

Role of 17 Beta Estradiol in Etiology of Premenstrual Syndrome in Medical Students

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ABSTRACT

Objective: To calculate the incidence of PMS (premenstrual syndrome) in young medical female students. To check relation of serum 17 β estradiol with affective symptoms of PMS. **Study Design:** Cross sectional study. **Settings:** The Department of Biochemistry, The University of Faisalabad (TUF). **Duration:** 3 months from September 2017 to November 2017. **Methodology:** The study groups included 50 controls and 31 patients of the age group 18-28 years. Their symptoms of PMS were noted by questionnaire. Blood sampling of participants was performed in luteal phase of cycle. Serum 17 β estradiol was estimated with the help of ELISA. **Results:** The T-test was used to consider a comparison between the affective symptoms of PMS in patients and controls and for comparison of estradiol between the both groups. While comparing estradiol between the both groups, P value is non-significant. For the symptoms of PMS, P value was significant between patients and control group. **Conclusion:** It suggests that the fluctuations in serum estradiol level are not the only cause of affective symptoms of PMS in this study. There may be other factors responsible for the symptoms in selected subjects such as life style, dietary habits or genetics.

Keywords: PMS, 17 beta estradiol, PMDD, Luteal Phase, ELISA

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Submitted for Publication: 07-11-2019

Accepted for Publication: 14-04-2020

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Citation: Saeed S, Saeed M, Azhar A, Saeed A. Role of 17 Beta Estradiol in Etiology of Premenstrual Syndrome in Medical Students. APMC 2020;14(2):160-3.

DOI: 10.29054/APMC/2020.744

INTRODUCTION

Psychological and physical symptoms happen during premenstrual phase of menstrual cycle. These symptoms get disappeared when menstruation occurs is known as premenstrual syndrome.¹ Affective symptoms comprise irritability, weepiness, fear, anger, fighting behavior, food craving and nausea. Somatic symptoms include leg cramps, headache, body aches, migraine, abdominal bloating, mastalgia.

These symptoms get worse near to menstruation cycle.² Premenstrual syndrome (PMS) occurs because of variations in the levels of hormones. Ovarian steroids show a crucial part for PMS symptoms.³ Almost 30-40% females with reproductive age have PMS. Whereas women (3-8%) have PMDD (premenstrual dysphoric disorder) i.e. severe premenstrual syndrome.⁴

Estrogens influence the female menstrual cycle as well as regulate brain functions.⁵ Naturally occurring estrogens are estradiol, estrone and estriol.⁶ Most effective estrogen of women is 17 beta estradiol.⁷ During the menstrual cycle, women have greater possibilities of mood changes because of unstable levels of estradiol.⁸ This act either with neurotrophic factors or it effects the serotogenic system.⁹

Aims of present research are to record frequency of affective symptoms of PMS in the medical female students and also to note relationship of 17 beta estradiol values with symptoms of PMS. Medical student is affected more by PMS as compared to other students because of more stress of academics on medical

students. Premenstrual syndrome causes negative effects on the performance of medical students. In our country, incidence of premenstrual syndrome in young medical students is 89%.¹⁰

METHODOLOGY

Study Design: Cross sectional study

Settings: Study was conducted on young female medical students in the Biochemistry department of "The University of Faisalabad, Faisalabad Pakistan".

Duration: 3 months from September 2017 to November 2017.

Sample Technique: Non-probability convenient sampling.

Sample Size: A total of 91 medical students were requested to participate in the study.

Inclusion Criteria: Out of these, 81 young medical students with regular menstrual cycles and having age between 18-28 years were included in the study.

Exclusion Criteria: 7 participants refused to give the consent and 3 participants were having irregular menstrual cycles so they were not included in the study.

Data Collection Procedure: The present research work was conducted after getting approval from ethical committee and written informed consent was taken from all participants.

The signs and symptoms of premenstrual syndrome were recorded by a questionnaire developed according to the American College of Obstetrician and Gynecologists (ACOG) criterion of diagnosis for PMS.¹¹ This criterion is used for diagnosis of premenstrual syndrome and its scoring. The

females have at least one somatic and one affective symptom 5 days before menstruation for consecutive 3 cycles. Symptoms get relieved as the menstruation proceeds according to ACOG. Nausea, anger, weepiness, food craving, irritability, fighting behavior and fear are the affective symptoms of premenstrual syndrome. Somatic symptoms contain headache, abdominal bloating, leg cramps, mastalgia and migraine. These all indications should not happen till after 12th day of cycle. Symptoms must be noted down in the absence of any drug or hormonal therapy and underlying pathology. PMS scoring was done on the basis of severity of symptoms. Symptoms severity (PMS scoring) was described in numbers from 1-4 as under.

