

Original Research Article

Study of iron status indicators in different phases of menstrual cycle in first year medical college females

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ABSTRACT

Background: Iron requirements are increased in adolescent girls with growth and the onset of menarche and remain high in women until menopause.

Methods: We conducted a study on first year medical college female students (age group 18-25 years) belonging to socioeconomic classes 1 and 2 as per the Modified Kuppuswamy's Scale to study the effect of the phases of menstrual cycle on the iron status indicators (ISI) (Hb, Serum Iron, TIBC, MCV and TS%). Menstrual phases were defined and blood samples were drawn from all the girls in all the 3 phases (menstrual, follicular and luteal) and Hb, Serum iron and Total iron binding capacity were assessed on a semi-auto-analyzer and MCV was estimated using a fully automated CBC machine. Transferrin Saturation was derived as Serum Iron / TIBC × 100.

Results: We found significant ($p < 0.01$) difference in iron status indicators (ISI) that varied significantly in accordance to the menstrual cycle, with values highest during the luteal phase and lowest during the menstrual phase.

Conclusions: The effect of hormonal fluctuations during the menstrual cycle plays a part in the variation of iron status measures, which has to be considered while measuring them in a female during her reproductive years.

Keywords: Iron status indicators, Menstrual cycle

INTRODUCTION

Iron has several vital functions in the body. WHO estimated that Iron Deficiency (ID) occurs in about 66–80% of the world's population. ID has many negative effects on health, including changes in immune function, cognitive development, temperature regulation, energy metabolism and work performance.¹

ID and anemia is a worldwide problem that is highly prevalent in developing regions of the world. In women, ID has been associated with low dietary iron intake and high levels of physical activity. The highest incidence of anemia is reported in South Asia in women of reproductive age and preschool children. It has serious

implications in terms of increased morbidity and mortality rates in vulnerable groups, impaired growth and cognitive abilities in children and reduced work capacity and poor obstetric performance in adult women.² In a tropical country like India where infestations and infections are a common occurrence in one's life combined with limited quality food intake, faulty cooking and eating methods, the iron as well as the overall nutritional status of females remains often compromised, especially in the females who are more physically active.

In developing nations, iron deficiency (ID) and iron deficiency anemia (IDA) occur most often in premenopausal women, mainly because of poor dietary intake and the regular loss of blood during menstruation.³

The mean menstrual iron loss, averaged over the entire menstrual cycle of 28 days, is about 0.56 mg/day. The marked variation of menstrual losses is a great nutritional problem.⁴ In boys, body iron stores may be increased during and after their rapid growth period, whereas in girls, iron stores remain low during the whole pubertal period. The lower iron status in girls, besides growth, are also because of the iron loss with menstruation.

Measurements of iron status in blood can be confounded by non-nutritional factors. The effect of such confounding factors must be considered when data are used to evaluate the iron status of population groups. In women of reproductive age, potential confounding factors include the possible fluctuations in measures of iron status associated with various phases of the menstrual cycle.

Physiologic changes that occur during the menstrual cycle, such as fluctuations in fluid volume, blood loss and significant iron loss associated with it, may cause variations in iron status indicators.⁵ So, while we conduct a nation-wide survey to assess the nutritional status, it is of foremost importance to assess, keeping in mind all the factors that can alter present results, specially menstrual cycle in females, girls at menarche, women right after child birth, women suffering from irregular/heavy menstrual cycle due to any gynecological disorder, post traumatic and post major surgical patients, people suffering from bleeding disorders. The present study was designed to study the variations in iron-status measures in young adult female students studying in first year of medical college (18-25 years).

Aims and objectives

To study the iron status indicators in in young adult female students studying in first year of medical college (18-25 years) and to determine whether normal physiological changes associated with menstrual cycle affect the iron status indicators in the present study group.

METHODS

The study was conducted at Department of Physiology, Moti Lal Nehru Medical College, Allahabad, Uttar Pradesh, India between year 2011 to 2012. Approval from the institute's ethical committee and written informed consent was taken from each girl participating in the study.

