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EVALUATING THE PLASMA SELENIUM AND FIBRINOGEN LEVELS IN THE LUTEAL AND MENSTRUAL PHASES OF THE MENSTRUAL CYCLE AMONGST A POPULATION OF YOUNG FEMALES IN BENIN CITY

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ABSTRACT: *Menstruation is a phenomenon unique to females. Variations in the concentration of plasma selenium and fibrinogen have not been clearly established. This study aimed at investigating the variations in the plasma selenium and fibrinogen concentrations amongst a population of young females. 100 healthy female subjects were engaged in this study. Subjects were asked to complete gynecological questionnaires. The clinical history of the subjects was noted and different phases of the menstrual cycle were determined. The results revealed a significant increase in the plasma selenium and fibrinogen levels during the luteal phase compared the menstrual phase (P<0.05).*

KEY WORDS: selenium, fibrinogen and menstruation

INTRODUCTION

The term menstruation was derived from the Latin word menstruus meaning monthly. Menstrual cycle is a repetitive phenomenon occurring during the reproductive life of a female. It involves structural, functional and hormonal changes in the reproductive system (Guyton and Hall, 2006; Sadiqua and Ashwini, 2012) with the periodic vaginal discharge of blood containing degenerated endometrial parts, as the only visible external sign (Rajnee *et al.,* 2010). It is associated with the secretion of estrogen and progesterone from the ovaries under the influence of the hypothalamus and pituitary gland (Guyton and Hall, 2006; Sembuligam and Sembuligam, 2006). Several studies have shown that the periodicity of the menstrual cycle ranges from 25 to 35 days with the recurrent discharge of blood lasting 3 - 5 days (Rajnee *et al.,* 2010).

Fibrinogen

Fibrinogen is the major plasma protein coagulation factor. Low plasma fibrinogen concentrations are therefore associated with an increased risk of bleeding due to impaired primary and secondary haemostasis. Fibrinogen is a classical positive acute-phase reactant protein (Van Der Bom *et al.,* 1997).Fibrinogen level are useful as part of the investigation of bleeding tendency or an unexplained prolongation of the activated partial thromboplastin time or prothrombin time. Elevated levels may correlate with increased risk of thrombosis in epidemiological studies although the significance in individual patients is unclear. Fibrinogen defects may be quantitative (hypo or hyperfibrinogenaemia) or qualitative (dysfibrinogenaemia). Inherited

dysfibrinogenaemia is rare with only 250-300 patients reported wordwide but an acquired defect of fibrinogen molecule is excessively glycosylated impairing its activity. Elevated levels of fibrinogen degradation product (FDPs) also impair the action of fibrinogen (Mackie *et al.,* 2003).

Selenium

The essential trace element selenium is an integral component of the enzyme glutathione peroxidase. Although originally discovered in 1817 by Jöns Jacob Berzelius , it was not until 1957 that Schwarz and Foltz proved that selenium is an essential nutrient for normal growth and reproduction in animals. (Mistry and Kurlak, 2015). Most of the selenium in the body comes from diet. The reference range for plasma selenium is about 60–150 ng/ml. Selenium deficiency (serum concentration <40 ng/ml) is rare (Smith and Garg, 2017). Selenium play some important role in humans health like, proper functioning of the immune system, it's also appears to be a key nutrient in counteracting the development of virulence and inhibiting HIV progression to AIDS. Another role being they it is required for sperm motility and may reduce the risk of miscarriage (Rayman, 2000).

MATERIALS AND METHOD

1. Spectrophotometer
2. Syringes and needles
3. Handgloves
4. Tourniquet
5. Centrifuge
6. Test tubes/rack
7. Timer
8. Cotton wool
9. Plain sample bottles
10. Sodium citrate bottles
11. EDTA bottles
12. 70% alcohol
13. Questionnaires.

The study was carried out in the physiology laboratory of the Department of Physiology, University of Benin, Benin City. Subjects were recruited across the geopolitical regions in Benin metropolis.

STUDY POPULATION:

A total of 100 apparently healthy females with regular cycle of 28 days were used in this longitudinal study with age range between 18 and 30.
Sample size will be estimated using the sample size expression (Araoye 2004).

One hundred subjects were used for the study as shown below.

$$n = \frac{z^2 \times p \times q}{c^2}$$

Where;

n = the desired sample size.

c = permissible error.

Z = the standard normal deviation, usually set at 1.96, which correspond to the 95% confidence interval.

p = the proportion in the target population estimated to have a particular characteristic. In this case, a reasonable estimate will be 0.15 (15.4%).

Q = 1.0−p = 1.0−0.15 = 0.846

D = degree of accuracy, usually set at 0.05.

n =100.

Inclusion Criteria: This study included healthy young females in a given population between the age group of 18-30 years having regular menstrual cycles and the normal menstrual cycle of 28+3 days.

Exclusion Criteria: Subjects on alcohol, Contraceptive pills, lactating women, sufferers from diabetes mellitus, cardiovascular abnormalities, Dysmenorrhoea, Oligomenorrhoea, Polymenorrhoea were excluded from the study. Also women with symptoms that could be attributed to other causes, women who been diagnosed of cancer, endometriosis, usual irregular menstrual cycles, or infertility before their reference year were excluded from this study.

Ethical Considerations: Approval and clearance for this study was sought and obtained from the Ethics and Research committee of College of basic medical sciences, School of Medicine University of Benin, Benin City. The Ethical clearance number is SMS/REC/2021/158.

METHOD/PROCEDURE:

The study protocol was explained to the subjects and oral and written informed consent were obtained so that the subjects would participate in the study.

PHASE1 (Administration of questionnaire):

Scientific reasons for questionnaires in the research:

Subjective health and well-being measurements offer a unique scope with which to capture latent health concerns and conditions that cannot be directly (or cost effectively) captured through objective measurement. These are reliable predictors of mortality than standard clinical biomarkers (Borenstein *et al*., 2003).

