Hematological modulation in different phases of menstrual cycle

Malipatil B.S1* and Shilpa Patil2

1Dept. of Physiology, M R Medical College, Gulbarga, India
2Postgraduate student, Dept. of Physiology, M R Medical College, Gulbarga, India

*Correspondence Info:
Dr. Malipatil B.S.
Associate Professor,
Dept. Of Physiology, M R Medical College,
Gulbarga, India
Email: malipatilbs@gmail.com

Abstract

Background: Menstruation is a phenomenon unique to females and nearly universal experience in women's lives and is poorly understood. It is characterized by co-ordinated sequence of hormonal changes but the changes occur in haematological parameters, have not been clearly established.

Objective: To compare haematological parameters in different phases of menstrual cycle.

Materials & methods: The present study was carried out on 92 healthy female medical students in the age group of 18 to 23 years with normal menstrual cycle of 27-33 days. Various haematological parameters were studied during menstrual, Proliferative and Secretory phases of menstrual cycle.

Result: The Red blood cell count, hemoglobin concentration, total leucocyte count, Differential leucocyte count, total platelet count showed no significant changes during various phases of menstrual cycle. The Erythrocyte Sedimentation Rate was significantly (P<0.01) higher in menstrual phase compared to proliferative phase.

Conclusion: This study revealed that ESR was significantly higher in menstrual phase compared to proliferative phase without affecting the level of other hematological parameters in different phases of menstrual cycle.

Keywords: Menstrual cycle, Haematological parameters, Biochemical parameters, Electrocardiography

1. Introduction

The menstrual cycle is a window into the general health and well-being of women, and not just a reproductive event. The hormonal changes occurring during menstrual cycle not only affect oocyte maturation and the endometrial and vaginal environment but can also have an effect on a number of other physiological & biochemical phenomena. It can indicate the status of bone health, heart disease, and ovarian failure, as well as long-term fertility. Apart from it being physiological there are various disorders associated with menstrual cycle which cause morbidity & mortality.

The menstrual cycle is characterized by cyclical fluctuations in the levels of FSH, LH, estrogen and progesterone. These hormones are known to have an effect on oxygen carrying capacity, immune response, bleeding and also changes in serum electrolytes which may be responsible for variable physical, psychological symptoms and autonomic changes. It is suggested that stressful situations during ovulatory periods and menstruation may cause increased 17-hydroxy corticosterone levels with resulting eosinopenia. Platelet function is periodically altered during the ovarian cycle due to the influence of progesterone and estrogen on Von Willebrand factor concentrations. Ovarian hormones influence almost all the systems of the body. They are known to alter the immune system like depression of the suppressor T cell activity.

Human & animal studies suggest that there is a change in the distribution of immune cells during different phases of menstrual cycle. 5–20% of women reporting severe dysmenorrhea (painful menstruation) which may be associated with
reproductive morbidities like infection, thus estimation of leucocyte count is an important tool. Females have more asthma throughout the reproductive years. Female sex steroids are pro-inflammatory and will increase the susceptibility to atopy. In developing countries, abnormal uterine bleeding appears to affect about 5–15% of women of reproductive age. It is a major cause of gynecological morbidity, affecting up to one in five women some point during their reproductive life span.

Reproductive-aged women of about 9-14% have blood loss that exceeds 80 ml and prolonged and excessive bleeding may provoke or exacerbate anemia and in a certain percentage of cases, may eventually be life threatening if left untreated, thus there arises a need to estimate Hemoglobin, Red Blood Cell count and ESR during the menstrual cycle. The lack of awareness about the potential importance of reducing menstrual flow when women are anemic and lack of knowledge among women about treatment alternatives is of some concern. The maintenance of different blood corpuscles at normal levels during the menstrual cycle is necessary. Therefore, in the present study, hematological modulation in the different phases of menstrual cycle was studied.

2. Materials and Methods

The study protocol was approved by the institutional ethical committee. Ninety two subjects were recruited after the informed and written consent. In the present study, apparently healthy ninety two female medical students aged between 18-23 years and Normal regular menstrual cycles of 27-33 days with ovulatory cycles were included. Subjects below 18yrs and above 23yrs of age, Subjects with endocrinal & gynecological disorders, chronic diseases, allergic conditions, presence of infection at the time of sampling, subjects with diabetes, pregnancy, subjects with irregular menstrual cycle, and subjects performing regular exercise were excluded.

