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HAEMORHEOLOGICAL CHANGES DURING THE MENSTRUAL CYCLE

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ABSTRACT

Objective: To determine changes in some haemorheological parameters: haematocrit (Hct), Whole Blood Relative Viscosity (WBRV), Erythrocyte Sedimentation Rate (ESR) and Fibrinogen Concentration (FC) during the menstrual cycle.

Design: Cross-sectional prospective study.

Subjects: Three hundred and fifty randomly selected female undergraduate students of the University of Port Harcourt, Port Harcourt, Nigeria.

Setting: Departments of Human Physiology and Anatomy, Faculty of Basic Medical Sciences, College of Health Sciences, University of Port Harcourt, Port Harcourt, Nigeria.

Main outcome measures: Significant variation ($p < 0.05$) were found in the values of all four haemorheological parameters assessed in the various phases of the menstrual cycle.

Results: Both haematocrit (Hct) and Whole Blood Relative Viscosity (WBRV) showed a similar trend, being highest in the ovulatory phase, followed by the luteal phase and follicular phase, and lowest in the menstrual phase. The Erythrocyte Sedimentation Rate (ESR) however, showed a pattern opposite to both Hct and WBRV, being highest in the menstrual phase followed by the luteal phase, and the follicular phase, and lowest in the ovulatory phase. The Fibrinogen Concentration (FC) was highest in the menstrual phase, followed by the ovulatory phase, the luteal phase and was lowest in the follicular phase.

Conclusion: The study shows that significant variation could occur in some haemorheological parameters during the phases of the normal menstrual cycle.

INTRODUCTION

Though previously neglected for over half a century, haemorheologic changes have recently gained attention, because of their possible role in the pathogenesis of arterial hypertension(1). Changes in whole blood viscosity, plasma viscosity and fibrinogen concentration, have all shown independent but strong correlation with blood pressure in large population studies(2-4). However, other reports have shown an inverse effect by fibrinogen concentration and a small contributory effect by haematocrit in males(5). In black Africans, an insidious role in the development of hypertension has been ascribed to haemorheologic changes(6).

Profound physiologic changes occur in females during the monthly menstrual cycle(7). These include changes in blood pressure(8), variations in haematocrit(9), cyclic changes in thrombocyte count(10) and white cell count(11). These changes are due to the effect of the female sex hormones: oestrogens and progesterone and the pituitary gonadotropins(7). These reported variations of vascular and haematologic parameters could possibly influence blood viscosity. Studies on haemorheological changes in black Africans are relatively scarce(12), this is especially with regard to changes during the menstrual cycle. Such studies are important to fully understand the possible role

of blood viscosity changes play in determining reported changes in blood pressure during the menstrual cycle(8).

The present study reports changes in some haemorheological parameters in female undergraduate students of the University of Port Harcourt, Port Harcourt, Nigeria during the menstrual cycle. Previous studies in Nigeria have focussed on haematologic changes during the menstrual cycle(13).

MATERIALS AND METHODS

Subjects: A total of 350 females aged between 18 and 27 years were recruited for the study. They were selected by systematic random sampling from the female undergraduate student population of the University of Port Harcourt, Port Harcourt, Nigeria. Each student gave informed consent and none had antecedent history of nutritional, hepatic, cardiovascular, endocrine, metabolic or neurologic disease. Each was physically examined and found apparently healthy. Subjects on any medication and subjects who were clinically pale and with haematocrit scores less than 30%(19) were also excluded from the study. Only subjects with 28 days menstrual cycles with three to five days of menstruation for at least one year were recruited into the study. All subjects were instructed to abstain from cigarette smoking, alcohol consumption and excessive physical activity during the study period.

Blood collection: Each subject reported to the laboratory between 9 am and 12 noon each day. On arrival they were

allowed to rest comfortably for at least 30 minutes before blood collection. Five millilitres of blood was collected from an antecubital vein with the subject comfortably seated and with minimum stasis. The blood was immediately transferred into trisodium citrate specimen bottles and carefully mixed. All specimens were analysed within two hours of collection.

Methods: Haematocrit (Hct) was determined using Hawksley microcapillary tubes centrifuged at 3000 rpm for 10 minutes. The mean of two separately obtained readings was taken as the haematocrit value. Erythrocyte Sedimentation Rate (ESR) was estimated by the method of Westergren as described by Dacie and Lewis (14). Fibrinogen Concentration (FC) was determined by the clot weight method as described by Ingram (15). The weight obtained was recorded in g/dl.

