

### **Variations in red blood cells and its indices during different phase of menstrual cycle**

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#### **Abstract**

**Background:** The menstrual cycle is a repetitive phenomenon occurring during the reproductive life of a female due to fluctuations in the concentrations of steroid sex hormones which can influence various organs of humans including hematological parameters.

**Aim & Objectives:** To assess the variation in Red blood cells and its related indices during different phases of menstrual cycle.

**Materials and methods:** Fifty healthy females in the age group of 13-45 years with normal menstrual cycle of  $30 \pm 3$  days were a part of this study. 2ml of venous blood sample was collected under aseptic condition on 2<sup>nd</sup>, between 9<sup>th</sup> to 13<sup>th</sup>, and between 21<sup>st</sup> to 24<sup>th</sup> day of the menstrual cycle. The blood sample was analysed using automated hematology analyzer.

**Results:** Red Blood Cells, Hemoglobin, Hematocrit, Mean Corpuscular Hemoglobin, Mean Corpuscular Hemoglobin Concentration values were lowest during menstrual phase and highest during secretory phase. Statistically significant variations were observed during different phases of menstrual cycles.

**Conclusion:** Significant variations in the mean values of Red blood cells, Hemoglobin, Hematocrit, Mean Corpuscular Hemoglobin and Mean Corpuscular Hemoglobin Concentration were observed in the present study.

**Keywords:** Red Blood cells, Hemoglobin, Hematocrit, Mean Corpuscular Hemoglobin, Mean Corpuscular Hemoglobin Concentration, Menstrual cycle.

#### **Introduction**

The normal reproductive years of the female are characterized by monthly rhythmical changes in the rates of secretion of the female hormones and corresponding physical changes in the ovaries and other sexual organs. This rhythmical pattern is called the female monthly sexual cycle or less accurately the menstrual cycle<sup>1</sup>. The first menstrual cycle is called menarche. The usual age for menarche is 12-14 years<sup>2</sup>. The menstrual cycle consist of three phases namely, menstrual phase (MP), proliferative phase (PP) and the secretory phase (SP)<sup>3</sup>. The menstrual cycle is due to fluctuations in the concentrations of estradiol, progesterone, luteinizing and follicle stimulating

hormones. These fluctuations can affect platelet count, hemoglobin concentration and other haematological parameters. Fluctuations in progesterone and oestrogen concentration can influence Von Willebr and factors in such a way that platelet function is periodically altered during the menstrual cycle<sup>4</sup>.

5-20% of women reporting severe dysmenorrhoea may be associated with reproductive morbidities like infection. Thus, estimation of leucocyte count is an important tool. 9-14% of reproductive women have blood loss that exceeds 80 ml, prolonged and excessive bleeding can provoke or exacerbate anaemia. Thus, there arise the need to estimate Haemoglobin, Red blood cells count and Erythrocyte Sedimentation Rate (ESR) during the menstrual cycle<sup>5</sup>.

Several researchers show that there are some fluctuations in different blood components during different phases of menstrual cycle in normal female. In addition, studies have also been undertaken to see complete blood cells during different phases of menstrual cycle but the results were contradictory and not conclusive. The present study is undertaken to study the variation of red blood cells and its related indices at three different phases of menstrual cycle in normal female.

### Materials and Methods

The present study was a prospective study carried out after getting approval from Medical Ethics Board, RIMS, Imphal. The nature and purpose of the study were fully explained to the subjects for their full cooperation and informed consent were obtained from all the participants. The study was carried out on 50 healthy subjects in the age group of 13 - 45 yrs with normal menstrual cycle of  $30 \pm 3$  days. Those subjects with irregular cycles, Gynaecological disorders, chronic

diseases, history of taking drugs affecting menstrual cycle were excluded from the study. The estimation of total red blood cell (RBCs) count, hemoglobin (Hb), hematocrit (Hct), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC) and red cell distribution width (RDW) were done under the following phases of menstrual cycle:

- a) Menstrual phase (2<sup>nd</sup> day)
- b) Proliferative phase (9<sup>th</sup> to 13<sup>th</sup> day)
- c) Secretory phase (21<sup>st</sup> to 24<sup>th</sup> day)

Blood samples were collected from the ante-cubital vein after taking aseptic precautions during single menstrual cycle. The blood samples were put in a vial containing EDTA anticoagulant. Estimation of RBCs, Hb, Hct, MCV, MCH, MCHC and RDW were performed using Hematology analyzer- Samsung Labgeo HC10.

