"Comparison of Hormonal Parameters Between Normal and PMS Affected Women in Luteal Phase of The Menstrual Cycle".

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Abstract

Background: Premenstrual Syndrome (PMS) is a condition affecting up to 47.8 per cent of women of reproductive age with severe symptoms occurring in 3-8 per cent. it is characterised by a range of emotional, physical, and behavioral symptoms occurring in the Luteal phase of the menstrual cycle. Symptoms include mood swings, bloating, fatigue, irritability and depression, significantly impacting daily life. Despite its prevalence, the etiology and pathophysiology of PMS remain poorly understood. This study aims to investigate the Comparison of Hormonal parameters between normal and PMS-affected women in the Luteal phases of the menstrual cycle, thereby shedding light on the physiological underpinnings of PMS.

Objective: The study aims to compare hormonal parameters and an electrolyte between normal and PMS-affected women of reproductive age.

Material and methods: This study was conducted on 80 women of which 40 were normal Control and 40 were as study population with PMS Symptoms, in the Department of Physiology in Collaboration Obstetrics & Gynecology department at Index Medical College Hospital and Research Centre, Malwanchal University, Indore. This study was carried out for three years from July 2021 to April 2024.

Observation and Result: In this study, we have calculated the mean and standard deviation of hormonal parameters. The mean estrogen level in control participants is 87.87 and the standard deviation is 29.46. The mean estrogen level in PMS-affected women is 66.5 and the standard deviation of is 21.91. The mean progesterone level in the control group is 1.97 and the standard deviation is 1.18. The mean Progesterone level in PMS-affected women is 1.52 and the standard deviation was 0.91. The mean FSH level in normal females was 2.65 and the standard deviation was 1.11. The mean FSH level in PMS-affected women was 3.03 and Std was 1.5. The mean LH level in normal women was 2.36 and Std 0.9 The mean LH level in PMS affected group was 3.34 and SD 1.42. The mean Prolactin in the control group of women was 6.13 and the standard deviation value was 2.09 The mean value of prolactin in PMS-affected women was 7.7 and the standard deviation was 1.18. The mean TSH level in normal females was 3.47 and the standard deviation was 1.2. The mean TSH level in PMS-affected females was 4.55 and the standard deviation was 1.53.

Keywords: PMS, PMDD Estrogen, Progesterone, LSH, LH, TSH, Prolactin

Introduction

Horney first referred to premenstrual syndrome as "premenstrual tension" in her 1930 study. (1) The term "premenstrual syndrome" (PMS) was coined in the 1960s by Dalton, based on observational accounts. (2) Psychiatrists first recognized the link between hormonal changes in the menstrual cycle and mental health in the 1980s. (3) The classification of PMS as a psychiatric disease remained debated until the fourth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM)

in 1994, when it was included in the appendix. (4) Over the next two decades, researchers found evidence that a new state, the luteal phase of the menstrual cycle, can improve the commencement of menstruation. (5) It causes severe suffering and interferes with work, school, social activities, and relationships, as evidenced by daily symptom severity ratings over two cycles. (6)
Most Indian research on PMS focuses on its prevalence, etiology, risk factors, and relationship with other psychiatric diseases. (7) Most research has focused on teens and college students. PMS is defined by the degree to which symptoms disrupt daily activities. (8) In Kerala, women make up 50% of the private sector labor and 34% of the public sector (9). Progesterone levels typically stay constant for most of the mid-luteal phase before abruptly dropping just before menstruation. (10) An animal study revealed that loss of progesterone could be a factor in PMS symptoms. (11) According to this theory, in healthy women, increased progesterone was linked to decreased irritation and fatigue symptoms. (12). Premenstrual syndrome is a term used to describe cyclic menstrual-related symptoms that are temporally associated with the late luteal phase (PMS). (13) In this study we have focused on what is the relation of hormones causing premenstrual symptoms. Female hormones e.g. Estrogen, progesterone play an important role in the menstrual cycle. However, there is a lack of studies in India on how PMS affects work quality.

METHODS

This study was conducted to evaluate the variation in Hormonal parameters in the Luteal phase of the menstrual cycle. A total of 80 females in the age group of 18 to 40 years, were recruited from Indore City and visited the Gynecology department of Index Medical College Hospital. Out of these 40 females were taken as the study group who had PMS-related problems on the basis Questionnaire of PMS (based on DSM criteria-5) 40 females were taken as control who had no PMS-related problems. The study was approved by the Institutional Review Board of Index Medical College and Teaching Hospital, Indore. This comparative correctional study was carried out from Jan 2022 to Feb 2024.