SAMPLE COLLECTION AND LABORATORY ANALYSIS

Sample collection:

The clinical history of the subjects were noted and different phases of the menstrual cycle (menstrual, follicular and luteal phases) were determined.

Ten (10) mls of blood was drawn by venipuncture after informed consent within the 1st to 5th days of menstruation and between 18th - 26th day of cycle during (Luteal Phase). All samples were collected from the cubital fossa's intravenous blood under standard phlebotomy guidelines.

Laboratory Analysis:

Four (4.0) milliliters were dispensed into Ethylenediamine tetraacetic acid (EDTA) containers for haematological parameters.

1.8mls of whole blood was dispensed into a 0.2ml of sodium citrate bottle and subjected to centrifugation at 4000 rpm for 15 min and the resulting plasma was separated into plain bottles and kept frozen at -20 °C for fibrinogen analysis. All analysis were carried out in the University of Benin Teaching Hospital (UBTH).

Five (5.0) milliliters was dispensed into Lithium heparin containers and subjected to centrifugation at 4000 rpm for 15 mins and the resulting plasma was separated into plain bottle using a Pasteur pipette and kept frozen at -20℃ for trace metals analysis.

The selenium analysis was carried out in University of Ibadan(UI).

STATISTICAL ANALYSIS

Data obtained was analysed by Graph Pad Prism 8.0.1(San Diego, California, USA).

https://www.eajournals.org/ https://doi.org/10.37745/ejbmsr.2013

The differences between the phases were analysed using the independent sample t-test, the differences were analysed using one way analysis 2 variance (ANOVA) and student t-test were used while comparing the phases. A value of $P < 0.05$ was accepted as significant.

RESULTS

Comparing the mean values of the haematological parameters and plasma fibrinogen concentration during the luteal and menstrual phase of young adult female individuals.

Parameters	Menstrual phase	Luteal phase	p-values
WBC	4.826 ± 0.214	4.654 ± 0.175	0.5371
Lymphocyte count	2.788 ± 0.386	8.234 ± 2.168	0.0151
MID count	0.4900 ± 0.05	1.428 ± 0.33	0.0062
Granulocyte count	1.924 ± 0.16	8.546 ± 2.54	0.0106
RBC	3.980 ± 0.05	3.971 ± 0.068	0.9207
Haemoglobin	11.66 ± 0.16	11.76 ± 0.21	0.7142
Haematocrit	33.93 ± 0.447	33.28 ± 0.562	0.3679
MCV	85.47 ± 0.90	84.16 ± 1.01	0.3372
MCH	29.36 ± 0.34	29.70 ± 0.43	0.5351
MCHC	34.37 ± 0.21	35.28 ± 0.20	0.0048
RDW-CV	14.67 ± 0.23	19.93 ± 1.84	0.0057
RDW-SD	48.44 ± 0.63	40.92 ± 1.67	< 0.0001
Platelet count	161.4 ± 8.955	201.8 ± 10.58	0.0044
Fibrinogen concentration	2.755 ± 0.259	3.494 ± 0.198	0.0336

$P<0.05$ indicates significant difference.

Table 1: Above shows the difference in test parameters between luteal phase and menstrual phase. The mean lymphocyte count, MID count, granulocyte count, platelet count and fibrinogen

concentration showed an increase in the luteal phase which was statistically significant while the mean red blood cell count, haemoglobin concentration, packed cell volume and white blood cell showed an increase in the menstrual phase but this was not statistically significant.

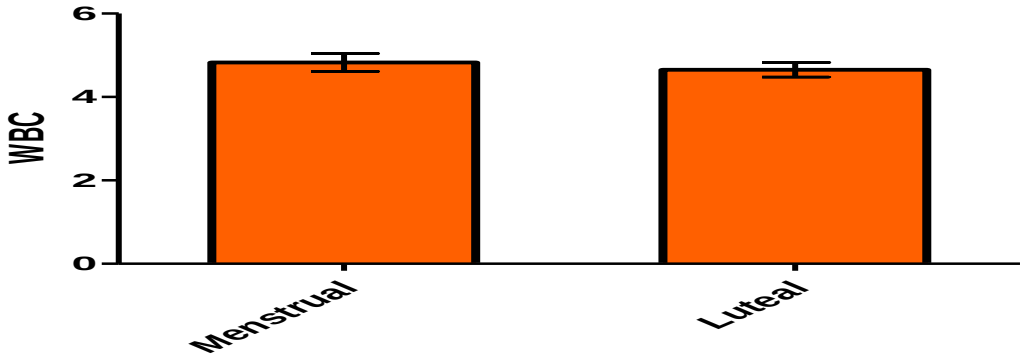

Figure 1: Showing ***WBC*** in luteal and menstrual phase of menstrual cycle in young females.

There was no significant changes in luteal phase compared with menstrual phase.