Inclusion criteria (n = 50)

- Young adult unmarried female students of age 18-25 years studying in M.L.N. Medical College, Allahabad.
- Having normal menstrual cycle of 25-32 days
- Living in same hostel
- Eating from the same mess

- Not on medication or hormonal supplements and of same educational and SES.

Exclusion criteria

- Non-compliant subjects
- Irregular menstrual cycle
- Any significant previous illness
- Any bleeding disorder or hemoglobinopathy
- History of major surgery, accident or blood transfusion
- Suffering from or suffered from any gynecological or hormonal disorder
- Family history of: Any blood related disorders/Menstrual irregularities/Infertility/Cancer of female reproductive organs/Any gynecological disorder.

Evaluation

After taking the informed consent, applying exclusion and inclusion criteria the detailed history was taken including name, age and the following:-

a) Dietary habits-veg./ non veg. with qualification and quantification of the daily intake

b) Menstrual history with: Age at menarche & following phase definition:

- Menstrual phase: day 1-5, menstruating at the time of survey
- Follicular phase : 6-16 days after menstruation
- Luteal phase: 17-30days after menstruation.

c) Detailed history regarding –Regularity/ Flow/ Debilitating pain/ Cyclical mastalgia/Last menstrual period.

Complete general and systemic examination was carried out on each subject as per the standard guidelines. The following measurements were carried out on each subject:

1. Anthropometry: Height, Weight and BMI

2. Iron status indicators:

a. Serum Iron: 11.6-31.7 $\mu\text{mol/lit}$ in males & 9.0-30.4 $\mu\text{mol/lit}$ in females.⁶

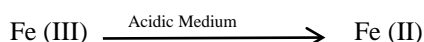
b. Total Iron Binding Capacity: 45 – 66 $\mu\text{mol/lit}$

c. Hemoglobin: 13.5-18 gm/dl in males and 11.5-16 gm/dl in females.

d. Transferrin Saturation: 20 – 50 % in males and 15-50% in females.

e. Mean Corpuscular Volume: 74 - 95 μm³

Intra-cubital venous blood (5ml) was collected from the subjects. The blood was allowed to stand for 60 minutes in incubator at 37°C. After that serum was obtained by centrifugation. Fresh serum was used for SI and TIBC, fresh whole blood for Hb and MCV determination. Estimation of serum iron and TIBC was done by ferrozine method (magnesium carbonate) obtaining the absorbance using the semi-auto-analyzer by ARTOS established in the Department of Physiology M.L.N.M.C Allahabad.



Fe (II) + Ferrozine → Violet colored complex

Hemoglobin estimation was done by Cyan-met-hemoglobin method (Drabkin's reagent), obtaining the absorbance using the semi-auto-analyzer

$$\text{Transferrin saturation} = \text{Serum Iron} / \text{TIBC} \times 100$$

Estimation of MCV was done by fully automated complete blood count machine (Medonic M series) installed in the Department of Pathology, M.L.N. Medical College, Allahabad. Fresh un-clotted whole blood was used for the MCV estimation.

Statistical analysis

The data obtained in the study group was expressed as the mean ± standard deviation. Statistical analysis was done with the help of statistical software SPSS 17.0. The p value of < 0.05 was considered as statistically significant

RESULTS

Present results show difference in the iron status indicators in the present study group. Also significant correlation was found between the iron status indicators during different phases of the menstrual cycle. Hb values were significantly associated with the menstrual phase for the study group.

Table 1: Mean and standard deviation of different parameters in the study group.

| Parameters | Study group (Mean ± S.D.) |
|--------------------------|---------------------------|
| Age (years) | 21.32±1.95 |
| Height (cms) | 157.60±6.09 |
| Weight(kgs) | 51.94±5.65 |
| BMI (kg/m ²) | 20.90±1.42 |
| SES | 1.58±0.72 |

Concentrations of Hb were lowest for girls in the menstrual phase and highest for girls in the luteal phase. Mean values of both SI and TS were also significantly associated with phases of the menstrual cycle, their

values were lowest for girls in the menstrual phase and highest for girls in the luteal phase. The patterns of TIBC values were opposite to those observed for Hb, SI, and TS.

