

## PLASMA FIBRINOGEN LEVELS DURING THE DIFFERENT PHASES OF MENSTRUAL CYCLE – A SCIENTIFIC INSIGHT

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### ABSTRACT:

This study was aimed at determining the association between levels of plasma fibrinogen, a marker of blood viscosity and the different phases of the menstrual cycle. Hence this study was conducted on 51 students in the age group of 17 to 19 years. Subjects with regular menstrual cycles were selected and blood samples were collected from them on the 7th and 25th day of the menstrual cycle that fall on the early follicular and late luteal phases respectively. Plasma fibrinogen level was estimated by Microturbidometric method. Plasma fibrinogen was

significantly elevated in the early follicular phase when compared to the late luteal phase. ( $P < 0.001$ ) Elevated plasma fibrinogen values in the early follicular phase suggest that ovarian hormonal activity influences haemorheology and blood flow. The clinical significance of these rheological changes remains to be established, but at least theoretically there may be an increased risk of thromboembolism, e.g. at surgery, during days 5-15 of the cycle.

**Keywords :** haemorheology, follicular phase, luteal phase microturbidometry.

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### INTRODUCTION:

Blood viscosity during the menstrual cycle in healthy women shows that it is the lowest at the start of the bleeding and increases to a peak at day 7. The clinical significance of these rheological changes remains to be established, but at least theoretically there may be an increased risk of thromboembolism, e.g. at surgery, during days 5-15 of the cycle<sup>1</sup>.

Therefore, in an attempt to establish possible correlations between blood viscosity with different phases of the menstrual cycle, a study in this regard is conducted where plasma fibrinogen level, a marker of blood viscosity is estimated during the follicular and the luteal phases of menstruation.

### Objectives:

1. To assess and compare the plasma fibrinogen level in the early follicular and luteal phases of menstrual cycle in healthy adult population.
2. To associate plasma fibrinogen level variations with the number of days of menstrual bleeding.
3. To study the associations if any between different grades of physical activity and plasma fibrinogen levels.

### MATERIALS & METHODS:

The study was conducted on 51 female students of Sri Ramachandra Medical College in the age group of 17 to 19 years after obtaining an ethical committee clearance and volunteer informed consent. Subjects with regular menstrual cycles were included for the study. Blood

samples were collected from them on their 7th and 25th day of menstrual cycle that fall on the early follicular and late luteal phases respectively. Subjects with history of any infection, inflammation and those who are under any treatment for any condition were also not included in this study.

The subjects were asked to provide a detailed history regarding their personal, menstrual and physical activity in the proforma handed out. Height and weight were also recorded.

Plasma fibrinogen level, a marker of blood viscosity was estimated by Micro turbid metric method of Parfentjev<sup>2</sup> and Johnson. Once the blood sample was collected, it was centrifuged and the plasma was separated out. The fibrinogen in the plasma was precipitated with ammonium sulphate and the resulting turbidity was estimated as optical density from the amount of light transmitted to the photoelectric cell of a spectrophotometer. A commercial preparation was selected and used as a standard protein solution and various concentrations were analysed. The relationship of increasing optical densities to increasing concentrations of fibrinogen are a straight line in a graph, indicating that the turbidity varies directly with the fibrinogen levels of the protein solutions studied. Now, the plasma fibrinogen concentration was derived from this optical density value using the standard line graph that was plotted to standardise the procedure.

The levels of physical activity are graded as follows.

Grade 0- Inactive; The subject has a sit-down job with no regular physical activity.

Grade 1- Relatively inactive; Three to four hours of walking or standing per day and the subject has no regular organized physical activity during leisure time.

Grade 2- Light physical activity; The subject is sporadically involved in recreational activities such weekend golf or tennis, occasional jogging, swimming or cycling.

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Grade 3- Moderate physical activity; The subject participates regularly in recreational/ fitness activities such as yoga, jogging, swimming or cycling at least three times per week for 30 to 60 minutes each time.

Grade 4- Very vigorous physical activity; the subject participates in extensive physical activity for 60 minutes.

The statistical analysis was conducted using SPSS version 7.0 software. P values less than 0.5 was considered statistically significant.

The levels of physical activity of the subjects were graded from zero to five(0-5) and were correlated with the corresponding plasma fibrinogen levels during both follicular and luteal phase.