Inclusion Criteria: for a subject as follows
I. Age: 18- 40 years
II. Regular Menstrual Cycle

Exclusion Criteria
I. Subject using oral contraceptive pills
II. Irregular menstruation (menorrhagia)
III. Under medication
IV Diabetes mellitus
V Psychiatric illness.

Collection of samples

The subject was asked to report to the Phlebotomy department on the 20^{th} to 22^{nd} day of the onset of the period (menses). From each subject 5 ml of whole blood was drawn from the vein puncture under all aseptic precautions with a disposable syringe. The needle was detached from the syringe and blood was transferred to the gel tube container blood was left for 20 min and then it was centrifuged at 2000 RPM for 5 minutes. Then serum sample was sent to the Biochemistry Lab for Hormonal test evaluation.

Statistical analysis

The data were collected based on reading given by sample fed in a fully automated Hormonal analyzer and data was arranged on MS Excel. Statistically significant differences among quantitative variables

were evaluated ANNOVA with the Help of SPSS software (version 27). A *p-value* less than 0.005 was considered statistically significant.

Result:

Table 1. Demographic Profile of the Patients

		Control		PMS	
		Frequency	Per cent	Frequency	Per cent
Age	18-25	16	40	12	30
	26-35	18	45	17	42.5
	36-40	6	15	11	27.5
Education Level	High School	8	38.9	7	17.5
	Intermediate	12	14.4	13	32.5
	Bachelor	16	15.6	12	30
	Masters	4	31.1	8	26.60
Employment Status	Employed	8	20	10	27.8
	Others	7	17.5	6	15
	Students	12	30	16	40
	Unemployed	13	32.5	8	20
Marital Status	Divorce	3	7.5	3	7.5
	Married	17	42.5	20	50
	Unmarried	20	50	17	42.5
Body Mass Index (BMI)	Normal (18.5-24.9)	17	42.5	15	37.5
	Obese (≥30)	7	17.5	10	25
	Overweight (25-29.9	6	15	5	12.5
	Underweight (<18.5	10	25	10	25

Table 1 shows the distribution of the demographic profile of normal and PMS-affected females. The present study observed that PMS symptoms are more common in 26-35 years of age group. It also signifies that PMS is more common in obese individuals. Somayeh Hashemi et al study showed there was no significance between obesity and PMS. (9)

Table 2 Comparison of Hormonal Parameters

Parameters	Day	Control Mean ± SD	PMS Mean ± SD	Significance
Estrogen	22	87.87±29.46	66.5±21.91	0.0004
Progesterone	22	1.97±1.18	1.52±0.91	0.0064
FSH	21	2.65±1.11	3.03±1.5	0.0034
LH	22	2.36±0.9	3.34±1.42	0.00019
TSH	21	3.47±1.2	4.55±1.53	0.0007
Prolactin	22	6.13±2.09	7.7±1.18	0.0006

Table 2 shows a comparison of hormonal parameters of women with and without PMS. Our results suggest that there was a significant decrease in estrogen, and progesterone levels in females having PMS compared to Normal females, whereas there was an increase in FSH, LH & TSH in PMS-affected females compared to Normal females. Prolactin levels were significantly high in PMS-affected females. After adjusting age and BMI linear regression analysis demonstrated a significant association Between PMS and fluctuation of Hormonal parameters. From the above table, it was

observed that P- value of estrogen is 0.0004, showing a significant decrease in estrogen levels in PMS-affected females compared to the control group. p-vale of progesterone is 0.0064, In PMS -affected females there is a significant decrease in Progesterone compared to normal females. FSH level in PMS-affected females is higher than normal control population. A P-value is 0.0034. Luteinizing hormone is higher in PMS-affected females in comparison to normal females. p- value is significant (0.00019). TSH of females with PMS was significantly higher compared to normal females. p-value is (0.0007). Prolactin in PMS-affected females is higher compared to normal females. P -value (0.0006).

Discussion

In this study, we assessed a wide range of hormones to establish their association with PMS. there was a significant decrease in estrogen and progesterone levels in PMS-affected females, while it was observed that there were increases in TSH, FSH and prolactin levels in PMS.

Thysi-Jacobs et al. (17) demonstrated that women with PMDD had lower free estradiol levels during the luteal phase. In the present study, the difference in estrogen was significant.

Previous reviews demonstrated that women with PMDD had lower free estradiol levels during the luteal phase. (14) Progesterone has been repeatedly reported to exaggerate premenstrual symptoms in women with PMDD.