1. Subjects having no symptoms (No PMS)
2. Patients having mild symptoms (Mild PMS)
3. Patients having moderate symptoms (Moderate PMS)
4. Patients having severe symptoms. (Severe PMS)

The confounding variables were controlled with the help of exclusion criteria. Samples of all subjects were used to estimate the serum 17β estradiol level. During the luteal phase of cycle, this estimation was done by standard assay technique.

Serum 17β estradiol was estimated by using enzyme linked immunosorbent assay (ELISA) technique. This was achieved with the help of ELISA kit by Calbiotech.¹² The underlying principle was competitive ELISA between the sample antibody and antigens present in the kit reagents. The values of serum 17 beta estradiol were noted by ELISA plate reader (Biotech, ELx800).

Statistical package for social sciences (SPSS) version 21 was used for data analysis. The T-test was used to compare qualitative variables between the two groups ¹³ i.e. for comparing the signs and symptoms of premenstrual syndrome between the patients and controls.

RESULTS

Most of our participants were of the age 22-23 years (Table I). Out of all the participants 50 were included in control group (without PMS) and 31 were involved in patient group (having PMS) on the basis of questionnaire filled by the respondents (Figure I). Several controls and patients had feeling of nausea. 50.6% of total included population did not have nausea. None of the controls ever had severe nausea (P<0.00).25.9% patients experienced mild nausea, 18.5% had moderate while4.9% had severe nausea respectively.

Due to premenstrual syndrome, one third of participants did not have mood swings and remaining subjects had mild (35.8%), moderate (24.7%) and severe (13.6%) mood swings (P=0.005). 40.7% of total involved population had not faced deficiency of sleep and weepiness before the periods where as 32.1% had mild symptoms, 13.65% had moderate and severe symptoms (P <0.104).

Mild angry behavior and fighting attitude were found in 30.9% subjects while 18.55 had moderate and 11.1% had severe symptoms. The symptoms are absent in 39.5% of total population (P<0.001). 51.9% never had food craving, 19.8% had mild food craving while moderate and severe food craving was found in 22.2% and 6.2% respectively (P<0.207).

From all study subjects, 39.5 percent claimed their symptoms get relieved when menstruation proceeds.18.5% claimed they never get relieved from the symptoms.23.5 percent population claimed some symptoms got relieved and others persist.18.5% populace often got relieved from symptoms (P<0.00). The T test was used to prepare comparison between patient and control groups about affective symptoms of PMS and 17β estradiol values (Table 2 and Table 3).

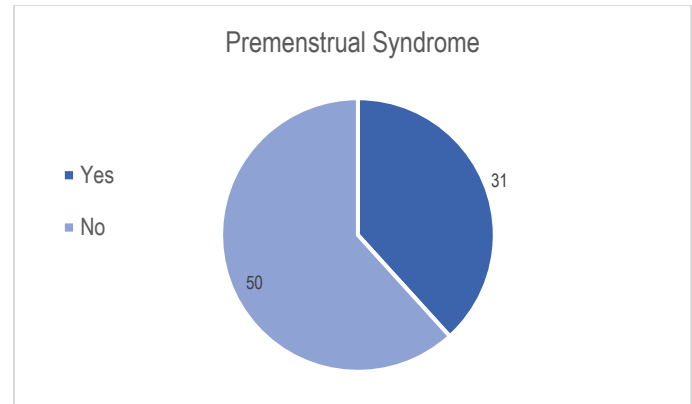


Figure 1: Pie chart showing true patients and control

Table 1: Distribution of respondents regarding age group

Age in years	Frequency	Percent
< 21	28	34.6
22 - 23	37	45.7
24+	16	19.8
Total	81	100.0

Table 2: Comparison between control and patient group regarding affective symptoms of PMS

	Group	N	Mean	SD	P -value
Feeling of nausea or change in taste	Control	50	0.42	0.67	<0.000
	Patients	31	1.35	0.98	
Mood swings	Control	50	0.96	0.95	<0.000
	Patients	31	1.74	0.89	
Lack of sleep or weepiness	Control	50	0.78	0.95	<0.016
	Patients	31	1.35	1.11	
Fighting with others	Control	50	0.68	0.91	<0.000
	Patients	31	1.55	0.96	
food craving	Control	50	0.66	0.89	<0.050
	Patients	31	1.10	1.08	
Mood swings and other symptoms get relieved	Control	50	1.04	0.83	<0.000
	Patients	31	3.00	0.00	

NS = Non-significant (P>0.05); * = Significant (P<0.05); ** = highly significant (P<0.01)

SD = Standard Deviation, SE = Standard Error

Table 3: Comparison between patient group and control group regarding serum estradiol levels

	Group	N	Mean	SD	P-value
Estradiol (pg/mL)	Control	50	32.34	20.29	0.470 ^{NS}
	Patients	31	35.71	20.38	

NS = Non-significant ($P>0.05$); * = Significant ($P<0.05$); ** = highly significant ($P<0.01$)