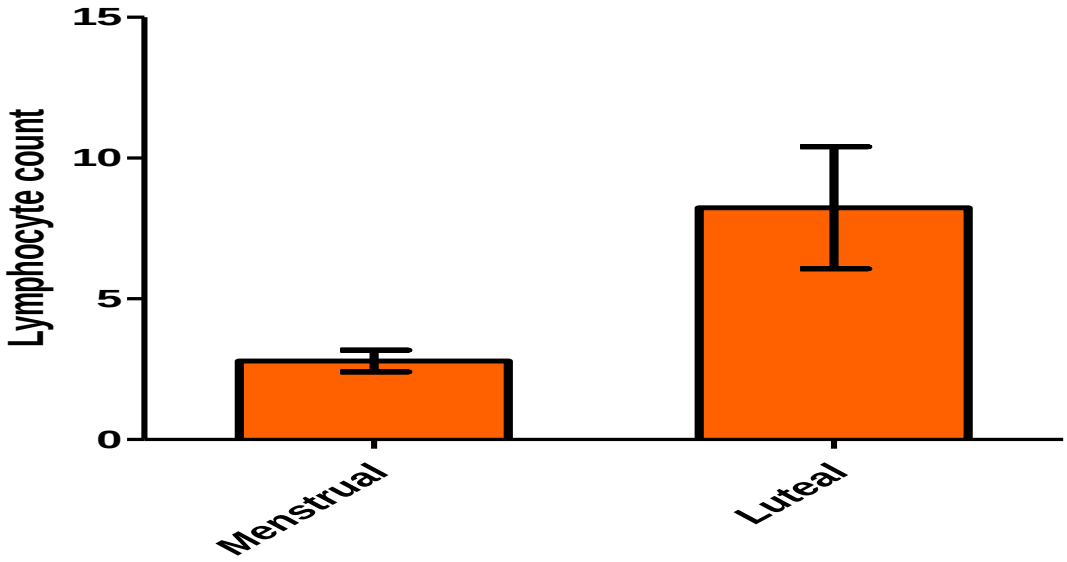

Figure 2: Showing ***lymphocytes count*** in luteal and menstrual phase of menstrual cycle in young females.

There was a significant increase in luteal phase compared with menstrual phase

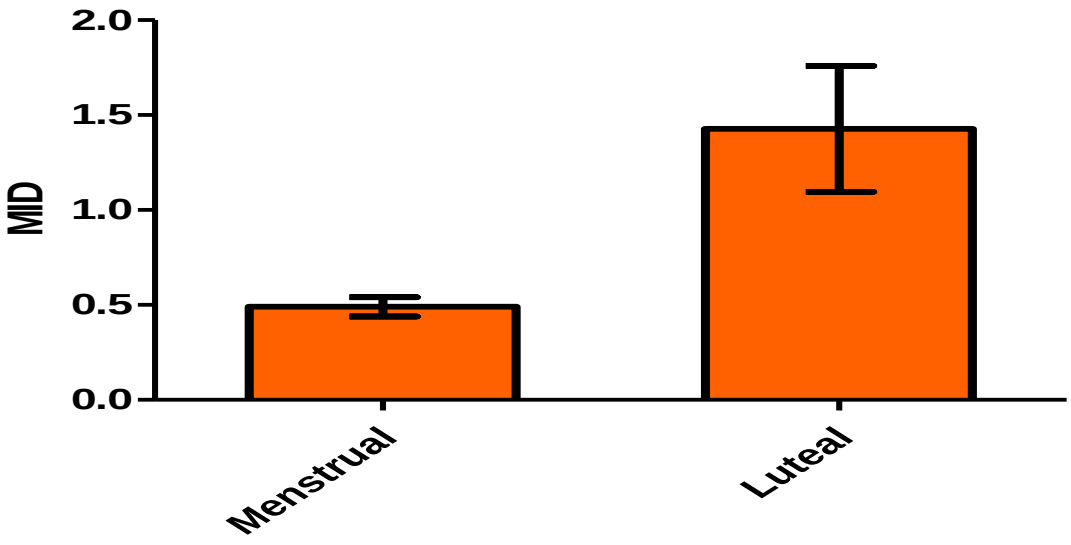

Figure 3: Showing ***MID*** in luteal and menstrual phase of menstrual cycle in young females.

There was a significant increase in luteal phase compared with menstrual phase.

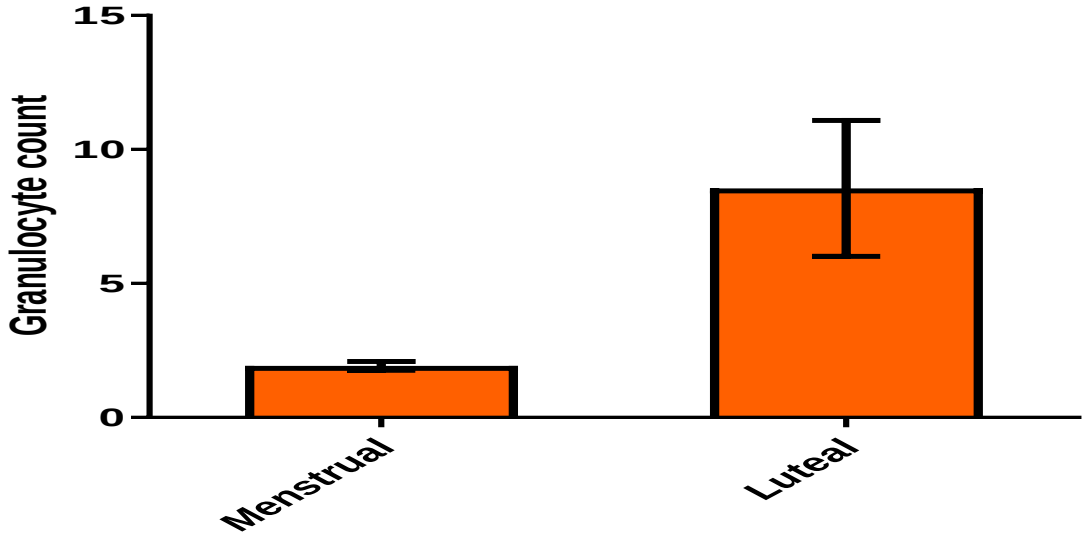

Figure 4: Showing ***granulocyte count*** in luteal and menstrual phase of menstrual cycle in young females.

There was a significant increase in luteal phase compared with menstrual phase.

