

# Vitamin D3 & Serum Calcium Levels in Premenstrual Syndrome

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## ABSTRACT

**Objective :** To determine vitamin D3 and serum calcium levels in premenstrual syndrome during luteal phase.

**Study Design :** Comparative case control study

**Place and Duration:** Department of Gynecology and Obstetrics and Department of Biochemistry, Isra University Hospital from June-December 2013.

**Material & Methods:** A sample of 85 unmarried female of age 18-28 years were selected through non-probability purposive sampling according to pre-defined inclusion and exclusion criteria. Subjects were divided in; to Group I. normal healthy female as controls (n=42) and Group II diagnosed cases of premenstrual syndrome (n=43). Serum 25-OH-D3 was estimated by ARCHITECT I 1000 system and serum calcium by Roche Automated Clinical Chemistry Analyzer 902 modular system. Data was analyzed on SPSS version 21.0. The continuous and categorical variables were analyzed by student's t-test and chi-square test respectively. Pearson's correlation was used to determine association between vitamin D3 and serum calcium. The significant p-value was taken at = 0.05.

**Results :** Mean±S.D age of controls and premenstrual syndrome (PMS) cases noted was 22.6±3.2 and 21.6±3.9 years (range 18-28 years) (p=0.91). The premenstrual subjects revealed a significantly low vitamin D3 levels compared to controls. The mean±S.D of vitamin D3 was noted as 26.20±4.30 and 14.88±2.39 ng/dl respectively. (p=0.0001). Vitamin D3 levels as low as 8 ng/dl were noted in premenstrual syndrome. Significant statistical difference was observed for serum calcium level between groups i.e., 9.30±0.81 vs. 8.52±1.18 (p=0.001) Positive correlation co-efficient was observed between serum Vitamin D3 and calcium levels (r=0.44, p=0.001).

**Conclusion:** The present study observed low vitamin D3 and calcium levels in female subjects suffering from premenstrual syndrome. Supplementation with vitamin D3 and calcium may help to alleviate the symptoms of premenstrual syndrome.

**Key Words:** Vitamin D3                      Serum calcium                      Premenstrual syndrome

## INTRODUCTION:

Premenstrual syndrome (PMS) is characterized by a complex group of signs and symptoms which occurs during the luteal phase of the menstrual cycle and ends on menstrual

flow<sup>1</sup>. It is a widely recognized recurrent cyclic disorder related to the hormonal changes during the menstrual cycle, effecting the emotional and physical well-being of a woman during her reproductive age group<sup>2</sup>.

The pathophysiology of PMS in reproductive age group still remains unknown. Treatment with drugs like antidepressants, oral contraceptives, GRH agonist, can reduce the symptoms of PMS but all of these drugs have their own side effects. Previous research suggests that the levels of vitamin D and electrolytes such as calcium have much importance in controlling the symptoms of PMS<sup>2</sup>.

The sign and symptoms are mainly

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depression, irritability, anxiety, tension, aggression; bloating, breast tenderness; headache, mastalgia, dysmenorrhea, muscular and joint pain, all are non-specific. In young females having premenstrual syndrome (PMS) and premenstrual exacerbation (PME), these symptoms can distract their social and personal life style. Cases of premenstrual suicide, asthma and epilepsy have also been reported<sup>3</sup>.

Dietary intake of fortified dairy foods and cereals, fish, multivitamins and mineral supplements specially calcium contribute importantly to vitamin D activity in elderly populations and those with low ambient sunlight exposure<sup>3</sup>.

It is noted that women in the luteal phase with the symptoms of PMS may be suffering from vitamin D3 deficiency<sup>5</sup>. A good dietary source of vitamin D3 may reduce the symptoms of PMS<sup>6</sup>.

