

Evaluation of changes in periodontal health during menstrual cycle-a longitudinal study

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Abstract:

Introduction: Hormonal fluctuation during menses alter the female's response to dental plaque. In present study it has been correlated with gingival and oral cavity changes.

Aims:

- 1) Evaluate gingival changes during 1st day of menses, ovulation day and 5 days before menses onset
- 2) Correlate these with dental plaque 3. Assess relationship between menstrual cycle and tooth mobility, oral ulcers, other dental complaints.

Materials and Methods: Total 86 female subjects in age group 18-25 years with gingival inflammation, normal and steady menstrual cycle were seen at 1st day of menses (M), ovulation (O) and 5 days prior to menses onset (PM). Plaque Index [PI], Gingival Index [GI], Papillary Bleeding Index [PBI] were recorded at these three points. Occurrence of oral ulcers and mobility was also noted.

Results: Mean value of PI at M, O & PM were respectively 0.79±0.88, 0.78±0.87, 0.79±0.86, of GI were respectively 1.79±0.13, 1.91±0.09, 1.87±0.12. Mean values of PBI at M, O & PM were respectively 2.55±0.50, 3.20±0.48, 2.94±0.53. Mean values of PI at M,O & P were almost identical. GI & PBI were significantly higher at ovulation & premenstruation in comparison to menstruation (p<0.001). Mean value of mobility at M, O and PM were 0.025+0.080, 0.025+0.08, 0.026+0.08 respectively and so no statistically significant difference was recorded. 6 patients reported pain and discomfort in gums and burning sensation in mouth just before menses. No correlation was found between the occurrence of ulcers and hormone fluctuation.

Conclusion: Significant changes were observed in the GI score and PBI score of females during various stages of menstrual cycle.

Keywords: Menstrual cycle, ovulation, gingivitis.

Introduction

Bacterial plaque has been implicated as the primary etiological factor for the initiation of periodontal disease. However a susceptible host is supposed to be a prerequisite for the dental plaque to elicit initiation or progression of gingival/periodontal disease. Susceptibility of the host can be modified by many factors like smoking, stress, diabetes, genetics, neutrophil dysfunction etc. Sexual hormones have been suggested to be an important among them. Fluctuation in estrogens and progesterone level starts affecting the periodontium from puberty itself^[1].

The effect of fluctuation in hormone levels during menstrual cycle on cardiovascular disease^[2], urinary tract function^[3] & the immune system^[4] has been described in numerous studies. Several women report bleeding and swollen gingiva^[5, 6], burning sensation, generalized pain and discomfort in gums^[7] & sometimes a minor increase in tooth mobility^[5, 8] during menses. A gradual increase in gingival crevicular fluid has been reported during the proliferative phase just before menstruation coinciding with the increased production of estrogen & progesterone^[6]. Some studies have shown that gingival exudates increases in menstruation from the inflamed gingiva^[9]. Other studies suggest that changes in sex steroid hormones during menstrual cycle might have a limited effect on the inflammatory status of gingival, but GCF cytokines levels were not affected^[10]. During luteal phase intraoral recurrent aphthous ulcers^[11], candida infection & herpes labialis lesions may also occur in some women^[12].

Perusal of the available literature reveals only a few studies^[7, 13-15] correlating the hormone levels at various stages of menstrual cycle with the level of inflammation in gingiva. An attempt was made in this study to evaluate the inflammatory changes involving gingiva, at three points of menstrual cycle that were menstruation, ovulation & premenstruation and correlate them with the dental plaque levels.

Materials and Methods

Female patients in the age group of 18-25 years having gingival inflammation and with normal and steady menstrual cycle were included in this longitudinal study. Each patient provided signed informed consent to participate in the study. Patients who consented to be included in the study were told of its nature.

Patients were recruited from pool of patients at the Department of Periodontics and Oral Implantology, PGIDS, Rohtak for treatment. The patients with any known metabolic or systemic condition or any iatrogenic factor affecting the periodontium, with dental caries, history of orthodontic treatment, using immunosuppressant's or antibiotics during the time of study or during last three months from the time of study, were excluded from the study.