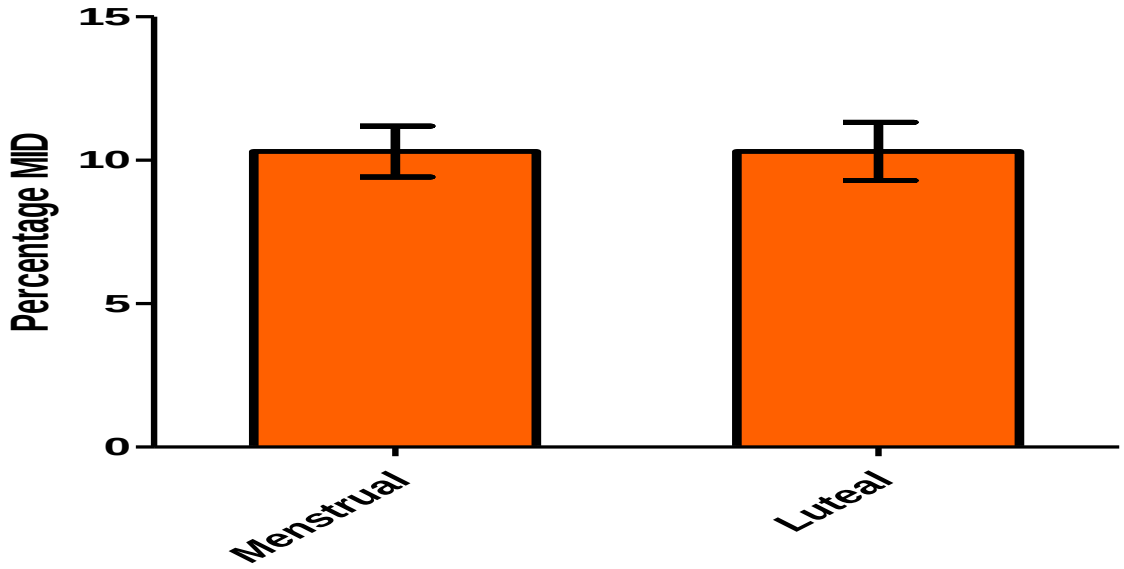

Figure 5: Showing percentage ***MID*** in luteal and menstrual phase of menstrual cycle in young females.

There was no significant changes in luteal phase compared with menstrual phase.

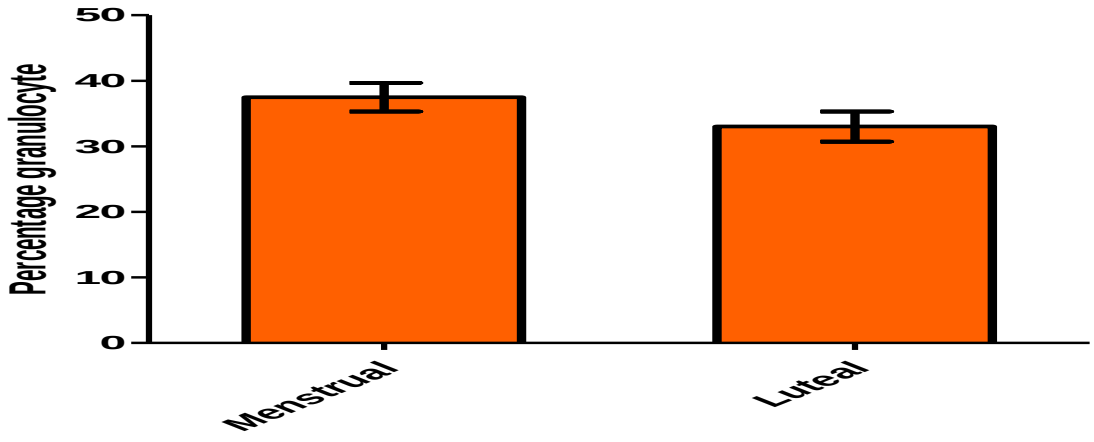

Figure 6: Showing percentage ***granulocyte*** in luteal and menstrual phase of menstrual cycle in young females.

There was no significant changes in luteal phase compared with menstrual phase.

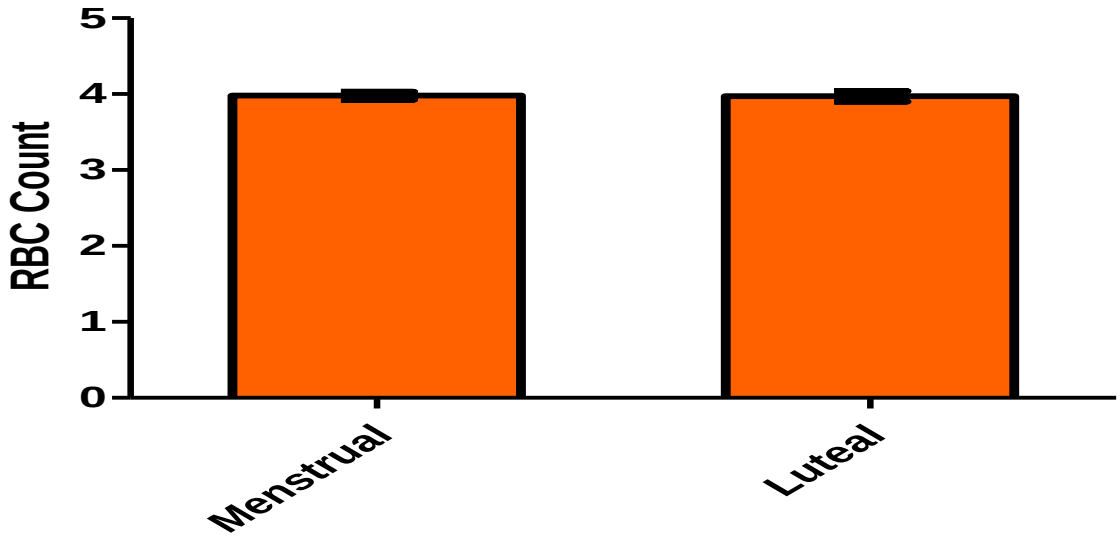

Figure 7: Showing ***RBC*** in luteal and menstrual phase of menstrual cycle in young females.