### Statistical methods

Data collected from the test were subjected to SPSS software version 21. Descriptive statistics such as mean, standard deviation was used to present the data, Data were expressed in mean  $\pm$  SD. Repeated measures ANOVA was used for comparison of the parameters during different phases of menstrual cycle. The p value of  $< 0.05$  indicates statistically significant. For the comparison of mean difference between menstrual phases Post Hoc analysis using Bonseroni test was performed. The p value of  $< 0.05$  was considered statistically significant.

### Results

In the present study, determination of RBCs count, Hb, Hct, MCV, MCH, MCHC and RDW were performed to investigate the modulation of these parameters during different phase of menstrual cycle. The levels were

represented as mean ± standard deviation. There is a significant variation in most of the hematological parameters we investigated such as Red cells, Hemoglobin, MCH and MCHC between different

phases of menstrual cycle. These parameters were highest during secretory phase and lowest during menstrual phase as shown in table 1.

Table 1: Red blood cell and its indices at three different phase of menstrual cycle

| Sn. | Parameters   | Menstrual phase<br>(Mean ±SD) | Proliferative phase<br>(Mean±SD) | Secretory phase<br>(Mean±SD) | P value |
|-----|--|-------------------------------|----------------------------------|------------------------------|---------|
| 1.  | Red blood cells( $\times 10^6$ / $\mu$ L)          | 4.82±0.95                     | 4.99±0.83                        | 5.40±0.87                    | 0.000*  |
| 2.  | Mean corpuscular volume(fL)                        | 86.64±7.25                    | 86.16±7.05                       | 86.28±7.52                   | 0.442   |
| 3.  | Red cell distribution width (%)                    | 15.29±2.93                    | 14.93±2.04                       | 15.16±2.06                   | 0.397   |
| 4.  | Hematocrit (%)                                     | 42.07±6.87                    | 41.88±6.64                       | 44.83±7.22                   | 0.013*  |
| 5.  | Hemoglobin(g/dL)                                   | 13.62±1.98                    | 13.71±1.97                       | 14.75±2.51                   | 0.001*  |
| 6.  | Mean corpuscular hemoglobin<br>(pg)                | 27.20±2.42                    | 27.55±2.49                       | 28.01±2.46                   | 0.000*  |
| 7.  | Mean corpuscular hemoglobin<br>concentration (g/L) | 315.52±14.95                  | 320.60±9.69                      | 322.12±22.08                 | 0.023*  |

\* Significant

Table 2: Multiple comparisons of RBCs, hemoglobin, hematocrit, MCV, MCH, MCHC and Red cell distribution width during different phases of menstrual cycle.

| Sn. | Parameters | Phases   | Mean difference | P value |
|-----|------------|----------|-----------------|---------|
| 1.  | RBCs       | MP vs PP | - 0.172         | 0.605   |
|     |            | MP vs SP | - 0.583*        | 0.000   |
|     |            | PP vs SP | - 0.411*        | 0.000   |
| 2.  | MCV        | MP vs PP | - 0.480         | 0.839   |
|     |            | MP vs SP | - 0.360         | 1.000   |
|     |            | PP vs SP | - 0.120         | 1.000   |
| 3.  | RDW        | MP vs PP | 0.334           | 0.806   |
|     |            | MP vs SP | - 0.132         | 1.000   |
|     |            | PP vs SP | - 0.202*        | 0.036   |
| 4.  | Hematocrit | MP vs PP | 0.183           | 1.000   |
|     |            | MP vs SP | - 2.761*        | 0.026   |
|     |            | PP vs SP | - 2.944         | 0.051   |
| 5.  | Hemoglobin | MP vs PP | - 0.082         | 1.000   |
|     |            | MP vs SP | - 1.124*        | 0.001   |