It is also reported that the level of vitamin D3 is lower than the normal in all subjects having PMS during their menstrual cycle. The possible cause may be the increased conversion of 25-OH vitamin D3 into 1,25-OH vitamin D3 during the luteal phase of their menstrual cycle which in turn increases the consumption of vitamin D3 causing its low level in the body<sup>7</sup>. The rationale of present study was to evaluate vitamin D3 and serum calcium levels in premenstrual syndrome during luteal phase.

#### **MATERIAL & METHODS:**

A prospective case control study was conducted at the Department of Gynecology and Obstetrics and Department of Biochemistry, Isra University, Hyderabad from July- December 2013. Informed written consent was sought from the participants. Study was approved by the ethics committee of the institute. A sample of 85 subjects was selected through non-probability purposive sampling according to well delineated inclusion and exclusion criteria. Unmarried female of age 18-28 years, regular menstrual cycle with symptoms of premenstrual syndrome not taking any drug were included in study protocol. Married female with concomitant systemic disease, multi-

vitamin and drug users were excluded. The study population was divided into two groups; Group I. as controls- normal healthy female (n=42) and Group II. Diagnosed cases of premenstrual syndrome (n=43).

Five ml of fasting venous blood sample was drawn from ante-cubital vein during luteal phase. The blood was centrifuged at 4000rpm for ten minutes and serum obtained was frozen at -20°C. The serum was used for estimation of calcium and vitamin D3 levels. The vitamin D3 was measured by ARCHITECT I 1000 system for estimation of 25-OH- D3 and serum calcium by Roche automated clinical chemistry analyzer 902 modular system. The data was recorded on a pre-structured proforma.

Data was analyzed on SPSS version 21.0. The continuous and categorical variables were analyzed by student's t-test and chi-square test respectively. The results were presented as mean±S.D and frequency (%) respectively. Pearson's correlation was used to determine association between vitamin D3 and serum calcium. The significant p-value was taken at = 0.05.

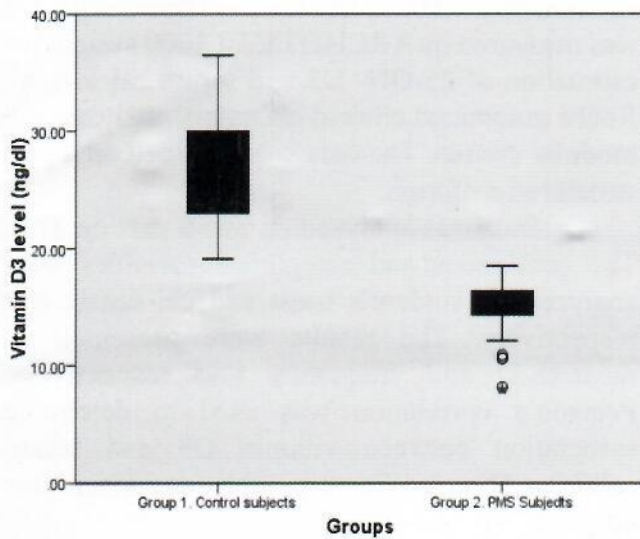
#### **RESULTS:**

The mean age of controls and premenstrual syndrome (PMS) cases noted was 22.6±3.2 and 21.6±3.9 years (range 18-28 years) (p=0.91). The premenstrual subjects revealed a significantly low vitamin D3 levels compared to controls. The mean±S.D of vitamin D3 was noted as 26.20±4.30 and 14.88±2.39 ng/dl respectively. (p=0.0001) (Table. I) (Graphs 1). Vitamin D3 levels as low as 8ng/dl noted in premenstrual syndrome. The serum calcium levels between groups were analyzed using students t-test. The mean±S.D of serum calcium levels in groups I and II were found as 9.30±0.81 and 8.52±1.18 mg /dl respectively. Significant statistical difference was observed for serum calcium level between groups (p=0.0001) (Table I) (Graphs 2).