Venous blood sample was collected from the antecubital vein (2 ml) in a disposable syringe between 1- 2 pm to avoid diurnal variation and counting was done within half an hour to avoid variations due to storage. Blood was taken in EDTA bottle and mixed well. The investigations were performed using Hemo auto analyzer-SYSMEX KX-21 whereas; ESR estimation was performed by Westergren’s method. Reading is taken at the end of 1st hour.

2.1 Statistical Analysis: Data was expressed as Mean ± S.D. and was analyzed for statistical analysis using SPSS 17.0 Software. To compare means of two independent groups, student’s t- test was used.

3. Results

In the present study, hematological parameters like Hemoglobin concentration, RBC Count, WBC Count, Differential Leucocyte Count, Platelet Count, PCV and ESR was performed to investigate the modulation of these parameters in different phases of menstrual cycle was studied. All the parameters in menstrual phase (MP), proliferative phase (PP) and secretory phase (SP) were represented in figure-1 to 5.

The hemoglobin concentration (g/dl), RBC Count, WBC Count, Neutrophil (%), Eosinophil (%), Basophil (%), Monocyte (%), Lymphocyte (%) and Hb Concentration in menstrual phase (MP), proliferative phase (PP) and secretory phase (SP) when compared did not show any significant variation. The Erythrocyte Sedimentation Rate (mm/hr) in MP, PP, and SP were 23.83±11.57, 15.67±9.71 and 18.50±11.31 respectively. It was significantly increased (P<0.01) in MP compared to PP.

![Fig-1: Red Blood Cell count in different phases of menstrual cycle.](https://www.ssjournals.com)

N=92. Variation of RBC Count is non significant between different phases of menstrual cycle.
Fig-2: White Blood Cell count in different phases of menstrual cycle.

N=92. Variation of WBC Count is non significant between different phases of menstrual cycle.

Fig-3: Hb Concentration in different phases of menstrual cycle.

N=92. Variation of Hb Concentration is nonsignificant between different phases of menstrual cycle.

Fig-4: Differential Leucocyte Count in different phases of menstrual cycle.

N=92. Variation of DLC is non significant between different phases of menstrual cycle.
N=92. Variation of ESR is significantly increased (P<0.01) in MP compared to PP whereas; between other phases it was insignificant.

4. Discussion

The human menstrual cycle involves physiological, biochemical, and ECG changes. Haematological and biochemical parameters are the indicators of health and nutritional status of females, which in turn affects its reproductive capability.

In the present study, Hemoglobin and Red Blood Cell Count exhibited a nonsignificant increase from Menstrual Phase (MP) to Secretory Phase (SP), which is in agreement with the earlier reports. Hemoglobin concentration may increase from menstrual phase to secretory phase due to increased erythropoiesis to compensate for the blood loss during menses. The menstrual cycle is affected by so many various factors--e.g., stress and changes in diet and iron. Several other studies showed no significant changes in Hb Concentration and RBC Count during various phases of menstrual cycle. There was a pronounced tendency towards an increase in Hb and RBC Count from the early menstrual phase until the post-ovulatory period, with a subsequent decrease towards the end of the cycle. The cyclic variations act as indicators of iron status and are a potential source of error when iron status is assessed in large population surveys that include women of reproductive age. Some studies showed that hemoglobin concentrations were significantly lower in follicular phase than in the luteal phase. The red blood cell count showed no statistically significant changes during the menstrual cycle. 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.

The Total Leucocyte Count (cells/cmm) was increased in PP compared to other phases but statistically significant values were not noted. Similarly several studies showed no significant changes in TLC during various phases of menstrual cycle. Various studies showed the total WBC count increase from menstrual phase to the secretory phase. Several studies are in general agreement with the fact that the leukocyte count increased during the mid cycle and decreased during secretory phase. Some studies showed no change in the number of circulating leucocytes in relation to the menstrual cycle.

