

# **Comparative study of the effects of the use of combined oral pills and progestin-only pills in Nigerian females**

Anslem O. Ajugwo<sup>1,\*</sup>, Teddy C. Adias<sup>2</sup>, Tosan A. Erhabor<sup>3</sup>, Andre M. Abouo<sup>1</sup>, Fredrick C. Anolue<sup>4</sup>, Ikechukwu R. A. Nnadozie<sup>5</sup>

<sup>1</sup>Department of Haematology and Blood Transfusion, Madonna University Elele, Nigeria

<sup>2</sup>Bayelsa State College of Health Technology Ogbia, Nigeria

<sup>3</sup>Medical Laboratory Science Council of Nigeria (MLSCN) Abuja, Nigeria

<sup>4</sup>Dept. of Obstetrics and Gynaecology, Imo State University Teaching Hospital Orlu, Nigeria

<sup>5</sup>Dept. of Parasitology/Microbiology, Imo State University Teaching Hospital Orlu, Nigeria

## **Email address**

slemjugwo@yahoo.com (A. O. Ajugwo)

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## **Abstract**

This study involved fifty apparently healthy females on oral contraceptives (test) and another fifty apparently healthy females not on oral contraceptives (control). Both groups were aged 16-40 years of age. The test group have been on oral contraceptive for at least 5 months. Test group was grouped into progestin-only pill (POP) users and combined oral pill (COP) users. The following parameters were analyzed, packed cell volume (PCV), erythrocyte sedimentation rate (ESR), Haemoglobin Estimation (Hb), Red cell indices, total white blood count (TWBC) and platelet count using standard manual methods. The results showed significant increase ( $P < 0.05$ ) in platelet counts, ESR and TWBC when compared with control. Significant difference ( $p < 0.05$ ) was also seen in platelet count and WBC when progestin-only pill (POP) users were compared with combined oral pill (COP) users. These findings suggest that oral contraceptive (OC) users could be predisposed to thrombosis with COP users having greater risk than POP users.

## **Keywords**

Oral Contraceptives, Thrombosis, Nigerian Females

## **1. Introduction**

Oral contraceptives are a group of oral drug preparations containing one or more synthetic female sex hormones taken by women in a monthly cycle to prevent pregnancy [1]. These preparations vary chemically and pharmacologically and have many properties in common. Oral contraceptives involve two types of preparations (1) combinations of oestrogen and progestins and (2) progestin-only therapy [2]. The combined drug is usually referred to as pill while the progestin-only drug is also usually referred to as mini-pill.

With perfect use, the protection that birth control pills

provide against pregnancy is nearly 100%. However, because of inconsistent or incorrect use, there is a surprisingly high annual failure rate of 8% in typical users [3]. Oral contraceptive pills come in tablet form, in containers designed to help women keep track of which tablet to take each day. The tablets are of different colours, indicating the amount of hormones they contain. These are included simply to help women stay in the habit of taking a pill each day as the hormone combinations need to be taken only on certain days of the menstrual cycle. It is only effective when taken properly, hence its obvious disadvantage is the daily requirement of taking a pill [4].

The combined pill increases the levels of progesterone

and oestrogen thereby interfering with the production of two hormones: luteinizing hormone (LH) and follicle-stimulating hormone (FSH) which in turn prevents ovulation. The progestin-only pill works mainly by making the mucus lining of the cervix too thick to be penetrated by sperm. Adverse effects associated with the use of OC have been partly linked to the dose of oestrogen component [5]. Most of these effects have been reported in other populations[6], hence the need to establish the effects in Nigerian females.

## 2. Subjects and Methods

### 2.1. Subjects

Fifty (50) apparently healthy Nigerian females aged between 16 and 40 years who have been on oral contraceptives for a period not less than 5 months were recruited for the study while another fifty (50) non-users of oral contraceptives (age and sex-matched) served as control group.

### 2.2. Approval

The study was approved by Madonna University ethical committee (MUEC). The participants were informed of their involvement in the study and they gave consent prior to sample collection.

### 2.3. Sample Collection

Four milliliters of blood samples were aseptically collected from both test and control subjects and transferred into EDTA bottles.

### 2.4. Methods

#### Haemoglobin Estimation

Method: Cyanmethhaemoglobin method.

#### Principle

Whole blood is diluted 1 in 201 in a modified Drabkin's solution, which contains potassium ferricyanide and potassium cyanide. The red cells are hemolyzed and the haemoglobin oxidized by the ferricyanide to methaemoglobin. This is converted by the cyanide to stable haemoglobinocyanide (HICN). Absorbance of HICN solution is read in a spectrophotometer at wavelength of 540nm.