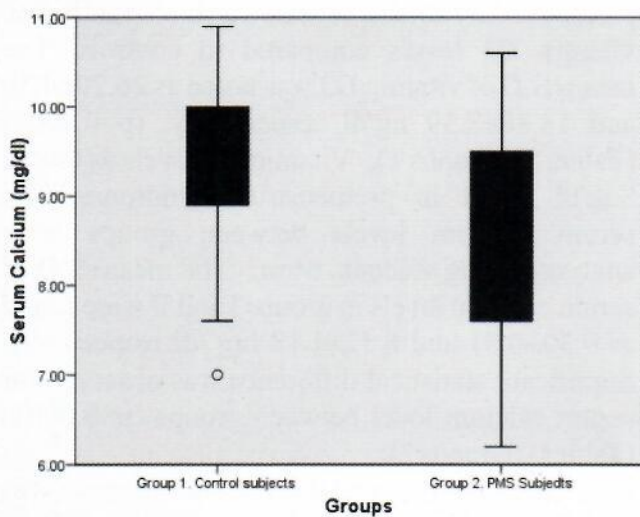
Positive correlation co-efficient was observed between serum Vitamin D3 and calcium levels (r=0.44, p=0.001) as shown in graph 3.

Table 1: Findings of controls & Premenstrual Syndrome Subjects (n=85)

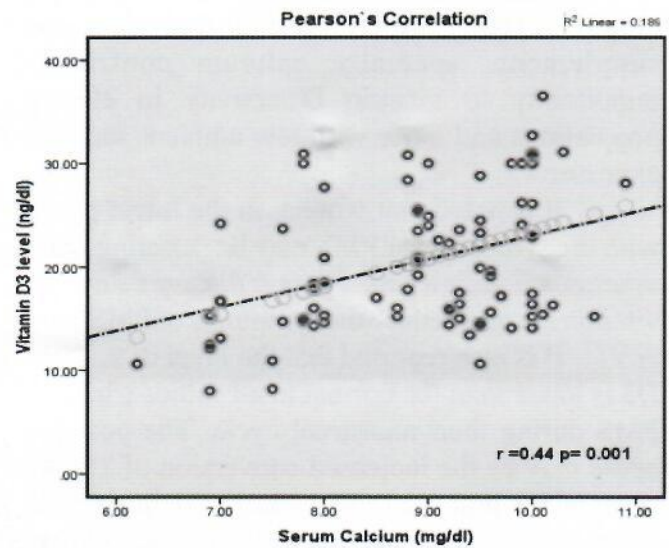
	Group 1. Controls (n=42)	Group II Cases (n=43)	P-Value
Age	22.64 ± 3.27	21.61 ± 3.91	0.91
Vitamin D3	26.20 ± 4.30	14.88 ± 2.39	0.0001
Calcium (mg/dl)	9.30 ± 0.81	8.52 ± 1.18	0.0001



Graph 1. Boxplots of Vitamin D3 distribution of Group 1 controls & Group 2. Premenstrual syndrome, Showing major difference in mean values.



Graph 2. Boxplot chart of calcium distribution (mg/dl) in study population.



Graph 3. Scatter plot: Positive correlation co-efficient was observed between serum vitamin D3 & calcium levels (r=0.44, p=0.001)

**DISCUSSION:**

The present cross sectional comparative study was planned to investigate the premenstrual syndrome (PMS) in young healthy unmarried females of 18-28 years of age. The present study observed low vitamin D and Calcium levels during luteal phase which are parallel to previous studies<sup>5-8</sup>.

Vitamin D3 levels fluctuate during luteal phase as has been proved in previous studies<sup>7-8</sup>. The observations of serum calcium and vitamin D3 levels of present study are comparable to previous studies. A previous study reported that the ovarian sex hormones increase the vitamin D3 metabolism. They observed the effect of the estradiol on 1-a-hydroxylase and 24-hydroxylase activity of liver and reported an enhanced effect of first enzyme and suppressed activity of the second enzyme. The changes in vitamin D3 metabolism showed an

increased utilization of vitamin D3 similar to previous<sup>5-8</sup> and present study. The previous studies<sup>5-8</sup> support the findings of present study that the vitamin D3 is found low also in human beings because of effects of ovarian hormones which disturbs serum calcium and vitamin D3 metabolism in cyclical fashion resulting in symptoms of premenstrual syndrome.