Table 2: Mean and standard deviation of iron status indicators during menstrual phase in the study group.

| Parameters | Study Group (Mean ±S.D.) |
|-----------------------|--------------------------|
| Hemoglobin (gm/dlit) | 11.85±1.01 |
| Serum Iron (μmol/lit) | 16.37±1.46 |
| TIBC (μmol/lit) | 62.37±1.96 |
| TS% | 26.28±3.11 |
| MCV | 89.51 ± 1.79 |

Measures of TIBC were highest for girls whose blood was drawn in the menstrual phase and lowest during the luteal phase. MCV values were different only during the follicular phase, significantly lower than the values observed during the menstrual phase. MCV values were only slightly different during the luteal phase from the menstrual phase (not significant). So, we found that the values of iron status indicators vary according to the menstrual cycle, with values highest during the luteal phase and lowest during the menstrual phase. Also it is seen that the females in the study group could be misdiagnosed as anemic if their menstrual phases were not taken into account.

Table 3: Mean and standard deviation of iron status indicators during follicular phase in the study group.

| Parameters | Study Group (Mean ± S.D.) |
|-----------------------|---------------------------|
| Hemoglobin (gm/dlit) | 12.14±1.01 |
| Serum Iron (μmol/lit) | 17.01±1.49 |
| TIBC (μmol/lit) | 61.71±2.00 |
| TS% | 27.63±3.22 |
| MCV | 88.37±1.80 |

Table 4: Mean and standard deviation of iron status indicators during luteal phase in the study group.

| Parameters | Study group (Mean ± S.D.) |
|-----------------------|---------------------------|
| Hemoglobin (gm/dlit) | 12.42±1.01 |
| Serum Iron (μmol/lit) | 17.67±1.53 |
| TIBC (μmol/lit) | 61.01±2.01 |
| TS% | 29.01±3.37 |
| MCV | 89.23±1.78 |

DISCUSSION

Present findings suggest that females in the reproductive age group (specially, during the active menstrual phase) are more prone to lower ISI as compared to women not actively menstruating and our findings are also confirmed by the work of Clung MJP et al, Kim I et al, Bentely et al and Elemo GN et al.^{3,5,8,9} The rhythms of ovarian hormones during the course of the menstrual cycle

influence the secretion of hormones that control the volume and content of the vascular space. Thus changes in plasma volume and rise in plasma protein concentrations are linked to the normal course of estrogen and progesterone fluctuations during the menstrual cycle.¹⁰ In present study we did not directly measure changes in plasma volume, but our observations are in accordance with the well-known hormonal changes of the menstrual cycle and their known influence on hemo-concentration and dilution.

Hemo-concentration due to estrogen, mediated changes in plasma volume or increased synthesis or secretion of plasma proteins, might explain the mechanism for higher iron-status values during the luteal phase. An increase in plasma progesterone concentrations also occurs during the luteal phase which has a natriuretic effect due to aldosterone antagonism, resulting in plasma loss of sodium and water.¹¹

Progesterone may also influence hemo-concentration during the early to mid-luteal phase when its concentrations peak. The fall in progesterone during the luteal phase is associated with a sharp rise in aldosterone activity observed few days before the onset of menses manifesting as weight increase, edema & hemo-dilution. Thus, the hormone-associated changes in plasma volume and plasma protein concentration occurring during course of the menstrual cycle offer a possible mechanism to explain differences in the values of iron-status indicators that we observed at different phases of the cycle.

CONCLUSION

From present observations we can conclude that the effect of hormonal fluctuations during the menstrual cycle has a part to play in the variation of iron status measures, which has to be considered while measuring them in a female during her reproductive years, as it may alter the results depending on the phase of the menstrual cycle.

Further modifications are possible in present study which may clarify our understanding in this area even more. For instance we could possibly study the levels of various reproductive hormones and correlate with them. We could also take more comparable parameters like serum ferritin and transferrin receptor.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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