Procedure for Haemoglobin Estimation

1. Two tubes labelled test and blank were placed on the rack.
2. 4.0ml of Drabkin's solution and 0.02ml of blood were added to the tube labelled test.
3. To the tube labelled blank only 4.0ml of Drabkin's solution was added.
4. The machine was zeroed with Drabkin's solution.
5. The absorbance of the test sample was read at 540nm wavelength and the reading was taken at 540nm
6. It was then calculated using

$$\frac{\text{Absorbance of Test}}{\text{Absorbance of standard}} \times \text{Concentration of standard}$$

#### Packed Cell Volume (PCV)

Method: Microhaematocrit method.

#### Principle

The packed cell volume is that portion of whole blood occupied by red cells, expressed as a ratio (litre/litre). Anticoagulated blood in a glass capillary of specified length bore size and wall thickness is centrifuged in a micro haematocrit centrifuge at RCF 1200-1500xg for 3-5 minutes to obtain constant packing of the red cells. A small amount of plasma remains trapped between the packed cells. The PCV values are read from a scale of a micro haematocrit reader or calculated by dividing the height of the red cell column by the height of the total column of blood.

Procedure

1. Three quarter of well-mixed anticoagulated blood was filled in a plain capillary tube.
2. The unfilled end was sealed preferably using a sealant material, if unavailable heat-seal the capillary tube using a small flame of Bunsen burner, rotating the end of the capillary tube in the flame.
3. It was centrifuged for 3minutes using the shorter time when the RCF is 15000xg.
4. Immediately after centrifuging, the PCV was read with a hand held micro haematocrit reader, the base of the red cell column was aligned (above the sealant) on the zero mark and the top of plasma column on the 100 mark, the PCV was read off from the scale, the reading point is the top of the red cell column, just below the Buffy coat layer (consisting of White blood cells and Platelets).

#### Erythrocyte Sedimentation Rate (ESR)

Method: Westergren method

#### Principle

When citrated blood in a vertically positioned Westergren pipette is left undisturbed, red cells aggregate together to form rouleaux. ESR is the rate at which red cells sediment after one hour and is measured in mm/hr.

Procedure

One part of tri-sodium citrate (anticoagulant) was mixed with 4 parts of whole blood. It was mixed properly and allowed to stand vertically for one hour in Westergren tubes. It was kept away from sunlight and vibrations. The result was read after one hour.

Mean cell volume (MCV), Mean cell haemoglobin (MCH) and Mean cell haemoglobin concentration (MCHC) were then calculated using appropriate formulas [7].

## 3. Results

Among the 50 oral contraceptive (OC) users studied, 31 (62%) use combined oral pill (COP) while 19 (38%) use the progestin-only pill (POP). The age interval of 26 – 30

years had the highest number of users with 37% and 39% for POP and COP respectively. The least number of users was seen in 36 – 40 years group with 10% and 3% for POP and COP respectively. This probably represents reduced sexual activity. Also within age 36 – 40 years, most Nigerian females would have been married hence getting involved in child-bearing and will find OC use unattractive.

**Table 1.** Distribution of OC users according to age and type of OC

Age Interval (years)	POP (Progestin only Pill)	COP (Combined oral Pill)
16 – 20	2	5
21 -25	4	11
26 – 30	7	12
31 – 35	4	2
36 - 40	2	1
Total	19	31

Most of the participants in the study use combined oral pill (COP). The least number of OC users was seen in the 36 – 40 years group while 26 – 30 years group had the highest number for both POP and COP use. In comparing the different parameters between OC users and non-users significant difference was seen in ESR, WBC and platelet counts while other parameters studied showed no significant difference (Table 2).

**Table 2.** Mean  $\pm$  SD of different parameters for OC users (Test) and nonusers (Control).

Parameters	Test	Controls	P value
PCV (l/l)	0.36 $\pm$ 0.04	0.39 $\pm$ 0.33	P>0.05
ESR ( mm/hr)	15.60 $\pm$ 3.17	10.30 $\pm$ 1.11	P<0.05
HB (g/dl)	12.02 $\pm$ 11.61	11.64 $\pm$ 9.01	P>0.05
RBC ( $\times 10^{12}$ /L)	4.48 $\pm$ 3.45	4.53 $\pm$ 1.26	P>0.05
MCV (fl)	81.87 $\pm$ 3.69	84.35 $\pm$ 2.93	P> 0.05
MCH (pg)	26.09 $\pm$ 7.91	27.32 $\pm$ 5.96	P>0.05
MCHC (g/dl)	33.09 $\pm$ 27.50	31.73 $\pm$ 1.70	P> 0.05
TWBC ( $\times 10^9$ /l)	11.3 $\pm$ 8.70	10.5 $\pm$ 5 .07	P< 0.05
Platelets ( $\times 10^9$ /l)	457.6 $\pm$ 174.0	209 $\pm$ 62.01	P<0.05

