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ORIGINAL ARTICLE

A STUDY OF VARIATIONS IN BONE PHYSIOLOGY DURING MENSTRUAL CYCLE

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ABSTRACT: BACKGROUND: The bone is subjected to Catabolic and Anabolic processes periodically like any other organ in the body. Apart from Growth Hormone, Thyroid hormone, Insulin and other hormones related to growth and decay of various body tissues and organs, estrogen and progesterone also play an important role in bone physiology. Both these promote osteoblastic activity of the bone more so estrogen. The present study was undertaken to compare the osteoblastic activity in both phases of menstrual cycle. **MATERIALS & METHODS:** This study was undertaken in the Department of physiology, Osmania Medical College, in collaboration with the Department of Bio-chemistry, over a period of two years i.e. 2007 – 09. A total of 50 female subjects in the reproductive age group (15- 45 years) were selected. These subjects were divided into 2 groups, one group in Proliferative phase and the other group in Secretary phase of menstrual cycle. They were subjected to Quantitative Ultrasonography of the calcaneum (to measure Bone Mineral Density -BMD), Serum Tartarate resistant Acid phosphotase, Bone specific Alkaline Phosphotase, Serum Calcium and Serum Phophorus estimation. **RESULTS:** We found increased Osteoblastic activity as measured by the increased levels of serum Bone specific Alkaline Phosphotase and by the T score and Z score of the subjects by Ultrasonography of the calcaneum, in the Proliferative phase of menstrual cycle. The Osteoclastic activity is decreased in the Secretary phase of the menstrual cycle as indicated by the increased levels of Tartarate resistant Acid Phosphotase and by the T score and Z score of the subjects. However the levels of Bone specific Alkaline Phosphotase were found to be normal. **CONCLUSION:** Throughout the duration of the menstrual cycle, the osteoblastic activity remained constant, the osteoclastic activity was found to be reduced during the secretary phase, - the BMD did not vary significantly.

KEYWORDS: Sex hormones, menstrual cycle, BMD.

INTRODUCTION: The physiology of bone like any other organ is addressed within the framework of role of different hormones in growth and decay process of the body.

Apart from the usual hormones related to growth and decay of various body tissues and organs like Growth hormone, Thyroid hormone, PTH, and Insulin, there is also said to be the role of Estrogens and Progesterones in a similar process.

In females cyclical variations of sex hormones are seen throughout the menstrual cycle. At the beginning of the Proliferative phase the estrogen levels gradually increase and peak during the pre-ovulatory period, following which they decrease and are maintained at a constant level never touching the base-line. Progesterones also steadily increase during the secretary phase and are maintained at a constant level (Fig. 1). So during the Secretary phase both these hormones are at a higher level and there by the Osteoblastic activity is maintained by decreasing the Osteoclastic activity.[1,2] So we can expect variations in the Osteoblastic and Osteoclastic activities during the whole of the menstrual cycle.[3]

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As there is cyclic variation of concentration of these hormones during normal menstrual cycle, the role if any has to be appreciated in terms of periodic variations of Biochemical parameters. When it pertains to bone, to its osteoblastic and osteoclastic activities,[4] this fact was emphasized by A. Zittermann et al.

In the present study we attempted to correlate the degrees of osteo-blastic and osteo-clastic activities observed during the two phases of the menstrual cycle so that objective assessment may be evolved.

The osteoblastic activity was objectively measured by measuring the serum concentrations of Bone Alkaline Phosphotase (BAP) and the Osteoclastic activity by Serum Tartarate resistant Acid Phosphotase (TRAP).[5,6,7] The Bone mineral density(BMD) was measured by the Ultra-sonography of the Right Calcaneum.

MATERIAL & METHODS: The study was conducted in the department of physiology, Osmania Medical College, Hyderabad, in collaboration with the Department of Biochemistry. A cross sectional study was conducted on 50 female subjects in the age group of 15 to 45 years(reproductive age group) after obtaining their consent. All the subjects were made to undergo BMD of right Calcaneum by Ultrasonography, in both the phases of menstrual cycle.

The serum levels of BAP, TRAP were measured in all the subjects in both the phases of the cycle.

EXCLUSION CRITERIA:

- History of amennorhoea, abnormal menstrual cycles, DUB, estrogen therapy, corticosteroid therapy.
- History of Hypertension.
- History of usage of drugs like Relaxifen, Vitamin D which may affect calcium metabolism.