There was no significant changes in luteal phase compared with menstrual phase.

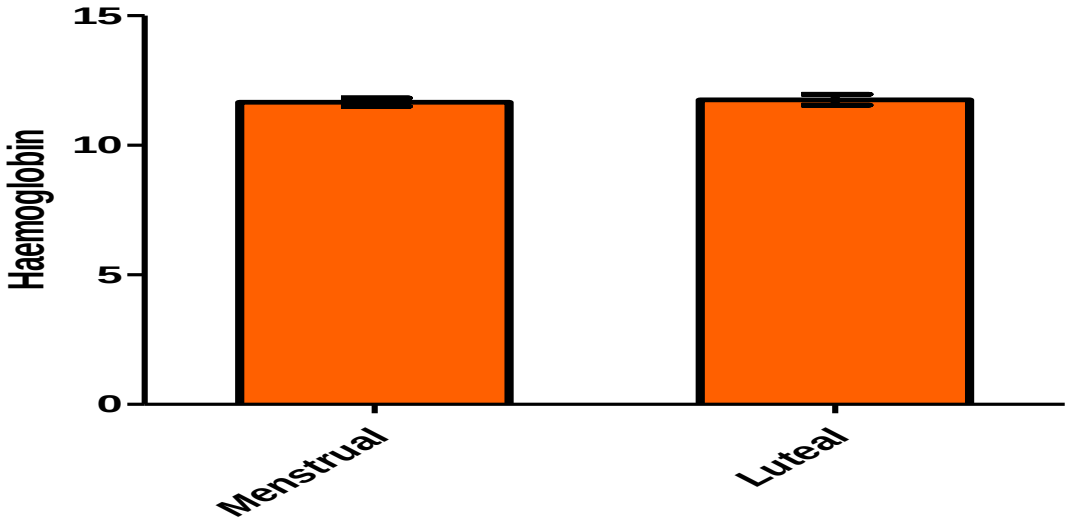

Figure 8: Showing **haemoglobin** in luteal and menstrual phase of menstrual cycle in young females.

There was no significant changes in luteal phase compared with menstrual phase

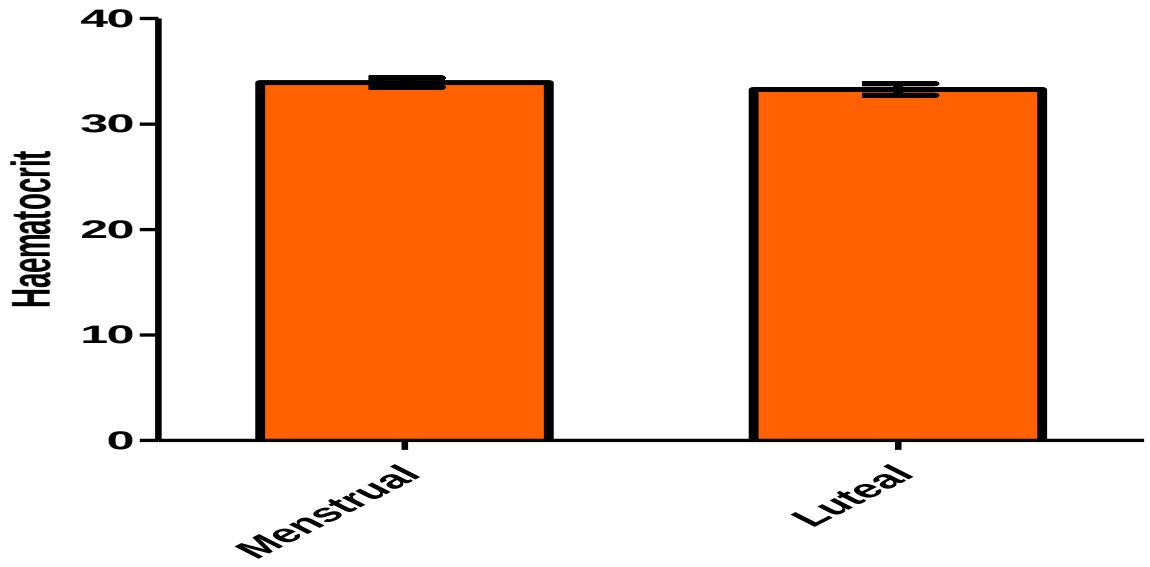

Figure 9: Showing **haematocrit** in luteal and menstrual phase of menstrual cycle in young females. There was no significant changes in luteal phase compared with menstrual phase.

