of childbirth. The efficacy of the oral contraceptives has never been in doubt, with only about 0.34 pregnancies per 100 woman year; however, more worrisome are the documented side effects. As a matter of fact, evidence suggesting that oral contraceptives might have negative effects on health other than the prevention of pregnancy began to appear shortly after the drugs were introduced.

The widespread use of hormonal contraceptives provides an opportunity for assessing the influence of estrogens and progesterogens on various biochemical parameters of the female. It is even possible that some of the side effects of these compounds might be associated with such metabolic effects<sup>1</sup>. Whichever way it is viewed, it seems important to ascertain whether there are changes in the results of various biochemical tests in women taking hormonal contraceptives.

Oral contraceptives have been implicated in many diseases such as thromboembolic disease<sup>2</sup>, myocardiac infaction<sup>3</sup> circulatory disorder and carcinogenicity<sup>4</sup>. Furthermore, it's negative effects on the liver, heart, diabetes, obesity, hypertension and high serum cholesterol levels are well documented<sup>5,6,7</sup>.

The biochemical profile of women on oral contraceptives showed different changes in plasma total protein, albumin and cholesterol levels<sup>8,9</sup>. Available data on this topic are mostly from developed countries and frequently on caucasians. On the contrary, there is paucity of information on the effects of oral contra-

ceptives on Nigerian women. Indeed, this is about the first time in our environment that such a comprehensive assesment of the biochemical parameters of oral contraceptive users in Nigerian women using oral contraceptives is undertaken, with a view to ascertaining changes, if any, on these biochemical parameters.

## Subjects and method

Twenty five healthy Nigerian women who have been on oral contraceptive for a period of six months to three years were selected for this study. Their ages ranged from 18 to 34 years with a mean of 22.76 years SD. All the subjects were regular clients of the family planning clinic of the Department of Obstetrics and Gynaecology, UCH, Ibadan. Similarly 25 control subjects were selected with age range 20-32 years with a mean of 24.6 SD  $\pm$  3.1 years. Students and staff of the University College Hospital, Ibadan formed the majority of the control group and they were non-users of oral contraceptives. Five mililitres of venous blood was collected from each of the 50 subjects using sterile syringes and hypodermic needles with the patients in sitting position. The blood samples were immediately centrifuged in an MSE/CENTAUR 2 centrifuge at 3000 revolutions per minute for five minutes. The serum was separated and stored frozen at  $-20^{\circ}\text{C}$ . The total serum protein was determined using the method described by Reinhold (1953). This is based on the ability of alkaline curpic solution to react with at least two peptide bonds to form a violet colour, which is estimated at 540nm. The colour development takes about 15 minutes.

Serum albumin was determined as described by Dourmas et al (1971) and modified by Spencer and Price (1978). This method is based on the fact that bromocresol green at a point below the isoelectric point of albumin reacts with albumin to cause a change in colour which is proportional to the amount of albumin present.

The determination of serum cholesterol is done according to the method by Trinder (1969) and modified by Richmond (1973) using the colorimetric end point cholesterol kit reagent from Randox Laboratories, Ireland. This method is based on the principle that free cholesterol and cholesterol released from its esters are oxidised after enzymatic hydrolysis. Statistical analysis of data was performed using student's t-test for comparison of two variables and the chi squared ( $X^2$ ) test for the degree of association between two variables.  $P = 0.05$  was taken as being significant.

## Results

The mean serum total protein, albumin and globulin levels in subjects on oral contraceptives are significantly higher compared with the control subjects whereby  $P < 0.001$ ;  $P < 0.05$  and  $P < 0.001$  respectively as shown in Table 1. The albumin/globulin is significant  $P < 0.001$ .

As regards the total serum cholesterol level, subjects on oral contraceptives show significantly increased serum cholesterol levels when compared with the control group.  $P < 0.001$  (table 1).

Table 2 shows the relationship between the degree of elevation of serum total protein in both subjects and their controls. All the users 25 (100%) had significantly elevated serum total protein levels of more than 72g/litre. About 12(48%) of the control group had serum total protein levels of between 45 - 72g/l ( $X^2 = 15.7895$ )  $P < 0.001$ .

The elevation of serum albumin levels in oral contraceptive

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users is marginally increased when compared with the control  $X^2 = 1.33$  and  $P < 0.20$  as shown in Table 3.