METHODS OF STUDY ADOPTED:

1. **Quantitative Ultrasonography of the calcaneum:** Non-invasive method of measuing bone mass by ultrasound of calcaneum of the right foot (heel) for the presence of osteopenia which indicates bone resorption This method was recently cleared by the US FDA(food and drug administration). It is relatively inexpensive, quick, painless, radiation free and safe[8]. It also provides additional information regarding trabecular bone formation[9]. It is an Out-patient procedure and can be done on large number of subjects in a limited time and place. (Fig. 2)

T SCORE: The WHO uses T score to define normal bone mass, low bone mass or osteopenia and osteoporosis. T score compares bone density to the average bone density of young healthy adults of same gender. (Table 1)

The formula used is T score= measured BMD—BMD reference range of women in their 30s (young normal)/ standard deviation.

T scores are based on statistical measurements called standard deviations (SD) that reflect the difference between one's bone density and normal bone density in the reference population. (Fig. 3)

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Z SCORE: It compares your bone density to the average value for a person of your same age and gender. A low Z score below -2.0 is a warning sign that you have less bone mass or losing bone more rapidly than expected for your age. Out of these two values T score measurement is of clinical significance.

BIOCHEMICAL PARAMETERS: Parameters assed were: Tartarate resistant acid phosphatase (TRAP), indicator of bone resorption, by King's method (normal values are 1.0 to 4.0 KA units).

Bone specific alkaline phosphatase, indicator of bone formation by pNPP-AMP (IFCC) method. Normal values are total alkaline phosphate 25 to 100 ALP activity in IU/L at 37degrees Centigrade. Heat stable Alkaline Phosphotase forms less than 20% of total.

RESULTS: The study group comprised of female subjects in reproductive age with a mean age of 31.3 yrs and standard deviation of 7.6. The variables considered were Serum Acid Phosphatase (Tartarate resistant), Serum Bone specific Alkaline phosphatase, T score and Z score.

PROLIFERATIVE PHASE: Regression analysis with Anova of data with Acid phosphatase as dependent variable and day of menstrual cycle as independent variable showed statistically significant values of F=2.793, R=.376, significance=.113, beta coefficient=.376, slope=0.064. (Tables 2, 3, 4, 5, 6, 7) and (Graphs 1, 2).

SECRETARY PHASE: Regression analysis with Anova of data with day of menstrual cycle as independent variable and Acid phosphatase as dependent variable showed statistically significant values of F=1.66, R=.269, significance=.297, beta coefficient=-.269 and slope =-.026. (Tables 8,9,10,11,12,13 and (Graphs 3, 4).

With respect to total duration of menstrual cycle regression analysis with Anova of data with day of menstrual cycle as independent variable and Bone Alkaline Phosphate as dependent variable showed statistically significant values of F=1.393, R=.198, significance=.246,beta coefficient =.198 and slope=.062.(Tables 14,15,16,17,18,19) and (Graphs 5, 6).

The study of subjects in reproductive age group comprised of mean age of 31.3 years, with a standard deviation of 7.6. We made an attempt to assess the role of Estrogen and Progesterone in the physiology of bone through the cyclical variation of certain parameters related to osteoblastic and osteoclastic activity during normal menstrual cycle. We have not made any direct estimation of Estrogens and Progesterones but relied mainly on established facts related to the different degrees of concentration of these hormones during normal menstrual cycle and clinical history of the subject. We took serum BAP as a marker for Osteoblastic activity, Tartarate resistant Acid Phosphatase as a marker for bone resorption. Concomitantly we also estimated the osteoblastic and osteoclastic activity through a non-invasive method of estimation of BMD by Ultra- sonography of the calcaneum basing on evolved values of T– score and Z- score.

In this study, we observed the relationship between Acid Phosphatase and day of menstrual cycle in proliferative phase. We did not find any statistically significant correlation, where as in secretary phase for the same parameters we found statistically significant correlation. This speaks of decreased osteoclastic activity during secretary phase as is evident from the negative slope of beta coefficient of regression analysis and negative slope in linear correlation. Our findings are similar to those of Chiu KM et al, whose studies emphasized the same finding.