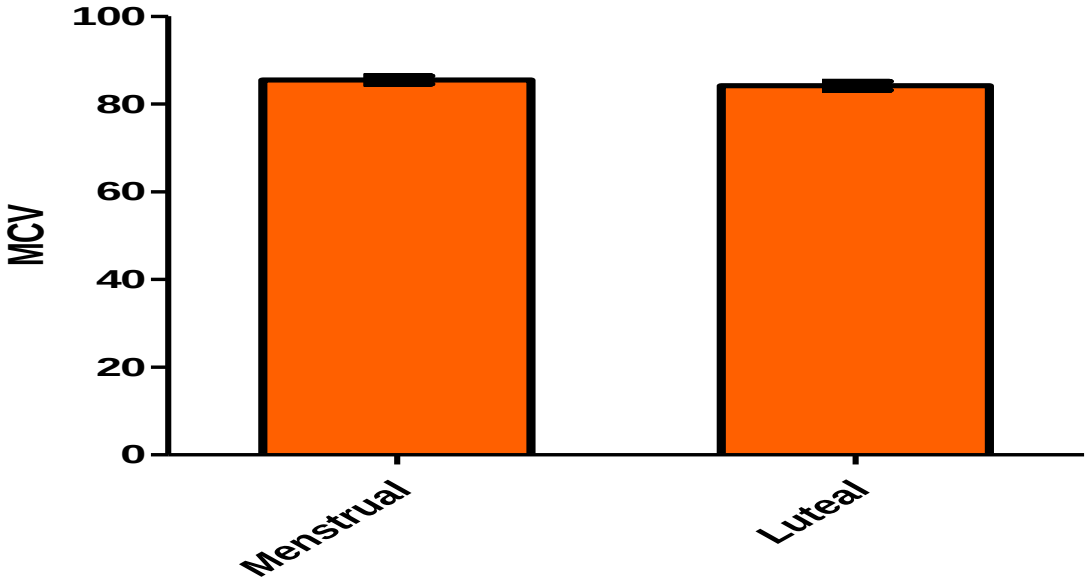

Figure 10: Showing **MCV** in luteal and menstrual phase of menstrual cycle in young females. There was no significant changes in luteal phase compared with menstrual phase

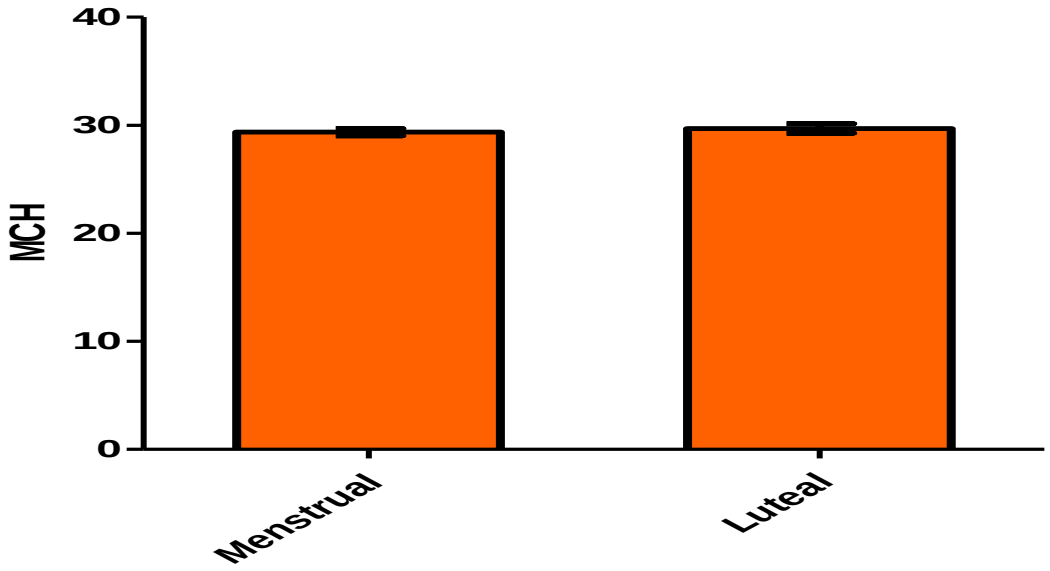

Figure 11: Showing **MCH** in luteal and menstrual phase of menstrual cycle in young females.

There was no significant changes in luteal phase compared with menstrual phase

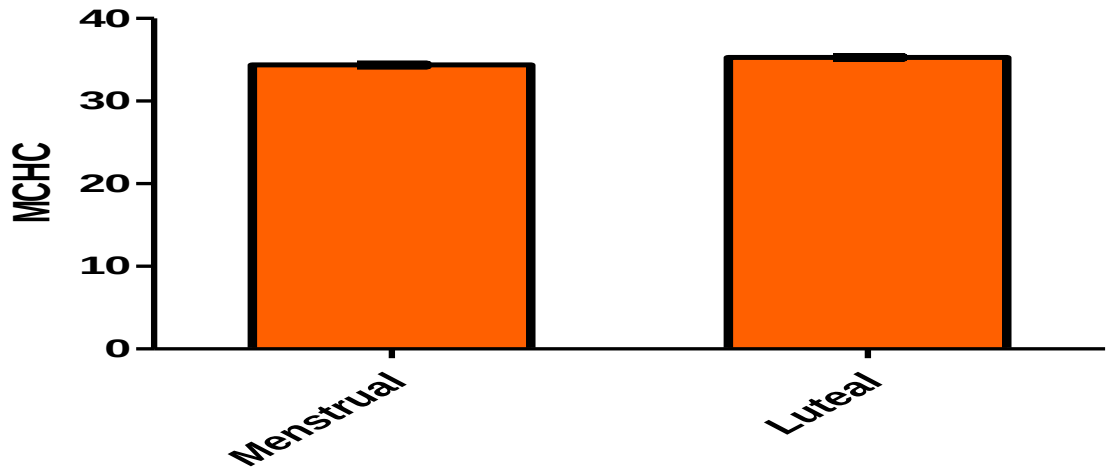

Figure 12: Showing **MCHC** in luteal and menstrual phase of menstrual cycle in young females.