Preliminary appointment schedule for clinical examination at menstruation (1st day of menstrual cycle), ovulation (generally 14th day of 28 day cycle) and premenstruation (5 days before the onset of menstrual bleeding) was set. The period between ovulation & next menstrual bleeding is constant i.e. about 14 days. So, on the basis of duration of cycle the day of ovulation was estimated. Plaque index (PI) ^[17], Gingival index (GI) ^[16] and Papillary Bleeding Index (PBI) ^[18, 19] were recorded at mesial, facial, distal and lingual surface of every tooth, by the same examiner on all the teeth (except third molars) with a Williams periodontal probe at all the three visits that were 1st day of menstrual cycle, ovulation day and 5 days prior to onset of menstrual bleeding (premenstruation). Presence of ulcers or any other complaints like tooth mobility ^[20], burning sensation in mouth, pain and discomfort in mouth, if present were also recorded in the enrolled subjects. Presence or absence of ulcers was noted at all the three visits and also patient was being questioned about the burning sensation or any other pain or discomfort in the mouth.

All clinical procedures were performed in accordance with the Declaration of Helsinki and Good Clinical Practice Guidelines. The research protocols were approved by Institutional Review Board.

A calibration exercise was performed to obtain acceptable intra-examiner reproducibility. Intra-examiner reproducibility was assessed with a calibration exercise performed at two separate occasions, 48 hours apart. Calibration was accepted if greater than 90 percent of the recording could be reproduced with a difference of 1 mm.

A total of 142 females were recruited for the study. 48 were excluded as they failed to meet inclusion criteria. So data was recorded in 94 females. But of those 94 females 2 didn't report for follow up, 1 became pregnant and in 3 there was unexpected fluctuation in dates. Hence, finally 86 females completed the study and were analysed for the results (Fig 1).

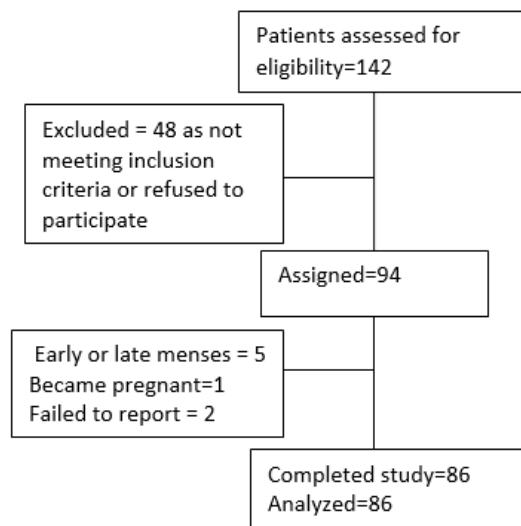


Fig 1: Flow diagram of study outline

Statistical Analysis

Analysis of variance (ANOVA) for repeated measures was done to determine differences in clinical parameters between the three examination time points. The mean values and the standard errors of the measured parameters were also assessed by Z test. All calculations were undertaken using a statistical software package. GI scores and PBI scores were significant at $p < 0.001$.

Results

Fig 2 and Table. 1 shows variations in clinical indices during menstrual cycle using ANOVA. Mean PI was basically identical for M, O and PM (0.7884 ± 0.0876), (0.7828 ± 0.0868), (0.7888 ± 0.0861) respectively throughout the study. Despite the similarities in PI, GI was higher at ovulation (1.9192 ± 0.0888) and premenstruation (1.8755 ± 0.1258) as compared to menstruation (1.7913 ± 0.1289).

Similarly PBI was also higher at ovulation (3.2021±.4789) and premenstruation (.029452±.5319) than the menstruation (2.5483±.5044) and their difference was statistically significant. Mean values of both GI and PBI were higher at ovulation than the premenstruation and this difference was also statistically significant. Fig.3 is a line diagram depicting the same.

No change in tooth mobility was found at menstruation, ovulation and premenstruation. Only six patients reported pain and discomfort in gums and burning sensation in mouth just before menses. But oral ulcers were not reported in any of the patients (Table 2).