In the study of correlation between Acid Phosphotase and day of menstrual cycle considering the total duration of cycle we did not find any statistical significance, whereas the relationship between BAP and day of menstrual cycle in the entire cycle we obtained highly significant correlation as is evident from positive beta coefficient of regression analysis positive slope of linear correlation.

When we studied combined relation of Acid Phosphatase and BAP with the day of menstrual cycle there was significant correlation only in secretary phase which indicates decreased osteoclastic activity, due to increased levels of oestrogen and progesterone during that phase. As the levels of estrogen and progesterone increase from proliferative to secretary phase with a peak increase on the day of ovulation, followed by sustained increase of their concentrations during the entire secretary phase.

We did not find statistically significant correlation between Z score, T score and day of menstruation.

CONCLUSION: The role of Estrogen and Progesterone in Osteoblastic and Osteoclastic activity is documented in our study, by assessing biochemical parameters and estimation of BMD in relation to phases of normal menstrual cycle and age.

There is decreased Osteoclastic activity in the secretary phase due to sustained elevations of Estrogen and Progesterone during that phase.

Future studies may be under taken on a similar line, on a larger population so that objectivity of the results may be strengthened further.

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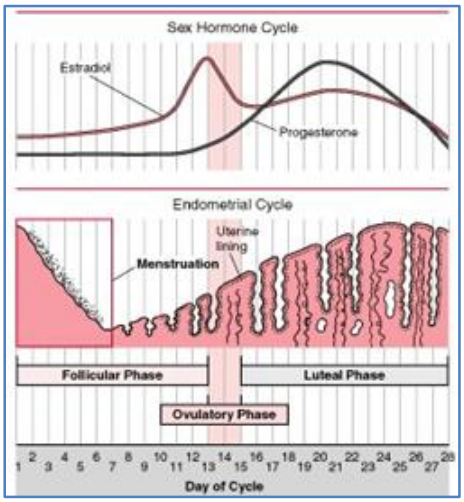


Fig. 1

Fig. 2

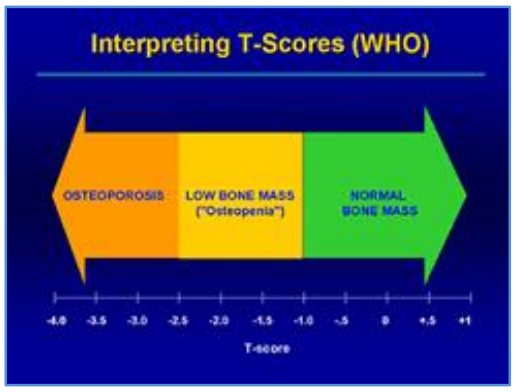
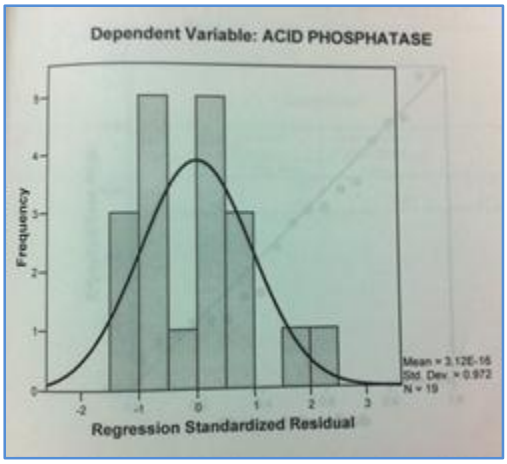
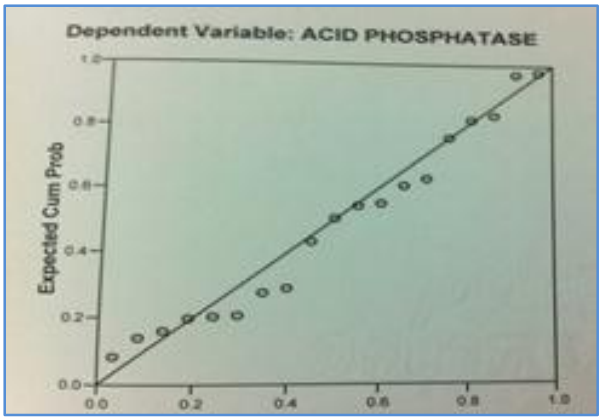