There was a significant increase in luteal phase compared with menstrual phas

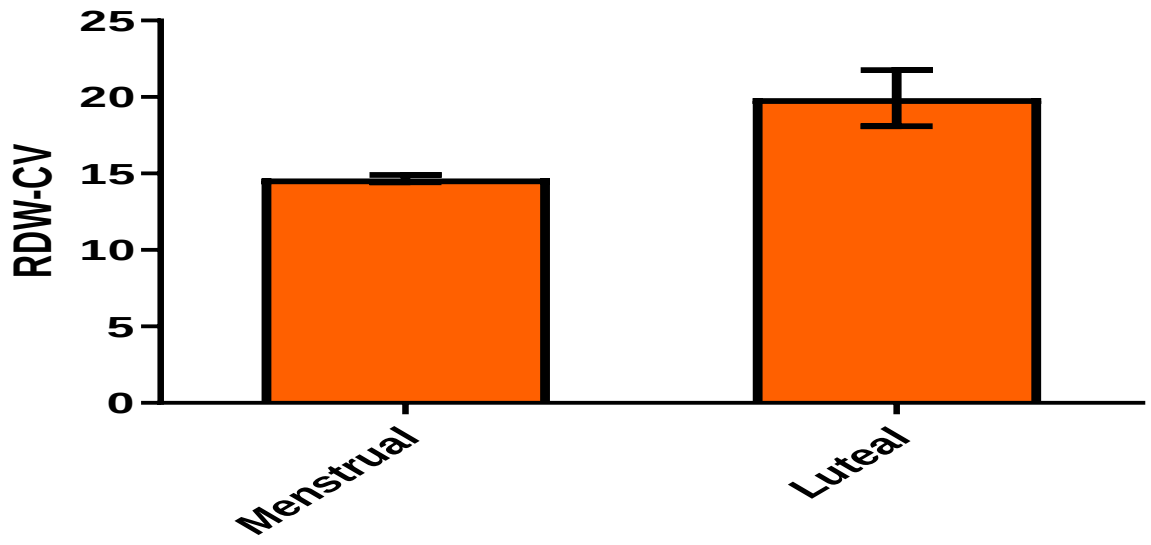

Figure 13: Showing **RDW-CV** in luteal and menstrual phase of menstrual cycle in young females. There was a significant increase in luteal phase compared with menstrual phase.

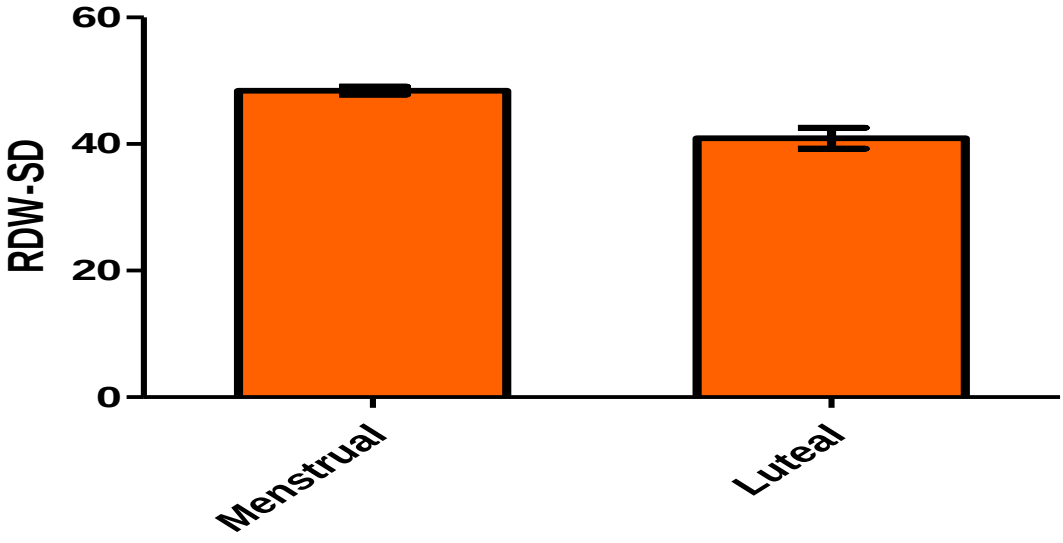

Figure 14: Showing **RDW-SD** in luteal and menstrual phase of menstrual cycle in young females. There was a significant decrease in luteal phase compared with menstrual phase.

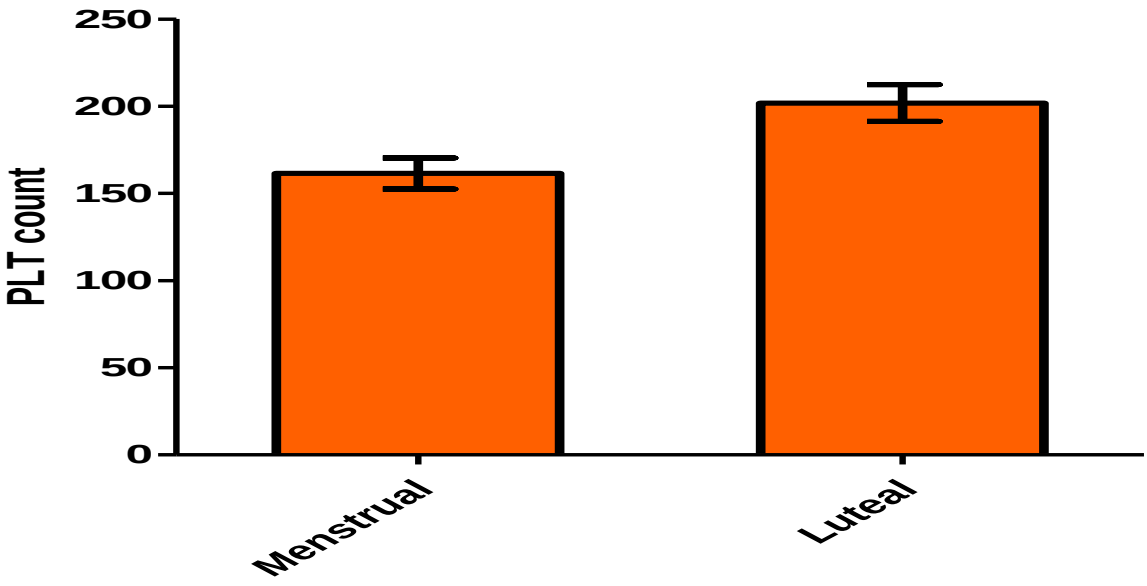

Figure 15: Showing **Platelet count** in luteal and menstrual phase of menstrual cycle in young females.