Variation of clinical indices (mean) during menstrual cycle

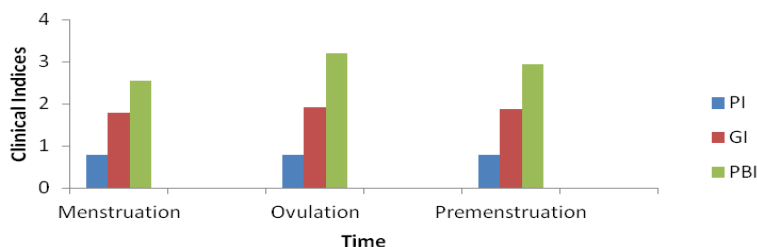


Fig 2

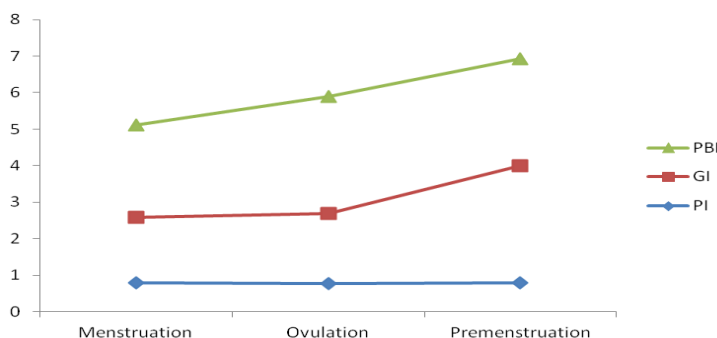


Fig 3: Line diagram

Table 1: Comparison of Clinical Indices during Menstrual cycle

Variable	Menstruation		Ovulation		Premenstruation		Z test		
	Mean	SD	Mean	SD	Mean	SD	M-O	O-P	P-M
PI	0.7884	0.0876	0.7828	0.0868	0.7888	0.0861	NS	NS	NS
GI	1.7913	0.1289	1.9192	0.0888	1.8755	0.1258	**	**	**
PBI	2.5483	.5044	3.2021	0.4789	2.9452	0.5319	**	**	**

Plaque index (PI), Gingival index (GI), Papillary bleeding index (PBI). Not Significant (NS), p<0.001**

Table 2: Comparison of mobility

Variable	Menstruation			Ovulation			Premenstruation		
	Mean	SD	SE	Mean	SD	SE	Mean	SD	SE
Mobility	.025	.080	.008	.025	.08	.008	.026	.080	.008

Discussion

The present study was undertaken with an attempt to gauge and correlate the inflammatory status of gingiva, at various stages of menstrual cycle that are menstruation, ovulation & premenstruation, with the local irritants in form of plaque.

Plaque Index (Silness and Loe) was used to assess the thickness of plaque at three different time points of menstrual cycle. No statistically significant difference was found in the amount of plaque at menstruation, ovulation and premenstruation. The findings reveal that local irritants cannot be accounted for the changes, if any, noticed in the inflammatory status of the gingiva. Gingival inflammation was assessed by Gingival Index & Papillary Bleeding Index. Statistically significant difference (p<.001) was found in the Gingival Index as well as Papillary Bleeding Index of gingiva at menstruation as compared with ovulation & premenstruation which was possibly due to fluctuation in hormone levels as plaque levels were same at all the three stages. Gingival Index & Papillary Bleeding Index of gingiva when compared at ovulation and premenstruation also showed significant change. (p<.001)

Chanda. *et al.* [13] also studied the effect of menstrual cycle on females exhibiting gingival inflammation

but their sample size was only 5, which was very small as compared to that of present study. Also, they did not find any change in inflammatory changes of gingiva at day 1, 7, 14, 21 of menstrual cycle, in females exhibiting gingival inflammation. The level of progesterone is at its peak at 24th day of 28th day menstrual cycle. So on 21st day the level might not be very high to cause inflammatory changes in gingiva. Results of this study are similar to study by E Macheti^[4] who also noted increase in gingival inflammation at ovulation and premenstruation in a longitudinal study of periodontally healthy premenopausal women. But their sample size was also (15) very small.

In the previous studies by C. Chanda^[13] and E Macheti^[4] only the Gingival Index was used to assess and correlate the inflammatory changes in gingiva with fluctuation in hormone levels during menstrual cycle. The Gingival Index (Loe and Silness) uses the presence of slight color change and the absence of bleeding when a blunt instrument is used to palpate the soft tissue wall of gingival margin to indicate initial gingival inflammation. However, the color changes may sometimes be so mild that they cannot be appreciated. Moreover, it is a subjective finding. The advantage of bleeding as a clinical sign is that it is an objective parameter to estimate inflammation in gingival tissue and there is less degree of subjective error inherent with trying to estimate the degree of color change^[21, 22]. It has the potential for diagnosing inflammatory lesions in regions inaccessible for visual monitoring^[23]. To know the extent and range of bleeding and further quantify it, graded bleeding index i.e. Papillary Bleeding Index (Saxer & Muhlemann) was used. Bleeding Index at menstruation, ovulation and premenstruation was shown by the present study.

Shourie V. *et al.*^[14] in their study showed that ovarian hormones have negligible effect on clinically healthy periodontium. However, these may exaggerate pre-existing inflammation in gingival tissues. Khosrovirmani M. *et al.*^[15] showed that changes occurring during menstrual cycle influence and induce inflammatory conditions in gingiva.