Schmidt et al (19) demonstrated that progesterone provokes premenstrual symptoms in women with PMDD but not in controls.

Ju-Yu Yen et al. (22) study suggested that a lower Early luteal-phase estrogen level may be involved in the vulnerability to the progesterone effect in women with PMDD. Thus, combining the moderating effect of lower EL-phase estrogen level and the provoking effect of progesterone, the participants with PMDD experienced exacerbation of symptoms after a timely increase in progesterone level under a lower estrogen level. Subsequently, symptoms rapidly improved as the progesterone reached the lowest level after the onset of menstruation.

Segebladh et al. (20) discovered that estrogen combined with progesterone provoked more premenstrual symptoms than estrogen only.

A study demonstrated increased sensitivity to the GABA receptor agonist effect of allopregnanolone when administered to women with PMDD in the luteal phase, this may explain why progesterone improves premenstrual symptoms in control.

Somayeh Hashemi et al (9) study showed there was no significance of TSH between normal and PMS-affected females. Prolactin (PRL) and triglycerides (TG) were significantly elevated in women with PMS, whereas their testosterone (TES), high-density lipoprotein (HDL) and 17-hydroxyprogesterone (17-OHP) levels were significantly less than they were in women without the syndrome ($P < 0.05$). After adjusting for age and body mass index (BMI), linear regression analysis demonstrated that for every one-unit increase in PMS score, there was a 12% rise in the probability of having metabolic syndrome ($P = 0.033$).

In this study, we also got a significant increase in TSH value in PMS-affected females compared to normal females.

Plasma prolactin and testosterone concentrations were measured during the luteal phase in women suffering from premenstrual tension syndrome (PMS). (14) The findings of these hormones were compared to those measured in women without PMS. (15) There were no differences between mean prolactin or testosterone levels in the patient group compared to those of the controls. (16)

M Steiner et al (24), elevated luteal phase prolactin (PRL) level was high compared to the normal control group so it has been suggested that an increase in prolactin may be associated with PMS. In this present study, we also found that there is an increase in prolactin in the PMS-affected female.

Conclusion: From this study, we have observed that the estrogen and progesterone level was significantly decreased in PMS-affected females compared to normal females. decreased in

Progesterone causes an increase in prostaglandins and cytokines and it also causes the uterine artery to become more fragile this all together may cause muscle cramps and pain before the menstrual cycle. The levels of FSH, LH, TSH and Prolactin was significantly higher in PMS-affected patients.

Bibliography

1. Stolberg M. The monthly malady: a history of premenstrual suffering. Medical history. 2000 Jul;44(3):301-22.
2. Di Giulio G, Reissing ED. Premenstrual dysphoric disorder: prevalence, diagnostic considerations, and controversies. Journal of Psychosomatic Obstetrics & Gynecology. 2006 Jan 1;27(4):201-10.
3. Figert AE. The three faces of PMS: The professional, gendered, and scientific structuring of a psychiatric disorder. Social problems. 1995 Feb 1;42(1):56-73.
4. Shrestha DB, Shrestha S, Dangol D, Aryal BB, Shrestha S, Sapkota B, Rai S. Premenstrual syndrome in students of a teaching hospital. Journal of Nepal Health Research Council. 2019 Aug 9;17(2)
5. Acikgoz A, Dayi A, Binbay T. Prevalence of premenstrual syndrome and its relationship to depressive symptoms in first-year university students. Saudi Medical Journal. 2017 Nov;38(11):1125-1131. DOI: 10.15537/smj.2017.11.20526. PMID: 29114701; PMCID: PMC5767616.
6. Chin LN, Nambiar S. Management of premenstrual syndrome. Obstetrics, Gynaecology& Reproductive Medicine. 2017 Jan 1;27(1):1-6.
7. Hanchinal VB, Sambrani A, Baljoshi V. A study on influence of different phases of menstrual cycle on hematological parameters. J Exp Clin Med. 2021;38(3):308–11.
8. Modzelewski S, Oracz A, Żukow X, Iłendo K, Śledzikowka Z, Waszkiewicz N. Premenstrual syndrome: new insights into etiology and review of treatment methods. Frontiers in Psychiatry. 2024 Apr 23; 15:1363875.
9. 9 Hashemi S, Ramezani Tehrani F, Mohammadi N, Rostami Dovom M, Torkestani F, Simbar M, Azizi F. Comparison of Metabolic and Hormonal Profiles of Women With and Without Premenstrual Syndrome: A Community Based Cross-Sectional Study. Int J Endocrinol Metab. 2016 Feb 14;14(2):e28422. doi: 10.5812/ijem.28422. PMID: 27679647; PMCID: PMC5035673.
10. Angst J, Sellaro R, Merikangas KR, Endicott JE. The epidemiology of perimenstrual psychological symptoms. Acta Psychiatrica Scandinavica. 2001 Aug 1;104(2).
11. Li Y, Pehrson AL, Budac DP, Sánchez C, Gulinello M. A rodent model of premenstrual dysphoria: progesterone withdrawal induces depression-like behavior that is differentially sensitive to classes of antidepressants. Behavioural brain research. 2012 Oct 1;234(2):238-47.12. Bloch M, Schmidt PJ, Su TP, Tobin MB, Rubinow DR. Pituitary–adrenal hormones and testosterone across the menstrual cycle in women with premenstrual syndrome and controls. Biological Psychiatry. 1998 Jun 15;43(12):897-903.
12. Bixo M, Ekberg K, Poromaa IS, Hirschberg AL, Jonasson AF, Andréen L, Timby E, Wulff M, Ehrenborg A, Bäckström T. Treatment of premenstrual dysphoric disorder with the GABAA receptor modulating steroid antagonist Sepranolone (UC1010)—A randomized controlled trial. Psychoneuroendocrinology. 2017 Jun 1; 80:46-55.
13. Halbreich U. The etiology, biology, and evolving pathology of premenstrual syndromes. Psychoneuroendocrinology. 2003 Aug 1; 28:55-99.
14. Halbreich U, Ben-David M, Assael M, Bornstein R. SERUM-PROLACTIN IN WOMEN WITI PREMENSTRUAL SYNDROME. The Lancet. 1976 Sep 25;308(7987):654-6.

