

## CYCLICAL MASTALGIA - IS IT A MANIFESTATION OF ABERRATION IN LIPID METABOLISM?\*

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**Abstract:** Several therapeutic and investigative studies suggest the possibility of the role of lipid profile aberrations in the pathophysiology of cyclical mastalgia. This prospective study is aimed to look for such aberrations. Fiftyseven patients of benign breast disease were included in this study who were symptomatic for at least 6 months prior to presentation. Detailed serum lipid profile work up was performed on day 1, 15 and 25 of menstrual cycle. The patients with symptoms of maximal severity (or limited to) during leuteal phase of menstrual cycle were included in group I (n = 32). Those who had mastalgia, but did not have above mentioned cyclical variation, were included in group II (n = 25). Since non-cyclical mastalgia is a group of heterogeneous disorders of varied etiology, the patients in group II were treated as controls. At day 25, there was an elevation in mean values of HDL-C (P = 0.03) and HDL-C/LDL-C ratio (P = 0.01), and reduction in TC/HDL-C ratio (P < 0.03), in group I. This has not been the case with group II patients. When the patients of mastalgia were treated with low fat dietary regimen, there was a significant difference in the responses of these two groups (P value < 0.0001).

Based on the results of lipid profile study and dietary intervention, we conclude that cyclical mastalgia is an entity which is distinctly different from non-cyclical mastalgia and needs a different therapeutic approach. Our data, both investigative and therapeutic, suggests that cyclical mastalgia may be a result of cyclical aberrations in lipid metabolism, and the physiological treatment in the form of an appropriate dietary regimen holds a considerable promise.

**Key words:** serum lipids mastalgia

### INTRODUCTION

Several studies (1, 2, 3, 4) indicate a possible role of lipid profile abnormalities in the pathophysiology of cyclical mastalgia. This concept has led to the reports of successful trial of low fat dietary regimen in cyclical mastalgia. The medications containing unsaturated fatty acids have been used with

fairly successful results (1). Physiological approach in this disorder appears to be quite promising in view of the fact that this disorder is an aberration of otherwise normal cyclical changes in breast (5). At this juncture, it is quite worthwhile to look into any demonstrable abnormality in lipid profile of such patients. This

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prospective study is an attempt in this direction.

## METHODS

At the Department of Surgical Endocrinology of Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, 57 patients of benign breast disease (BBD) were studied in 1990-91. These patients presented with mastalgia, nodularity and nipple discharge of at least 6 months duration. Cytopathology of needle aspirate of the nodularity (FNABC) and that of discharge was performed to rule out malignancy. All these patients were subjected to the estimations of serum total cholesterol (TC), triglycerides (TG), high density lipoproteins cholesterol (HDL-C), low density lipoproteins cholesterol (LDL-C) and very low density lipoproteins cholesterol (VLDL-C). The serum lipids were scheduled for estimation on day 1, 15 and 25 of menstrual cycle. Serum lipid values have been tabulated separately for these 2 groups and the mean, standard deviation were calculated. Hypothesis test for means was used to find out the comparability of fluctuations. The patients were divided into two groups based on the presence, or the lack, of cyclical features. The patients with cyclical mastopathy (group I) had pain, nodularity heaviness and discharge occurring either during one phase of menstrual cycle regularly, or the continuous symptoms worsening during a particular (leuteal) phase. The patients with non-cyclical symptomatology (group II) either had continuous pain or irregular phase of worsening of symptoms. Both the groups were age matched. The patients of group I were reported to have fibroadenosis (including mammary papillomatosis or hyperplasia) or fat cells on FNABC. In contrast the patients in group II had features of interstitial mastitis, chronic mastitis, granulomatous mastitis or fat cells.

Since non-cyclical mastalgia is a group of heterogeneous disorders of varied etiology (4), the patients in group II were treated as controls. The authors thought it was appropriate to include the patients with

non-cyclical symptoms as control as non-cyclical mastalgia is not because of abnormality in lipid physiology (1).

Fifty patients were kept on dietary treatment who were followed up on a monthly basis for 6 months and, thereafter, every 3 months. The pain was self-evaluated by the patients and recorded on a '10 cm' linear analogue scale charts provided to them. The response to the pain, on linear analogue scale, was categorized as follows : (i) reduction of less than 3 cm - no response; (ii) reduction of 3 to 7 cm - partial response; (iii) reduction of more than 7 cm - good response. Daily diet charts and diary were maintained by the patients. The patients in the treatment group were advised low fat diet (calorie from fat source less than 15% of total calorie requirement), minimal saturated fats and normal or high calorie (depending upon the weight of patient). The follow-up in the treatment group ranged from 3 months to 24 months (median 13 months). Statistical significance of the comparison of the effect of dietary treatment was tested by Chi-Square test.