## RESULTS:

**Table 1 :** Estimation of plasma fibrinogen in the different phases of menstrual cycle.

Period	Mean plasma fibrinogen level mg/dl	significance
Follicular Phase	364.10 + 65.39	0.000P <0.001
Luteal Phase	256.25 + 59.58	

**Table 2 :** Correlation between plasma fibrinogen level and the number of days of menstrual bleeding.

Period	No of days of bleeding	Mean plasma fib. Level in mg/dl	SIG.
Follicular phase	< 4 days	366.37+62.57	0.053 P>0.005
	> 4 days	308.50+139.30	
Luteal Phase	< 4 days	253.69+54.19	0.003 P<0.01
	> 4 days	319.00+168.29	

**Table 3 :** Correlation between plasma fibrinogen level and the levels of physical activity.

### Follicular phase :

Level of physical activity	Mean plasma fibrinogen level in mg/dl	Sig
0	0	0.128P >0.05
1	413.4+20.27	
2	356.19+67.10	
3	385.11+59.80	
4	332.33+69.82	

**Table 4 :** Luteal Phase

Level of physical activity	Mean plasma fibrinogen level in mg/dl	Sig
0	0	0.512P >0.05
1	278.0+76.11	
2	258.10+58.84	
3	256.56+78.09	
4	228.17+23.68	

**Table 5 :** Mean plasma fibrinogen and mean plasma estrogen during the different phases of menstrual cycle

Period	Days in a cycle	Mean estrogen value in pg/ml	Mean plasma fibrinogen level mg/dl
Follicular phase	1-9	57.6	364.10 + 65.39
Luteal phase	24-29	132.8	256.25 + 59.58

## DISCUSSION:

Based on the results obtained, I have analysed the plasma fibrinogen level in relation to plasma estrogen, duration of menstrual cycle and the levels of physical activity during the different phases of menstrual cycle and also compared with the results of the other studies.

It is quite evident from the results that the plasma fibrinogen level in the early follicular phase is elevated when compared to the luteal phase and the increase is found to be statistically significant.

Comparison of standard plasma mean estrogen values with that of the mean plasma fibrinogen levels estimated during different phases of menstrual cycle have clearly shown a negative relation between the plasma fibrinogen level and the corresponding estrogen values i.e a decreased estrogen during the follicular phase and an increased level during the luteal phase.

The above findings are in concurrence with the study done by Solerte SB et al<sup>3</sup>st on blood rheology in healthy women throughout a normal menstrual cycle. Significant increases in fibrinogen, blood and plasma viscosity, was demonstrated during the follicular and ovulatory phase in comparison with mid- and late luteal phase of the menstrual cycle. Associations were found between oestradiol levels and the haemorheological variables suggesting that ovarian hormonal activity influences haemorheology and blood flow.

Larsson H et al<sup>1</sup> studies on blood viscosity during the menstrual cycle in healthy women showed that it was the

lowest at the start of the bleeding and increased to a peak at day 7. The clinical significance of these rheological changes remains to be established, but at least theoretically there may be an increased risk of thromboembolism, e.g. at surgery, during days 5-15 of the cycle.

The levels of physical activity of the subjects were graded from zero to five (0-4) and were correlated with the corresponding plasma fibrinogen levels during both follicular and luteal phase. The results obtained in this regard during both the phases, though the physical activity showed no relation with the plasma fibrinogen levels statistically and there is a difference in the plasma fibrinogen level between grade 0 and 4 indicating that fibrinogen level is moderately high in the physically inactive persons.

Rankinen T, et al studied the relationship between habitual physical activity and plasma level of fibrinogen in a cohort of 180 postmenopausal women, aged 60-69 years<sup>4</sup>. For further analysis, the association between physical activity and fibrinogen level of the subjects were classified into three categories according to their weekly physical activity frequency: i.e 0 to 1, 2 to 3, and 4 or more during the preceding month. The data suggests that in postmenopausal women a low level of physical activity is associated with a high level of plasma fibrinogen. In our study the insignificant relation between plasma fibrinogen and physical activity may be due to the younger age group of the subjects we have selected.

#### CONCLUSION:

- A statistically significant elevated plasma fibrinogen level in the early follicular phase was observed when compared to the luteal phase.
- Though there was an increased plasma fibrinogen in inactive persons, the physical activity did not correlate significantly with the plasma fibrinogen levels.

Overall this study revealed that blood viscosity during the menstrual cycle in healthy women is the lowest at the start of the bleeding and increases to a peak at day 7. The clinical significance of these rheological changes remains to be established, but at least theoretically there may be an increased risk of thromboembolism, e.g. at surgery, during days 5-15 of the cycle.

There were few limitations encountered in the study. Subjects with irregular menstrual cycles and any history of inflammation, trauma, drug intake and systemic diseases had to be eliminated from the study. Though it was planned to collect four samples from a subject in one cycle initially, on the early and late follicular and also on the early and late luteal phases, most of the subjects were not willing for the same for ethical reasons.

Plasma fibrinogen level can also be estimated from subjects who have undergone natural and surgical menopause. Thereby, the effect of estrogen on plasma fibrinogen level in the above said groups can be studied and the cardiovascular risks involved can be assessed. Also a clinical study looking at incidence of thromboembolic events in female patients with respect to follicular/ luteal phase may be beneficial.

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