There was a significant increase in luteal phase compared with menstrual phase.

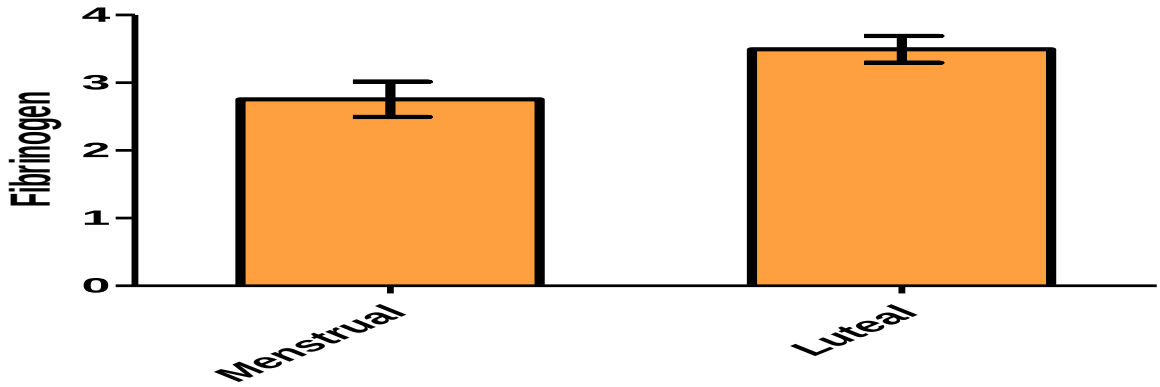

Figure 16: Showing **fibrinogen concentration** in luteal and menstrual phase of menstrual cycle in young females.

There was a significant increase in luteal phase compared with menstrual phase

Table 2: Comparing the mean values of selenium during pre-menstrual and menstrual phase of young adult female individuals.

Parameters	Menstrual phase	Luteal phase	p-values
selenium	46.48 ± 1.712	58.03 ± 3.372	0.0043

P<0.05 indicates significant difference.

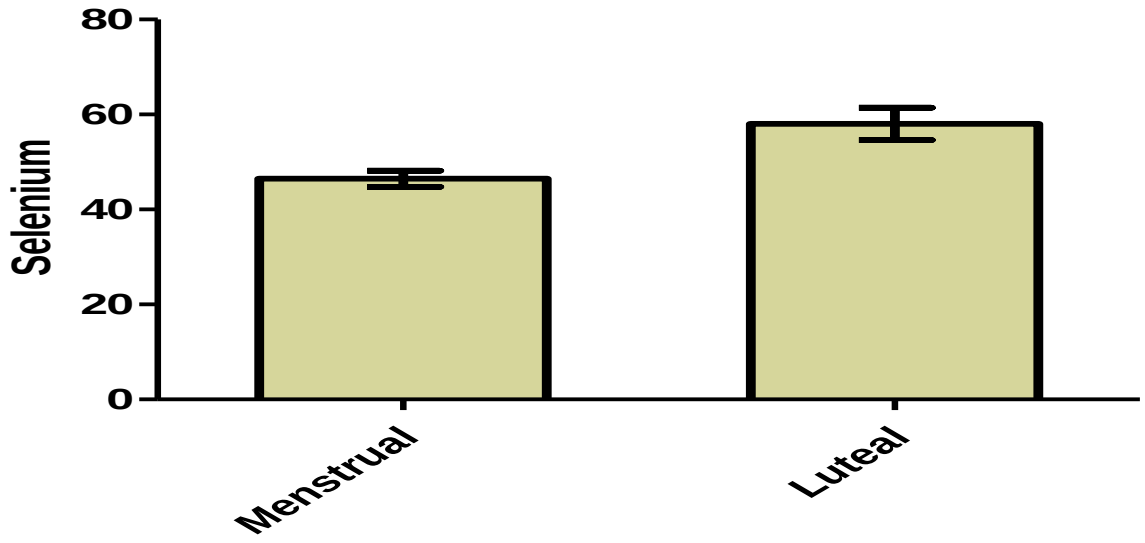

Fig 17: Showing ***selenium level*** in luteal and menstrual phase of menstrual cycle in young females.

There was a significant increase in luteal phase compared with menstrual phase.

DISCUSSION

Result obtained from the study presented that there is a significant increase in the levels of Selenium and fibrinogen during the luteal phase compared to the menstrual phase. The mean fibrinogen concentration showed an increase in luteal phase compared to menstrual phase and this was in agreement with the fact that this increase in fibrinogen concentration could be a progesterogenic effect (Cederblad *et al*., 1977). An elevated level of fibrinogen content during menstrual phase has been attributed to the absence of fibrinogen in menstrual blood leading to raised level of serum (Bhatnagar *et al.,* 1979). Red blood cell count show no significant difference which is in agreement with what was reported by Makinoda *et al.,* 1996.

It was seen that Selenium concentration increased during the luteal phase, and decreased during the menstrual phase. The reason for this difference could be as a result of an inverse relationship

that exists between selenium and estrogen i.e in cases where there is estrogen rise, there is a fall in Selenium concentration and vice versa. This inverse relationship could be as a result of some interactions between Selenium and estrogen receptors Selenium has affinity for estrogen receptors . Another major reason why Selenium concentration us high in the luteal phase and low in the menstrual phase could be because of its importance to aid pregnancy i.e because the luteal phase is characterised by preparation for possible pregnancy, Selenium is needed in this phase to carry out it's supportive function, this is in line with (Hidiloglou,1979) who stated that selenium supplements have been shown to prevent early pregnancy loss.

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