The Neutrophil (%) was increased in PP compared to other phases but statistical significant values were not noted. In other study granulocyte count were significantly higher in the luteal phase compared to the follicular phase. Estrogen seems to enhance granulocyte proliferation in vitro and probably promotes the release of neutrophil from the bone marrow rather than from the marginated pool. Progesterone that is secreted by the ovaries regulate the neutrophil count. The Eosinophil (%) was increased in MP compared to other phases but statistical significant values were not noted. This result was contradictory to in another study, which showed no significant variation during proliferative phase and secretory phase, but demonstrated a significant (p<0.05) fall around mid-cycle. This difference could be due to smaller sample size and different study population.

Similarly menstrual cycle showed no significant change in absolute eosinophil count. In contrast the eosinophil
count significantly dropped at mid-cycle and menstruation, and then its level increased during the secretory phase which occurred as a response to physiological stress where in the levels of steroid hormones increase causing eosinopenia. The Basophil (%) was Zero in different phases of menstrual cycle. In other study the basophil count increased during the luteal phase. In other study basophil count decreased around the secretory phase versus menstrual phase which was probably due to migration of the cells from the peripheral blood into the rupturing follicle of the ovary and into the ischemic premenstrual endometrium.

The Lymphocyte (%) was increased in SP compared to other phases but statistical significant values were not noted. Study showed increase in differential lymphocyte count during proliferative & secretory phase in comparison to menstrual phase probably due to increase in number of Helper T cells, cytotoxic T cells & Natural killer cells, that occurs under the influence of steroids. Several studies showed significant decrease in SP. The Monocyte (%) was increased in MP compared to other phases but statistical significant values were not noted. Several studies showed significant decrease in SP. In other study monocyte count was significantly higher in the luteal phase than in the follicular phase and their pattern followed closely that of progesterone.

The Erythrocyte Sedimentation Rate (mm/hr) was significantly increased in MP compared to PP (P<0.01). Fibrinogen being an acute phase protein could rise during MP due to necrosis of the uterine endometrium because of vasospasm of its blood vessels and inflammatory cell infiltration of the uterine endometrium due to menses and these changes are due to sudden loss of estrogen and progesterone support of the endometrium leading to desquamation. In our study we found significantly increased ESR which might be due to low level of serum albumin. Since in the present study, the RBC count was decreased in MP thus there was decrease in the ratio of RBCs to plasma and hence there was increase in rouleaux formation and ESR in MP. Several studies showed no significant changes of ESR in different phases of menstrual cycle. Some study showed significant increase in fibrinogen whereas significant decrease in Hematocrit & Erythrocyte Sedimentation Rate (ESR) in the menstrual phase.

5. Conclusion

This study revealed that ESR was significantly higher in menstrual phase compared to proliferative phase without affecting the level of other hematological parameters in different phases of menstrual cycle.

References

1. P. Dullo, N. Vedi. Changes in serum calcium, magnesium and inorganic phosphorus levels during different phases of the menstrual cycle. J Hum Reprod Sci. 2008; 1(2):77-80.
2. Feuring M, Christ M, Roell A, Schueller P, Losel R, Dempfle CE, Schultz A, Wehling M. Alterations in platelet function during the ovarian cycle, Blood coagulation and fibrinolysis. 2002 Jul; 13(5):443-7.
3. Drici MD, Burklow TR, Haridasse V et al. Sex hormones prolong the QT interval and downregulate potassium channel expression in the rabbit heart, Circulation. 1996;94:1471–4.
4. Dixon Northern AL, Rutter SM, Peterson CM. Cyclic changes in the concentrations of immune cells during the normal menstrual cycle, Physiol Society of Expt Biol and Med. 1994; 27: 81-88.
5. Pehlivanoglu B, Balkanchi ZD, Ridvanagaoglu AY, Durmazlar N, Ozturk G, Erbas D, Okur H. Impact of stress, gender and menstrual cycle in immune system: Possible role of nitric oxide, Arch Physiol Biochem. 2001; 109:383-387.
6. Sioba’ D, Harlow, Oona M.R. Campbell. Epidemiology of menstrual disorders in developing countries: a systematic review. BJOG: an International Journal of Obstetrics and Gynaecology. January 2004; Vol. 111, pp. 6–16
7. Osman M. Therapeutic implications of sex differences in asthma and atopy, Arch Dis Child. 2003 Jul; 88(7):587-90.
8. Coulter A, Noone A, Goldacre M. General practitioners’ referrals to specialist outpatient clinics. BMJ 1989; 299:304–308.
9. Hallberg L, Hogdahl AM, Nilsson L, Rybo G. Variation at different ages and attempts to define normality and Menstrual blood loss-a population study. Acta Obstet Gynecol Scand. 1966; 45:320–351.
10. Rajnee, Vinod Kumar Chawla, Raghveer Choudhary, Bijendra Kumar, Binawara, Sunita Choudhary. Haematological and electrocardiographic variations during menstrual cycle. *Pak J Physiol* 2010; 6(1): 18-21.