Relative viscosity of whole blood was determined by capillary viscometry, using a method first described by Reid and Ugwu in 1987 and modified by Korobo-Owiye *et al* (12) in 1997.

All haemorheological parameters were determined at the different phases of the menstrual cycle i.e. menstrual, follicular, ovulatory and luteal in all subjects. All parameters were determined at room temperature ($20^{\circ}\text{C} \pm 0.05$).

Statistics: The means, standard deviation and standard error of mean were calculated and statistical significance determined using the single factor analysis of variance (ANOVA). Results are as presented in Table 1.

RESULTS

Table 1 shows the means, standard deviation and ranges of the Haematocrit (Hct), Whole Blood Relative

viscosity (WBRV), Erythrocyte Sedimentation Rate (ESR) and Fibrinogen Concentration (FC) obtained in the different phases of the menstrual cycle for all subjects. Analysis of variance showed significant differences ($p < 0.05$) in the values of all four haemorheological parameters in the different phases of the menstrual cycle.

The mean value of haematocrit (Hct) was found to be highest in the ovulatory phase ($40.86 \pm 0.91\%$), followed by the luteal phase ($39.82 \pm 0.82\%$) and the follicular phase ($39.26 \pm 0.98\%$). The lowest value of $38.09 \pm 1.34\%$ was recorded also in the menstrual phase. The values of WBRV showed a pattern similar to that of haematocrit (Hct), being highest in the ovulatory phase (2.41 ± 0.16),

followed by the luteal phase (2.37 ± 0.08) and the follicular phase (2.36 ± 0.07). The lowest value was recorded in the menstrual phase (2.17 ± 0.12). However, ESR showed a pattern opposite that of both haematocrit (Hct) and WBRV. The mean value of the erythrocyte sedimentation rate ESR was found to be highest in the menstrual phase ($10.66 \pm 2.07\text{mm/hr}$) followed by the luteal phase ($9.17 \pm 1.15\text{mm/hr}$) and the follicular phase ($8.80 \pm 0.87\text{mm/hr}$). The lowest value of $8.29 \pm 0.67\text{mm/hr}$ was recorded in the ovulatory phase.

The values of FC were found to be highest in the menstrual phase ($3.57 \pm 0.40\text{g/dl}$), followed by the ovulatory phase ($2.53 \pm 0.40\text{g/dl}$) and the luteal phase ($1.79 \pm 0.29\text{g/dl}$). The lowest value was found in the follicular phase ($1.47 \pm 0.44\text{g/dl}$).

Both FC and the ESR were found to be highest in the menstrual phase, unlike the haematocrit (Hct) and the whole blood relative viscosity (WBRV) which were lowest in the menstrual phase. However, fibrinogen concentration (FC) and erythrocyte sedimentation rate (ESR) did not show the same pattern in the other phases of the menstrual cycle compared to both haematocrit (Hct) and WBRV.

DISCUSSION

The results of the present study clearly indicate that all four haemorheological parameters studied show significant ($p < 0.05$) changes during the menstrual cycle.

Table 1

Values of the Haemorheological parameters in the different phases of the menstrual cycle

	Menstrual phase (n=350)	Follicular phase (n=350)	Ovulatory phase (n=350)	Luteal phase (n=350)	F value	Fcrit	Significance (ANOVA)
Haematocrit (Hct) (%)	38.09 ± 1.34 (34-40)	39.26 ± 0.98 (37-41)	40.86 ± 0.91 (39-42)	39.82 ± 0.82 (38-41)	43.96	2.67	Yes ($P < 0.05$)
Whole Blood Relative Viscosity (WBRV)	2.17 ± 0.12 (2-2.3)	2.36 ± 0.07 (2.3-2.5)	2.41 ± 0.16 (2-2.6)	2.37 ± 0.08 (2.2-2.5)	32.32	2.67	Yes ($P < 0.05$)
Erythrocyte Sedimentation Rate (ESR) (mm/1 hr)	10.66 ± 2.07 (7-15)	8.80 ± 0.87 (7-10)	8.29 ± 0.67 (7-9)	9.17 ± 1.15 (7-12)	21.35	2.67	Yes ($P < 0.05$)
Fibrinogen Concentration (FC) (g/dl)	3.57 ± 0.04 (3-4)	1.47 ± 0.44 (1-2.5)	2.53 ± 0.40 (2-3)	1.79 ± 0.29 (1.5-2.5)	202.8	2.67	Yes ($P < 0.05$)

Viscosity (WBRV), Erythrocyte Sedimentation Rate (ESR) and Fibrinogen Concentration (FC) obtained in the different phases of the menstrual cycle for all subjects. Analysis of variance showed significant differences ($p < 0.05$) in the values of all four haemorheological parameters in the different phases of the menstrual cycle.