SD = Standard Deviation, SE = Standard Error

DISCUSSION

Many enrolled participants had no fighting attitude to other people in this study of premenstrual syndrome. Almost half controls did not have complain of fighting attitude and most patients had mild fighting behavior. The severity level of above-mentioned symptom of PMS in this present research project is similar to symptoms of PMS in another research work which was performed by Nisar and co-workers on students of medical field in Pakistan.¹⁰

More than half included subjects had not food craving. The patients suffering from such symptoms, many of them had moderate food craving. Maximum control group had no food craving. Seedhom *et al.* performed a study on the students from medical field in Egypt, they presented most of their subjects had mild to moderate food craving. They also showed a very less about 6.7% medical students had worse indications.¹⁴

Half involved subjects did not have nausea but many of them had mild. None of the control subjects of this research work experienced severe type of nausea. Most patients had mild and moderate feeling of nausea. Result regarding nausea feeling of this project similar to other research work which was performed by Tolossa and Bekeleon on the students of medical in Ethiopia. Maximum subjects having mild nausea symptoms in both studies.¹⁵

The assessment of estradiol concentration was conducted between patient and control groups. Mean value of 17 β estradiol in patients are 35.71 \pm 20.38 pg/mL and the mean estradiol value in control group is 32.34 \pm 20.29 pg/mL. 0.470 is the p value which is not much significant in this regard. This result explains that there is no noticeable difference in the value of estradiol between patient and control groups. These estradiol results in both groups of patient and control of this study have same findings with another research work that was done by Thys-Jacobs and colleagues on women who had PMDD and also on healthy controls.

Our findings of research work presented that mean estradiol value in luteal stage in both patient and control groups are 153.2 \pm 46.4pg/mL and 150 \pm 57.8pg/mL respectively. The p value is calculated and considered as 0.76 which is also not much significant. Such results proposed no clear difference in estradiol values between both patient and control groups. Estradiol concentration bound to the sex hormone binding globulin (SHBG) could be varied between patient and control groups.¹⁶

The p value for 17 β estradiol results in both patient and control groups is not much significant ($P>0.05$) in this study. This shows estradiol levels have no important part in PMS symptoms in these study groups. This is contradicting to present research project hypothesis that low level of estradiol has a great part in symptomology of PMS.

Hammarbäck and his colleagues conducted a research project in 1989 on females with premenstrual syndrome. They checked estradiol and progesterone levels in their serum. They also assessed and kept record of their severity of premenstrual symptoms. Their findings presented an increased value of estradiol which was linked to intense PMS symptoms. Their study suggested that during luteal phase of cycle, level of severity of symptoms related to PMS cannot be associated to decreased levels of estradiol. These results are contrary to this present hypothesis.¹⁷

CONCLUSION

In this current study, the prevalence of premenstrual syndrome is 38.3% i.e. from all the participants 31 were suffering from premenstrual syndrome and 50 participants i.e. 61.7% were healthy controls. The study data suggests that many of the patients do not have symptoms and many of the controls show the symptoms of premenstrual syndrome and p-value is not significant between the patients and controls.

Therefore, it is concluded that variations of 17 beta estradiol do not affect solely the premenstrual syndrome signs and symptoms in these study subjects. There may be other factors involved in the etiology of premenstrual syndrome such as serum calcium, zinc or iron levels and vitamins deficiencies like vitamin B6 or vitamin C etc.

LIMITATIONS

Only 81 participants were included in the study. Number of patients and controls can be increased to elaborate this study. Furthermore, only parameter compared in patients and controls is serum levels of 17 beta estradiol. More variables like age of menarche, role of vitamins and minerals in PMS and factors like BMI etc. can also be studied in relation to premenstrual syndrome.

SUGGESTIONS / RECOMMENDATIONS

This study will help to highlight the importance of PMS in young female students of medical field and to explore more causative factors involved in the etiology of premenstrual syndrome. It will also help to formulate strategies for reducing the negative impact of PMS on academic activities of medical students.

CONFLICT OF INTEREST / DISCLOSURE

No conflict of interest is involved.

ACKNOWLEDGEMENTS

All the praises and thanks are to Allah, the Lord of the worlds, who is the ultimate source of all knowledge to mankind. Bow in

obeisance, I before my Lord, WHO bestows me to fortitude and impetus to accomplish this work.

I feel an immense love and respect for my parents, their prayers and limitless efforts helped me a lot in my life. My heartiest thanks to my father late Muhammad Saeed who has always been a source of inspiration for me in all the aspects of life and has supported me to accomplish this research work.

Special thanks to Prof. Dr. Muhammad Saeed and Dr. Ayesha Azhar for the help and moral support.

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AUTHORSHIP CONTRIBUTION

Sadaf Saeed	Performance of experimental work and manuscript writing
Muhammad Saeed	Conceived the idea and supervised the experimental work
Aysha Azhar	Help in Manuscript writing
Adnan Saeed	Proof reading and clinical input