**Table 1 Comparison of mean value of Total serum protein albumin and Globulin, albumin/globulin ratio, cholesterol in subjects on oral contraceptives and the control subjects.**

Parameter	Control (n=25)		Oral Contraceptive users (n = 25)			
	Means	SD	Mean	SD	Value	P-Value (n = 25)
Total protein	72.0	7.7	93.7	8.2	6.644	<0.001s
Albumin	49.0	6.4	55.2	6.8	1.333	<0.005
Globulin	22.8	6.0	38.4	16.5	4.445	<0.001
Albumin/globulin Ratio Total	2.5	1.6	0.8	0.8	39.333	<0.001
Serum/Cholesterol	5.4mmo	7.2	0.4	0.4	10.112	<0.001
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**Table 2 Relationship between degree of hyperproteinaemia on control subjects and subjects on oral contraceptives**

Subjects	Serum total protein concentration				Total
	45 - 72g/l		>>72g/l		
	n	%	n	%	
Controls	12	48	13	52	25
Contraceptive user	0	0	25	100	25
Total	12	-	38	-	50

$X^2 = 15.7895$   $P < 0.001$

**Table 3 Relationship between degree of increased serum albumin in Control subjects and subjects on oral contraceptives**

Subjects	Serum albumin concentration				Total
	27 - 49g/l		>>49g/l		
	n	%	n	%	
Controls	12	48	13	52	25
Subjects on oral contraceptive	8	32	17	68	25
Total	12	-	30	-	50

$X^2 = 1.333$   $P > 0.20$

**Table 4 Relationship between elevated serum globulin in oral contraceptive users and their controls**

Subjects	Serum globulin concentration				Total
	05 - 22.84		20.38.4		
	n	%	n	%	
Controls	12	48	13	52	25
Subjects on oral contraceptive	8	32	17	68	25
Total	12	-	30	-	50

$X^2 = 15.385$   $P < 0.001$

**Table 5 Relationship between increased total serum cholesterol levels in control subjects and subjects on oral contraceptives**

Subjects	Total serum cholesterol concentration				Total
	4.0 - 5.4 mmol/l		>>5.4m		
	n	%	n	%	
Controls	12	48	13	52	25
Subjects on oral contraceptive	0	0	25	100	25
Total	12	-	38	-	50

$X^2 = 15.7895$   $P < 0.001$

Majority 24 (96%) of the contraceptive users had serum globulin levels of more than 22.84g/l while the controls showed significantly lower levels of between 05-22.84g/l  $X^2 = 15.385$   $P < 0.001$  see table 4. As shown in table 5 all subjects 25(100%) of oral contraceptive users had higher serum cholesterol levels more than 5.4m mol/l compared with the controls with values between 4.0 - 5.4mmol/l  $X^2 = 15.7895$   $P < 0.001$ .

### Discussion

During contraceptive medication the most pronounced changes are usually in the concentrations of total serum proteins and albumin, with an increase in proteins and a decrease in albumin concentration. The quantitative pattern of alterations is in accord with the results of previous electrophoretic determinations which had

shown a decrease of albumin and increases in globulins during the administration of contraceptives<sup>6,10</sup>.

In our study, we arrived at similar results with regards to significant elevation of serum protein, globulin and cholesterol, but serum albumin level showed no significant difference in oral contraceptive users compared with controls ( $P > 0.20$ ). This result of serum albumin level is at variance with a reported moderate decrease of serum albumin in oral contraceptive users as reported by other workers<sup>10,11</sup>.

It has been suggested in previous studies that the increased total protein levels in subjects on oral contraceptives might be due to an increase in certain carrier proteins such as transferrin, ceruloplasmin, hormone binding globulin, and thyroxin binding prealbumin. Also, the estrogen content in oral contraceptives is said to be responsible for the increased total proteins<sup>12,13</sup>.

Furthermore, quantitative determinations of serum proteins by other workers have also demonstrated an increase in lipoproteins, ceruloplasmins, alpha 1 - antitrypsin and transferrin after administration of estrogens or oral contraceptives<sup>6,10,14</sup>. It is also documented that pregnancy and oral contraceptives appear to produce similar changes in serum proteins as reported by other researchers<sup>6,15,16</sup>. However, these reports had been contradictory in certain respects.

It has also been established that the serum levels of some coagulation related proteins such as fibrinogen, factors VII, VIII, Antithrombin - III and plasminogen as well as some acute phase proteins such as alpha 1 - antitrypsin tend to rise in oral contraceptive users<sup>17</sup>.

Our study has also shown that serum globulin is significantly increased in oral contraceptive users compared with controls ( $P < 0.001$ ). This result is similar to the findings of previous workers<sup>6,18</sup>. The study further shows that albumin/globulin ratio (1.6) in subjects on oral contraceptive is significantly decreased compared with control value (2.5)  $P < 0.001$ . This disparity in the ratio is apparently due to the significantly increased serum globulin levels in subjects, compared with controls.

The level of serum cholesterol in subjects on oral contraceptives in this study is significantly increased compared with controls  $P < 0.001$ . This elevation of serum cholesterol level may have been influenced by the oestrogen content in oral contraceptives. Several previous workers came to similar results<sup>17,18, 19</sup>.

In conclusion this study has demonstrated the need to periodically reassess the biochemical parameters of oral contraceptive users, especially those who have been on the steroids for a long time. This is necessary in view of the subtle but significant biochemical changes as regards increases of total protein, albumin and cholesterol levels demonstrated here. However, further studies that will recruit a larger number of subjects on the oral contraceptive pill for a longer duration of time would be valuable in this regard before conclusive statements can be made on the effect of oral contraceptive use on these parameters.

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