## RESULTS

Table I and Fig. 1 and 2 demonstrate the means, standard deviation (S.D.) and value of lipid profile on day 1, 15 and 25. Notable feature during leuteal phase was: an appreciable elevation in HDL-C and HDL-C/LDL-C ratio, and statistically significant reduction in TC/HDL-C ratio in group I patients. This was not the case with group II patients.

The data of 36 patients, who could follow the diet properly and were on regular follow up, was available. None of the responders has had recurrence of symptoms when on dietary treatment. The response to pain was much better in the patients with cyclical mastalgia (n=21, good and partial response in 16 and 3 patients respectively) than in those with non-cyclical mastalgia (n=15, good and partial response in 2 and 9 patients, respectively); Chi-square value 13.94, D.F.-2, P value <0.0001.

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TABLE I: Fluctuations in serum lipid values of various components in the patients presenting with cyclical mastalgia (Group I), and others with non-cyclical mastalgia (Group II).

	Group I (n = 32) Mean ± SD (mg/dl)	Group II (n=25) Mean ± SD (mg/dl)
<b>TC</b>		
Day 1	160.3 ± 81.8	164.3 ± 80.6
Day 15	163.9 ± 70.5	151.2 ± 69.8
Day 25	165.2 ± 71.2	164.0 ± 60.8
<b>TG</b>		
Day 1	154.7 ± 96.7	146.1 ± 91.2
Day 15	160.6 ± 137.8	116.2 ± 64.9
Day 25	165.9 ± 108.4	138.0 ± 82.4
<b>HDL-C</b>		
Day 1	43.6 ± 17.6	46.9 ± 25.0
Day 15	42.8 ± 15.9	56.7 ± 62.8
Day 25	53.0 ± 23.7*	60.9 ± 37.3
<b>LDL-C</b>		
Day 1	91.6 ± 56.4	89.3 ± 56.1
Day 15	90.5 ± 55.5	83.5 ± 45.7
Day 25	78.5 ± 48.5	81.8 ± 37.4
<b>VLDL-C</b>		
Day 1	30.9 ± 19.3	29.4 ± 17.3
Day 15	31.9 ± 27.5	25.9 ± 15.2
Day 25	32.0 ± 21.0	28.6 ± 16.3

TC - total cholesterol; TG - triglycerides; HDL-C - high density lipoprotein cholesterol; LDL-C - low density lipoprotein cholesterol; VLDL-C - very low density lipoprotein cholesterol.

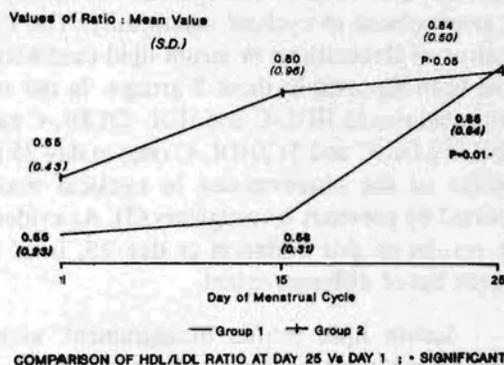


Fig. 1: Fluctuations during menstrual cycle in HDL/LDL ratio of serum lipids in mastalgia patients; cyclical mastalgia (Group I) and non-cyclical mastalgia (Group II). S.D. - standard deviation, \* - statistically significant (P value < 0.05). Comparisons have been made between the values of day 25 with those at day 1 (as base line). HDL/LDL - ratio of high density lipoprotein cholesterol to low density lipoprotein cholesterol.