The mean value of haematocrit (Hct) was found to be highest in the ovulatory phase ($40.86 \pm 0.91\%$), followed by the luteal phase ($39.82 \pm 0.82\%$) and the follicular phase ($39.26 \pm 0.98\%$). The lowest value of $38.09 \pm 1.34\%$ was recorded also in the menstrual phase. The values of WBRV showed a pattern similar to that of haematocrit (Hct), being highest in the ovulatory phase (2.41 ± 0.16),

An interplay of several factors, including the effect of menstruation and of the female sex hormones: oestrogen and progesterone, could possibly account for these haemorheological changes.

Cyclic changes in haematocrit (Hct), during the menstrual cycle have earlier been described (9,13) and were confirmed in the present study. The lowest value of haematocrit reported during the menstrual phase is likely due to the blood loss that occurs at this phase of the cycle, leading to a reduction in red cell population. Unexpectedly however, the highest value of haematocrit (Hct) was observed during the ovulatory phase of the menstrual cycle, the subsequent luteal phase value being slightly lower. This variation cannot be fully explained by menstrual

loss alone. Perhaps changes in the concentration of the female sex hormones: oestrogen and progesterone during the menstrual cycle could contribute. From initially low levels during the menstrual phase, oestrogen levels begin to rise gradually and peak towards the end of the follicular phase(20). Oestrogen levels subsequently falls during the ovulatory phase, following which progesterone levels begin to rise. Both hormones rise again during the luteal phase, with progesterone now reaching peak levels. oestrogens exert several effects that could reduce haemoglobin concentration and thus haematocrit values. Oestrogens cause fluid retention, depress erythropoietin synthesis and reduce the bone marrow response to available erythropoietin(21). These effects are however, antagonised by progesterones(21). The reduced haematocrit observed during the luteal phase is therefore probably due to the effects of the peak oestrogen towards the end of the follicular phase. The combined effects of oestrogen and erythropoietin on erythropoiesis would require a minimum of five days to manifest(20).

Expectedly, the whole blood relative viscosity (WBRV) showed a trend similar to that of haematocrit (Hct), being highest at the ovulatory phase and lowest at the menstrual phase. Though several interdependent factors largely influence blood viscosity(14,17), haematocrit plays a primary role(17), therefore blood viscosity would largely increase and decrease along with haematocrit(22).

Fibrinogen being an acute phase protein would expectedly rise during the menstrual phase of the menstrual cycle. This is because of the necrosis of the uterine endometrium due to vasoplasm of its blood vessels and inflammatory cell infiltration of the uterine endometrium during the process of menstruation. These endometrial changes are initiated by the sudden loss of hormonal: oestrogen and progesterone, support of the endometrium leading to its desquamation(7,20). The elevated fibrinogen concentration could account for elevation of the erythrocyte sedimentation rate, (ESR) during the menstrual phase. This is because rouleaux formation and the process of erythrocyte sedimentation are enhanced by increases in fibrinogen concentration(12,14,19). It is also an established fact that the ESR is higher in females compared to males, likely because of the effects of menstruation and pregnancy(18).

The present study clearly demonstrates that significant haemorheologic changes could occur during the menstrual cycle. Results of this study suggests that blood viscosity apparently is highest during the ovulatory phase and lowest during the menstrual phase of the menstrual cycle. The physiological and clinical significance of these changes is at present unclear.

In conclusion, we report significant ($p < 0.05$) variation of haematocrit (Hct), whole blood relative viscosity (WBRV), erythrocyte sedimentation rate (ESR) and fibrinogen concentration (FC) during the different phase of

the menstrual cycle. Our results suggest that blood viscosity is apparently highest during the ovulatory phase and lowest during the menstrual phase of the menstrual cycle.

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