Brommage, et al<sup>9</sup>. investigated an effect of ovarian hormones on calcium absorption. They reported that calcium absorption is affected by the ovarian hormones resulting in calcium dysregulation. They concluded that this physiological phenomenon might contribute also to the symptoms of menstrual cycle in human beings. Currently as mentioned above, the cyclical changes in mineral metabolism involving healthy premenopausal women during the menstrual cycle are responsible for symptoms of premenstrual syndrome. These findings support our present study. In Pitkin's study<sup>10</sup> of healthy premenopausal women, the concentration of parathyroid hormone is shown progressively increased through the follicular phase of the cycle. It is peaked from 30% to 35% above earlier follicular and late luteal phase concentrations in association with reduced ionized calcium concentrations. Hence it can be concluded from previous and present studies that the calcium metabolism is disturbed during luteal phase and contributes to symptoms of premenstrual syndrome.

The study of Gray, et al<sup>11</sup>. is contrary to the present and most of the studies mentioned in medical literature on this current research topic. The Gray, et al<sup>11</sup>. conducted study on seven normal females and collected blood samples on Day 1, 8, 15 and 22 of menstrual cycle. This previous study reported contradictory results of serum calcium and vitamin D3 and mentioned that their concentration increases during all phases of menstrual cycle instead of any reduction observed during luteal phase.

The Das, et al<sup>12</sup>. measured plasma concentrations of metallic ions in normally menstruating women. The concentrations of magnesium, zinc, selenium and manganese were

highest during menses and lowest at the ovulatory phase. A rise in serum magnesium and selenium levels, with a fall in zinc and manganese during the luteal phase is highly contradictory not only to present but most of the published studies<sup>13-15</sup>.

The Bertony J, et al<sup>16</sup>. conducted case control study with a very large sample size of 1057 females. The study was intended to observe effects of calcium and vitamin D3 on the risk of developing symptoms of premenstrual syndrome. A significantly low risk of developing symptoms of premenstrual syndrome with calcium and vitamin D3 supplementation was reported. The study design had very strong internal validity because of prospective nature, patient selection and follow ups. It was reported for the first time that high doses of calcium supplemented with vitamin D3 was useful to prevent the initial development of symptoms of premenstrual syndrome. In the present study, the mean±S.D of vitamin D3 was found as 26.20±4.30 and 14.88±2.39 ng/dl respectively. (p=0.0001) (Table. I). Vitamin D3 levels as low as 8.0 ng/dl were noted in premenstrual syndrome subjects (p=0.0001). While serum calcium, mean±S.D in groups I and II were found as 9.30±0.81 and 8.52±1.18 mg /dl respectively. A statistically significant difference was found in serum calcium level between groups (p=0.0001) (Table I). Our results of low vitamin D3 and serum calcium are in consistent with the previous studies<sup>13-18</sup>. The cause-effect relationship of vitamin D3 and serum calcium with premenstrual syndrome cannot be ascertained because of the cross sectional design of present study. The study could not measure the parathyroid hormone, hypothalamo-pituitary gonadal hormones, sex steroid hormones and other parameters which might have an effect on the results of present study. Since the sample size of present study was small, the results cannot be generalized to other settings. The study was conducted on a population of specific age, race, ethnicity, hence results may not be authentic for other population and must not be interpreted by others. It needs extensive study to assess.

## CONCLUSION:

The present study witnessed low vitamin D3 and calcium levels in female subjects suffering from premenstrual syndrome. Supplementation with vitamin D3 and calcium may help to alleviate the symptoms of premenstrual syndrome which is a complex of clinical manifestations of vitamin D3 and serum calcium deficiency.