MCV – Mean Cell Volume, MCH – Mean Cell Haemoglobin, MCHC – Mean Cell Haemoglobin Concentration

Similarly, significant difference was also seen in WBC and platelet counts when progestin-only users was compared to combined oral pill users.

**Table 3.** Mean  $\pm$  SD of Progesterone only pill (POP) and combined oral pill (COP)

Parameters	Progestin-only pill (POP) n =19	Combined oral Pill (COP) n =31	P value
PCV (l/l)	0.37 $\pm$ 0.06	0.35 $\pm$ 0.05	P>0.05
ESR (mm/hr)	14.57 $\pm$ 2.82	16.23 $\pm$ 3.23	P>0.05
HB (g/dl)	12.38 $\pm$ 0.69	11.78 $\pm$ 1.11	P>0.05
RBC ( $\times 10^{12}$ /l)	4.48 $\pm$ 2.51	4.38 $\pm$ 1.23	P>0.05
MCV (fl)	83.20 $\pm$ 2.51	83.30 $\pm$ 2.83	P> 0.05
MCH (pg)	35.23 $\pm$ 11.95	27.32 $\pm$ 5.96	P>0.05
MCHC (g/dl)	33.09 $\pm$ 27.50	31.73 $\pm$ 1.70	P> 0.05
TWBC ( $\times 10^9$ /l)	13.6 $\pm$ 1.70	7.2 $\pm$ 2 .30	P< 0.05
Platelets ( $\times 10^9$ /l)	282.9 $\pm$ 85.0	436.2 $\pm$ 102.2	P<0.05

MCV – Mean Cell Volume, MCH – Mean Cell Haemoglobin, MCHC – Mean Cell Haemoglobin Concentration

## 4. Discussion

Erythrocyte Sedimentation Rate (ESR) showed significant increase ( $p<0.05$ ) in OC users ( $15.6 \pm 3.17$  mm/hr) when compared to nonusers ( $10.3 \pm 1.11$  mm/hr). Though ESR is a non-specific test [7], it is known to be increased in certain physiological conditions. The physiological effect of oral contraceptives are in many ways similar to those of pregnancy [2]. This possibly could be the reason for increased ESR in OC users. White blood cell count (WBC) was significantly increased ( $P<0.05$ ) in OC users. Such increase have also been recorded [8]. Reference [9] documented increased WBC though statistical significance was not achieved.

Significant ( $p<0.05$ ) platelet count was seen in OC users ( $457.6 \pm 174.0 \times 10^9/l$ ) compared to nonusers ( $209 \pm 62.01 \times 10^9/l$ ). This is in agreement with previous work [10], which suggested that the incidence of thromboembolism in women on oral contraceptive was about 10 times the expected rate. The increased platelet count could predispose OC users to blood clotting and thrombosis. Reference [11] suggested that the oestrogen content of oral contraceptive determine the risk of cerebral thrombosis. Though OCs have procoagulatory effects, at the same time the effect is balanced with fibrinolytic activity [12],[13],[14].

Other parameters like PCV, Hb, red cell count and red cell indices (MCV, MCH and MCHC) were not statistically significant ( $p>0.05$ ). Many investigators suggest that OC do not significantly affect haemostatic parameters [15,16], but studies involving white females suggest otherwise [17],[18].

Oral contraceptive users were also grouped into progestin-only pill (POP) group and combined oral pill (COP) group and compared (Table 3). Significant difference ( $p<0.05$ ) was seen in WBC and platelet count with those on COP having increased platelet counts. This comparative increase will likely increase the risk of thrombosis associated with oral contraceptive and put COP users at higher risk. POP have relatively less side effect on platelets because it has no estrogen receptor site for platelets to adhere to, causing thrombosis.

Oral contraceptives have been associated with increased blood pressure [19]. Oestrogen-based pills should be avoided in women with hypertension, liver disease or who are at increased risk of a thrombosis [1]. Conclusively, in Nigerian females, oral contraceptive users are at risk of thrombosis with COP users being at higher risk.

## Conflict of Interest

We declare that we have no conflict of interest.

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