15. Bäckström T, Aakvaag A. Plasma prolactin and testosterone during the luteal phase in women with premenstrual tension syndrome. Psych neuroendocrinology. 1981 Jan 1;6(3):245-51.
16. Carroll BJ, Steiner M. The psychobiology of premenstrual dysphoria: the role of prolactin. Psychoneuroendocrinology. 1978 Jan 1;3(2):171-80.
17. Thys-Jacobs S, McMahon D, Bilezikian JP. Differences in free estradiol and sex hormone-binding globulin in women with and without premenstrual dysphoric disorder. The Journal of Clinical Endocrinology & Metabolism. 2008 Jan 1;93(1):96-102.
18. Walf AA, Koonce CJ, Frye CA. Estradiol or diarylpropionitrile decrease anxiety-like behavior of wildtype, but not estrogen receptor beta knockout, mice. Behavioral neuroscience. 2008 Oct;122(5):974.
19. Schmidt PJ, Nieman LK, Danaceau MA, Adams LF, Rubinow DR. Differential behavioral effects of gonadal steroids in women with and in those without premenstrual syndrome. New England Journal of Medicine. 1998 Jan 22;338(4):209-16.
20. Segebladh B, Borgström A, Nyberg S, Bixo M, Sundström-Poromaa I. Evaluation of different add-back estradiol and progesterone treatments to gonadotropin-releasing hormone agonist treatment in patients with premenstrual dysphoric disorder. American journal of obstetrics and gynecology. 2009 Aug 1;201(2):139-e1.
21. Timby E, Bäckström T, Nyberg S, Stenlund H, Wihlbäck AC, Bixo M. Women with premenstrual dysphoric disorder have altered sensitivity to allopregnanolone over the menstrual cycle compared to controls—a pilot study. Psychopharmacology. 2016 Jun; 233:2109-17.
22. Yen JY, Lin HC, Lin PC, Liu TL, Long CY, Ko CH. Early-and late-luteal-phase estrogen and progesterone levels of women with premenstrual dysphoric disorder. International Journal of Environmental Research and Public Health. 2019 Nov;16(22):4352.
23. NIKOLAI TF, MULLIGAN GM, GRIBBLE RK, HARKINS PG, MEIER PR, ROBERTS RC. Thyroid function and treatment in premenstrual syndrome. The Journal of Clinical Endocrinology & Metabolism. 1990 Apr 1;70(4):1108-13.
24. Steiner, Meir, Haskett, Roger F., Carroll, Bernard J., Hays, Sally E., Rubin, Robert T. (1984)."Plasma prolactin and severe premenstrual tension." Psychoneuroendocrinology 9(1): 29-35.