11. Harewood WJ, Gillin A, Hennessy A, Armitstead J, Horvath JS, Tiller DJ. The effects of the menstrual cycle, pregnancy and early lactation on haematology and plasma biochemistry in the baboon (Papio hamadryas). *J Med Primatol*, 2000; Dec; 29(6): 415-20.

12. Kim I, Yetley EA, Calvo MS. Variations in iron-status measures during the menstrual cycle. *Am J Clin Nutr*, 1993 Nov; 58(5): 705-9.

13. Hallberg L., A. Hogdahl, L. Nilsson and G. Rybo, Menstrual blood loss a population study. *Acta Obstet Scand Gynecol*. 1966; 45: 320-322.

14. Simmons, Butterworth Heinemann. Microcytic Hypochromic Anemias in Hematology: A Combined Theoretical and Technical Approach. 1997; 2nd Edn, pp: 53-58.

15. Loraine IA, Bell ET. Hormone excretion during the normal menstrual cycle. *Lancet*. 1963; 1: 1340-2.

16. Makinoda S, Mikuni M, Sogame M, Kobamatsu Y, Yamada H, Yamamoto R, Fujimoto S, Furuta I. Erythropoietin, granulocyte–colony stimulating factor, interlukin-1 beta and interlukin-6 during the menstrual cycle. *Int J Gynaecol Obstet* 1996; 55: 265-71.

17. Pathak NR, Desai CA, Chandwani S. Hematological changes during normal menstrual cycle. *Indian J Physiol Pharmacol*. 1981; 25(4): 440.

18. Pohle FJ. The blood platelet count in relation to the menstrual cycle in normal Women. *Am J Med*. 1939; 197: 40-47.

19. Bouman A, Moes H, Heineman MJ, de Leij LF, Faas MM. The immune responses during the luteal phase of the ovarian cycle: increasing sensitivity of human monocytes to endotoxin. *Fertil Steril*. 2001; 76: 555-559.

20. Bain BJ, England JM. Variations in leucocyte count during menstrual cycle. *Br Med J*. 1975; 2: 473-5.

21. Mathur S, Mathur RS, Goust JM, Williamson HO, Fudenberg HH. Cyclic variations in white cell subpopulations in the human menstrual cycle: correlations with progesterone and estradiol. *Clin Immun Immunopath*. 1979; 13: 246–253.

22. Hulot JS, Demolis JL, Riviere R, Strabach S, Maître S, Brentano C. Influence of endogenous oestrogens on QT interval duration. *Eur Heart J*. 2003; 24: 1663–7.

23. D.V.B. Dapper & B.C. Didia. Haemorrheological changes during the menstrual cycle. *East African Medical Journal* vol. 2002; 79(4): 181-183.

24. Faas MM, Bouman A, Moes H, Heineman MJ, Leij LF, Schuiling G. The immune response during the luteal phase of the ovarian cycle: a Th2-type response. *Fertil Steril*. 2000; 74: 1008–1013.

25. Leon S, Robert H, Nathan G. Clinical Gynecologic Endocrinocology and Infertility, 4th Edn, William and Willkins Publication; pg-132.

26. Guyton AC. Textbook of Medical Physiology. Eighth edition. W. B. Saunders Philadelphia; 1991

27. A.K. Jain, Manual of Practical Physiology. 4th edn. Arya publications; 2012: 50-53

28. Indu Khurana, Text book of Medical Physiology. 1st edn. Elsevier publication; 2006: 143-144.

29. Korubo Owiye T, Dapper & Emakpor A C. The effect of cigarette smoking on some haemorrheological parameters. *Nig Med Pract*. 1997; 33: 52-55.