Fig. 3



Graph 1



Graph 2

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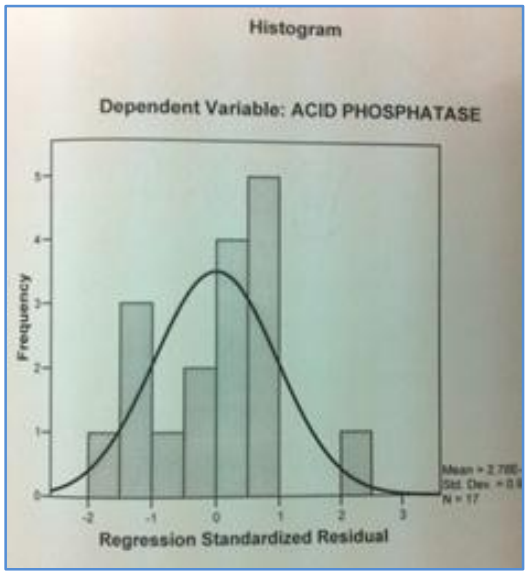

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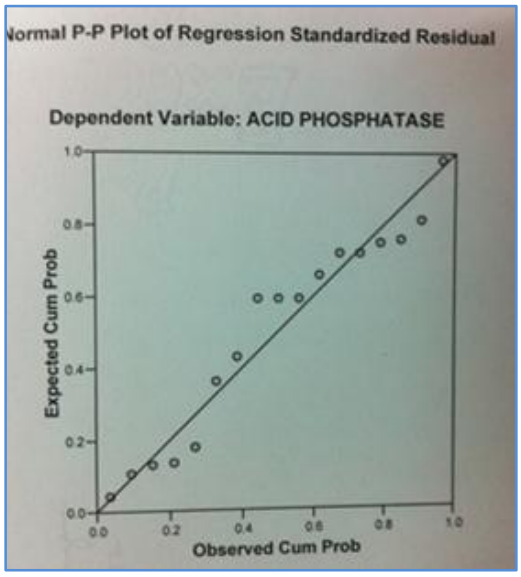

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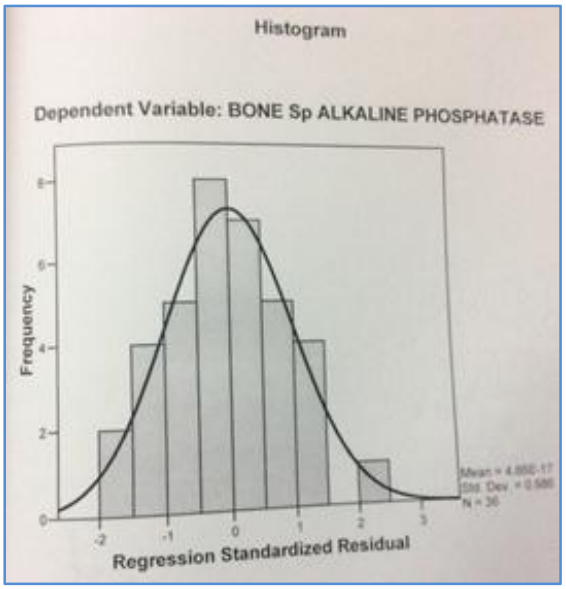
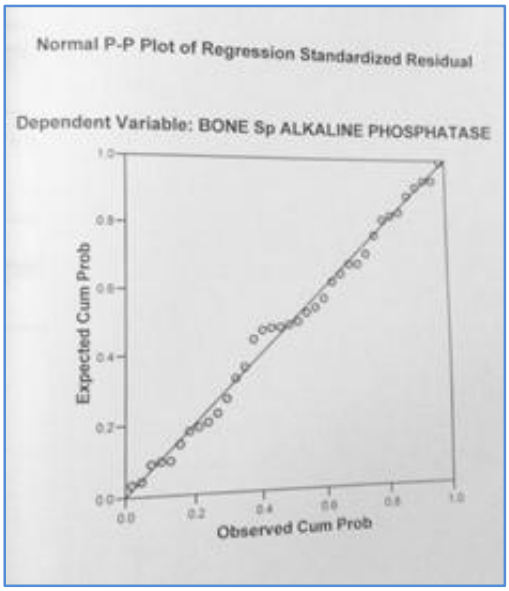


Graph 5



Graph 6

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