|    |      |          |          |       |
|----|------|----------|----------|-------|
|    |      | PP vs SP | - 1.042* | 0.025 |
| 6. | MCH  | MP vs PP | - 0.348* | 0.039 |
|    |      | MP vs SP | - 0.086* | 0.000 |
|    |      | PP vs SP | - 0.458* | 0.005 |
| 7. | MCHC | MP vs PP | - 5.080* | 0.034 |
|    |      | MP vs SP | - 6.600  | 0.095 |
|    |      | PP vs SP | - 1.520  | 1.000 |

\* Significant

### Discussion

In the present study, we observed variations in RBCs, hemoglobin, MCH, MCHC and hematocrit during different phases of menstrual cycle. These variations were found to be statistically significant.

The mean value of red cell count is lowest during MP (13.62±1.98) and highest during SP (14.75±2.51). Statistically significant difference were observed between MP and SP (p = 0.000), PP and SP(p = 0.000), but not between MP and PP (p = 0.605). In a study conducted by Arthur Omorgiuwa and Tosin Igeleke<sup>4</sup> among unmarried young girls, they observed a significant decrease in red blood cell indices such as RBCs, hemoglobin and hematocrit during menstruation in comparison to follicular phase of the cycle. This is in agreement with the present study. The decrease red cell count during menstruation cause a decrease in the ratio of red blood cells to plasma. Hence, there is an increase in rouleaux formation and erythrocyte Sedimentation Rate after menstruation<sup>4</sup>. A comparative study of hematological values during ovulation and luteal phases of menstrual cycle conducted by A. Omorogiuwa and E. Egbeluya<sup>6</sup> do not observed any change in red cell parameters during ovulation and luteal phases of menstrual cycle stating that these phases do not involved haemorrhage. Several other studies<sup>3,7,8</sup> reported a non significant increase in red cell count

along with hemoglobin from menstrual phase to secretory phase which is in contrast with the present study.

The mean hemoglobin concentration observed is highest during SP (14.75±2.51) and lowest during MP (13.62±1.98). Statistically significant variation in the mean hemoglobin concentration were found between MP and SP (p=0.001), PP and SP (p=0.025) and non-significant difference between MP and PP as shown in table 2. The haemoglobin level observed is lowest during menstrual period similar to the findings of other studies<sup>6,8,9,10,11</sup>. Hemoglobin exhibit a significant increased from proliferative phase to secretory phase similar to the study conducted by Rajnee et al<sup>12</sup>. The significant difference in hemoglobin concentration may be due to increased erythropoiesis to compensate for the blood loss that occur during menstruation<sup>3,12</sup>. This could possibly affect the levels of hemoglobin in red blood cells<sup>9</sup>. Oestrogen exerts several effects that could reduce hemoglobin concentration and thus the hematocrit values. Oestrogen cause fluid retention, depress erythropoietin synthesis and reduce the bone marrow response to available erythropoietin whereas progesterone antagonises these effects<sup>3</sup>.

There are also other studies which reported a non significant increased from proliferative phase to