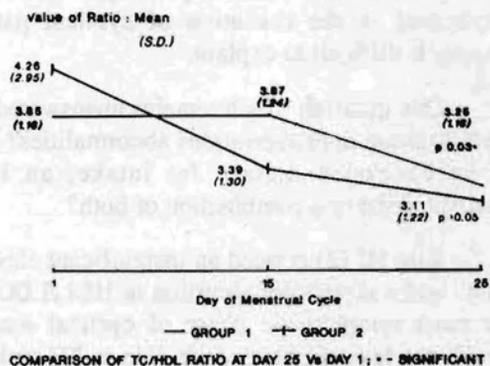


Fig. 2: Fluctuations during menstrual cycle in TC/HDL ratio of serum lipids in mastalgia patients; cyclical mastalgia (Group I) and non-cyclical mastalgia (Group II). S.D. - standard deviation; \* - statistically significant (P value < 0.05). Comparisons have been made between the values of day 25 with those at day 1 (as base line). TC/HDL - ratio of total cholesterol to low density lipoprotein cholesterol.

unlike those in non-cyclical mastalgia (1). The latter disorder includes a number of conditions of heterogeneous etiopathology (1). Goodwin et al (1) noted that the results of non-cyclical mastopathy cannot be extrapolated to cyclical mastopathy. The different patterns of fluctuations in serum lipid (and hormones) have been reported in these 2 groups. In our study, a consistent rise in HDL-C and HDL-C/LDL-C ratio and a fall in LDL-C and TC/HDL-C ratio at day 25 is quite similar to the observations in cyclical mastalgia, reported by previous investigators (3). As evident from the results of this variation at day 25, is of similar pattern but of different extent.

Serum lipid profile measurement, alone, has certain limitations because it does not truly reflect the process of mobilization of fat in the breast during the symptomatic phase of cyclical mastalgia i.e., in leuteal phase. In fact, there is a reciprocal relationship between serum lipids and the breast fat as demonstrated by a few experimental studies. The studies in rats have demonstrated that lipoprotein lipase in the breast tissue is responsible for the mobilization of lipoproteins (6, 7, 8). Whether lipoprotein lipase, and the prolactin (9) play an etiological role in the causation of cyclical symptomatology and lipid profile fluctuations, is a matter of speculation at present. Presently the precise mechanism as to how these cyclic lipid aberrations are implicated in the causation of cyclical pathologic process is difficult to explain.

One question which remains unanswered is what leads to these lipid aberrations abnormalities? Is it due to an excessive dietary fat intake, an inherent predisposition or a combination of both?

Kim HJ (2) noticed an insignificant elevation in HDL, and a significant elevation in HDL/LDL ratio in the most symptomatic phase of cyclical mastopathy i.e., in the leuteal phase. A decline in TC and TG has been reported in leuteal phase of healthy women (10). In our study such a decline has been recorded in group II patients at day 15 in mean values of TC, TG, VLDL-C and in LDL-C and in LDL-C in group I patients. Perhaps a larger sample size could have improved the statistical significance of the above mentioned findings

(which is handicapped by large deviation from the mean values of lipid profile).

Cyclical mastopathy is now considered a lipid disorder (1) and is more common in a society where dietary fat intake is high (1). The results of dietary manipulations suggest the possible role of high fat diet in the causation of cyclical mastalgia. The mechanism of action of this regime could either due to alteration in lipid or due to changes in hormonal metabolism (11).

Preece et al have used evening primrose oil in mastalgia patients with good results (12). Different agents (1) used in the treatment of cyclical mastalgia are considered to bring about the desired changes by hormonal and/or lipid alteration. Following effective treatment, the normalization of HDL and LDL abnormalities have paralleled the achievement in remission (1). Intake of evening primrose oil, and low-fat diet have been found to be effective in mastalgia by causing reduction in serum TG, LDL and HDL (1). Danazol has been found to cause reduction in HDL : LDL ratio (13). Norethisterone, too, is effective in cyclical mastopathy which is associated with lowered HDL : LDL proportion (14). There are speculations that Tamoxifen and primrose oil are effective in mastalgia by reducing HDL, LDL, and total cholesterol.

A physiological therapeutic approach to such a common, and often distressing disorder has not been tried due to two reasons. Firstly, there is a lack of appreciation that a large number of female patients have this problem. Secondly, lack of awareness that cyclical mastopathy may improve with such a treatment. In our country such medications are not available, we have been able to achieve similar results just by dietary alterations as apparent by preliminary results. A distinct pattern of serum lipid fluctuations in cyclical mastalgia patients is quite remarkable in view of parallel worsening (or appearance) of cyclical symptoms and signs during leuteal phase. This has not been the case with non-cyclical patients. These findings raise a question whether cyclical mastalgia is an entity with distinctly different underlying pathophysiology, in comparison to non-cyclical mastalgia. Nonetheless, the possibility of these 2 groups of mastalgia being two

comparison to non-cyclical mastalgia. Nonetheless, the possibility of these 2 groups of mastalgia being two

separate manifestations of a single, though of different extent, spectrum of lipid profile aberrations.

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