The differences observed in gingival inflammation may be attributed to interaction between sex steroid hormones and specific inflammatory cells in periodontium. Receptors for estrogen and progesterone have been demonstrated in the gingiva, and thus gingiva can be thought of as a target organ for progesterone and estrogen^[24-30]. The pathway for this hormonal tissue interaction in the periodontium could be due to various factors. Brannstrom and coworkers^[31] reported that tumour necrosis factor (TNF α) showed significant fluctuation during the whole cycle, with surge just before OV and PM. TNF alpha regulates the inflammatory response by ligating at the site of epithelial lesion by specialized membrane channel aquaporin 3 and ICAM-1 protein and it is closely implicated in development of periodontitis mechanism.³² These findings might implicate TNF α as one of the mediators of gingival inflammation.

Gornstein *et al.*^[33] and Lapp *et al.*^[34] reported that IL-6 production was down regulated by progesterone. They concluded that increased sex hormones modulate the development of localized gingival inflammation. Another possible mechanism for the increase in gingival inflammation is the effect of monocytes. Miyagi and coworkers^[35] studied the effect of sex hormones on prostaglandin synthesis by peripheral monocytes. Both estradiol and progesterone (in various concentrations) resulted in an elevated PGE₂ production. This could turn up the inflammatory process *in vivo*, thus being responsible for higher gingival scores at ovulation and premenstruation.

A direct effect of sex hormones on periodontal pathogens might also play a role in promoting gingival inflammation during the ovulation and premenstruation period. Klinger *et al.*^[36] showed an increase in sulcular *Prevotella intermedia* species after treatment with oral estradiol preparations the fluctuation in estrogen levels during the menstrual cycle could be accompanied by similar fluctuation in bacterial flora, thus resulting in changes in gingival scores.

The effect of steroid sex hormone on angiogenesis could also play a role^[37, 38]. Yuan *et al.*^[39, 40] showed that female sex hormones can modulate angiogenetic factors in pyogenic granuloma. It is also possible that similar to other organs, vascular endothelial growth factors (VEGF) and VEGF receptors in the gingiva are modulated by estrogen/progesterone, thus contributing to the increase in gingival inflammation in the ovulation and premenstruation stages of the menstrual cycle. Progesterone increases vascular permeability due to vascular dilatation^[41]. It increases the production of prostaglandins^[42]. It increases PMN and prostaglandin E₂ in the gingival crevicular fluid^[42].

Lindhe and Branemark^[38, 43] have shown increase cellular proliferation in blood vessel by estrogen. It inhibits PMN chemotaxis^[44]. Estrogen decreases keratinisation that results in the diminution in the effectiveness of the epithelial barrier. The reduction in keratinisation can result in change in the color of the gingiva. Increase in inflammation can also cause color change in gingiva. The exact cause can only be confirmed by the histological section. The present study being clinical one, histopathological changes could not be established.

Relationship could not be established in the present study between the occurrence of ulcers and menstrual cycle. Studies by Segal and Ship^[45, 46] have also failed to demonstrate any influence of menstrual cycle. On the other hand several other investigators have described specific population of women who develop ulcers during the luteal phase of the cycle^[47]. However, the specific mechanism of how steroid sex hormones influence vesicle/ulceration formation remains to be determined. Similar to study by Lawrence A Friedman^[48] this study also did not show any significant change in tooth mobility during various stages of menstrual cycle.

Burdine^[49] observed increased tooth mobility during the fourth week of menstrual cycle. However, there were certain limitations in this study. In the present study mobility was recorded using the criteria given by Lindhe which was not effective in detecting very minute changes, if any, tooth mobility during various stages of menstrual cycle. In the present study, Williams probe (Hu Friedy Co.) was used to test for bleeding response while recording the indices. Since standardization of force could not be ensured because of manual probing, chances of error in bleeding score cannot be ruled out. Use of pressure sensitive probe might have nullified those chances of error. Recording the level of hormones also at all the three visits of the patients would have provided a more substantial evidence and would have added to the authenticity of the study. Changes in the microbial flora and the level of GCF cytokines at all the three visits, if recorded, would have added to the potential of the study.

Further studies to investigate other possible cellular pathways to explore the effects of the menstrual cycle on the markers of gingival inflammation should be undertaken. It is also required to examine whether these transitional changes have any long lasting negative effects on periodontium. Also, the impact of sex hormones during this period on gingival pathologies need to be determined. More studies are required to explore how this phenomenon actually occurs.

This study suggests that changes in sex steroid hormones during menstrual cycle might affect periodontal health. This led us to speculate that studies concerned with the changes in the periodontal parameters should consider the menstrual cycle when including women in their study. Dentist knowledge about the effect of hormonal changes that occur in oral tissues is essential for clinical routine as it can help in diagnosis and treatment of these patients, treating early and teaching to prevent major problem in future through clarification of daily routine.

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