## REFERENCES:

1. Shaughn O, Brein M. The premenstrual syndrome. In : Edomns K. (editor). Dewhurst's Textbook of Obstetrics and Gynecology. John Wiley & Sons UK. 2012:544-52.
2. Thys-Jacobs S, McMohan D, Bilezikian JP. Cyclical changes in calcium metabolism across the menstrual cycle in women with premenstrual dysphoric disorder. *J Clin Endocrinol Metab.* 2007;98(8):2952-9.
3. Najam R, Bano N, Ahmed SP. The therapeutic role of magnesium in different depressive syndromes of female patients. *Pak J Pharmacol.* 2010;27(2):1-8.
4. Holick MF. Vitamin D deficiency. *NEJM.* 2007;357(3):266-81.
5. Thys-Jacobs S. Micronutrients and the premenstrual syndrome: the case for calcium. *J Am Coll Nutr* 2005 ; 19:220-7.
6. Bertone-Johnson ER, Hankinson SE, Bendich A, Johnson SR, Willet WC, Manson JE. Calcium and vitamin D intake and risk of incident premenstrual syndrome. *Arc Intern Med* 2005; 165(11):1246-52.
7. Thys-Jacobs, Alvir MAJ. Calcium regulating hormones across the menstrual cycle: evidence of a secondary hyperparathyroidism in women with PMS. *J Clin Endocrinol Metab* 1995 ; 80:2227-32.
8. Tanaka Y, Castillo L, Deluca HF. Control of renal vitamin D hydroxylases in birds by sex hormones. *Proc Natl Acad Sci* 1976 ; 73: 2701-5.
9. Brommage R, Binuacua C, Carrie AL. Ovulation-associated increase in intestinal calcium absorption during the rat estrous cycle is blunted by ovariectomy. *Biol Reprod* 1993 ; 49:544-8.
10. Pitkin R, Reynolds WA, Williams GA, Hargis GK. Calcium regulating hormones during the menstrual cycle. *J Clin Endocrinol Metab* 1978 ; 47:626-632, 1978.
11. Gray TK, Mc Doo T, Hatley L, Lester GE, Thierry M. Fluctuation of serum concentration of 1,25 dihydroxyvitamin D during the menstrual cycle. *Am J Obstet Gynecol* 1982 ; 144:880-4.
12. Das K, Chowdhury AR. Metallic ions during menstrual cycle in normally menstruating women. *Indian J Med Sci* 1997; 51:52-4.
13. Yucel U, Bilge A, Oran N, Ersoy MA, Gencdogan B, Ozveren O. Adolesanlarda premenstruel sendrom yayginligi ve depresyon riski arasindaki iliski. *Anadolu Psikiyatri Dergisi* 2009;10(1):55-61.
14. Zaffrane F, Faleh R, Melki W, Sakouhi M, Gaha L. An overview of premenstrual syndrome. *European Journal of Obstetrics, Gynecology and Reproductive Biology* 2007 ; 36(7):642-52.
15. Bakhshani NM, Mousavi MN, Khodabandeh G. Prevalence and severity of premenstrual symptoms among Iranian female university students. *J Pak Med Assoc* 2009 ; 59(4):205-8.
16. Bertone-Johnson ER, Hankinson SE, Bendich A, Johnson SR, Willet WC, Manson JE. Calcium and vitamin D intake and risk of incident premenstrual syndrome. *Arc Intern Med* 2005; 165(11):1246-52.
17. Dullo P, Vedi N. Changes in serum calcium, magnesium and inorganic phosphorus levels during different phases of the menstrual cycle. *J Human Repord Sci* 2008 ; 1(2): 77-80.
18. Ebrahimi E, Motlagh SK, Nemati S, Tavakoli Z. Effects of magnesium and vitamin B6 on the severity of premenstrual syndrome symptoms. *J Caring Sci* 2012 ; 1(14): 183-9.