secretory phase<sup>3,7,9</sup>. The Hemoglobin concentration were found significantly lower during PP than SP in the present study which is similar to other studies<sup>3,8,9,13</sup>. The natural fluctuations in ovarian hormones during the course of the menstrual cycle influence the secretion of hormones that control the volume and content of the vascular space<sup>9</sup>. Non significant variation of hemoglobin values between menstrual and follicular phase were reported by Mary Jane et al<sup>10</sup> and Y.S Usharani et al<sup>8</sup> which is in line with the present study. The menstrual cycle is affected by so many factors, e.g stress and changes in the diet and iron<sup>9</sup>. Several other studies<sup>7,8,14</sup> show no significant changes in haemoglobin concentration during various phases of menstrual cycle. There was a pronounced tendency towards an increase in red blood cells and haemoglobin from the early menstrual phase until the postovulatory period with a subsequent decrease towards the end of the cycle<sup>3,9,15</sup>. The cyclic variation acts as an indicators of iron status and are a potential source of error when iron status is assessed in a large population surveys that include women of reproductive age<sup>16</sup>. The haemoglobin levels obtained were higher during the secretory phase. This could be due to blood loss during menstruation. This could possibly affect haemoglobin level in red blood cells. The blood loss during menstruation results in negative iron load in women and increases the risk for developing iron deficiency anaemia<sup>10,13,14,17</sup>. Other studies<sup>9,13</sup> indicated that postmenopausal women have higher hemoglobin levels than premenopausal women during the luteal phase. This may be due to high levels of progesterone during the luteal phase in premenopausal women. The present study also observed significant variations in other red cell indices such as hematocrit (MP vs SP)

MCH (MP vs PP, MP vs SP, PP vs SP), MCHC (MP vs PP) during different phases of menstrual cycle. The hematocrit is highest during SP (44.82±7.22) and lowest during MP (42.07±6.87) similar to the findings of other studies<sup>13,18</sup>. The variation in hematocrit value was found significant between MP vs SP (p=0.001) and PP vs SP (p=0.025). Non significant value was reported during follicular and luteal phase in another study<sup>13</sup>. Non significant difference in hemoglobin and hematocrit during menstruation and follicular phase was also reported by Rajnee et al<sup>6</sup>. Moses D Lugos et al<sup>18</sup> stated that, the significance in p values obtained reflects that menstrual bleeding indeed could be a predisposing factor to anaemia, any decrease in hematocrit value observed was due to physiologic condition being experienced as the study was focused on apparently healthy unmarried young girls with no abnormal menstrual bleeding. This finding is in agreement with our study.

MCH and MCHC were highest during SP and lowest during MP (Table 1). A. Omorogiuwa and E.E.Egebeluya<sup>6</sup> observed that red cell indices - red blood cells, MCV, RDW, MCH and MCHC show no significant variation during ovulatory and luteal phase of menstrual cycle. Ibeh Nancy C et al<sup>17</sup> observed statistically increased MCV and MCH level in menopausal women when compared with premenopausal and menstruating women (p = 0.001). The increase was observed to occur progressively from the microcytic to normal range from premenopausal to the menopausal study groups. Pre-existing iron depletion/deficiency stands to be exaggerated by the monthly blood loss that occurs from menarche till the onset of menopause in women.

The hematological and biochemical parameters are indicators of health and nutritional status of women and in turn affect her reproductive capacity. The effect of menstruation alongside several factors such as female sex hormones- oestrogen and progesterone interplay and could possibly affect haematological parameters<sup>4</sup>. This could be the reason why significant variations were observed in red blood cells count, hemoglobin, hematocrit and other indices during different phases of menstrual cycle. The decrease in red blood cells, hemoglobin and hematocrit observed during menstruation may not necessarily lead to an Anemic state. But it is important to have a regular check on these parameters so as to avoid eventual onset of anaemia in menstruating women<sup>17</sup>.

The present study limitations include- study conducted involving only 50 healthy females subjects of reproductive age groups, only specific blood parameter is investigated, we do not estimate the blood loss for each participant nor studied the interaction of factors such as weight, body mass index, level of physical activity, stress and nutritional status of the participants. Further study conducted in larger sample size considering all the above factors may bring conclusive results about the detailed variations in haematological parameters that occur during different phases of menstrual cycle.

### **Conclusion**

In the present study, it has been found that statistically significant variations occur in Hemoglobin, Red blood cells, Hematocrit, MCH, MCHC levels whereas non significant variations were found in MCV and RDW during different phases of menstrual cycles.

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