MÆDICA - a Journal of Clinical Medicine

ORIGINAL PAPER

MAEDICA – a Journal of Clinical Medicine
2017; 12(4): 258-266

Plasma Prolactin and Total Lipid Levels and Subsequent Risk of Breast Cancer in Pre- and Postmenopausal Women: Experience from an Indian Rural Centre

Nidhi GUPTA, Gautam MENDIRATTA*, Rikki SINGAL, N.S SHARMA

Department of Surgery, M.M. Institute of Medical Sciences and Research, Mullana (Distt-Ambala), Haryana, India

ABSTRACT

Aims and objectives: 1) To analyze serum lipid and prolactin levels in breast cancer patients and normal subjects; 2) to correlate those levels with risk and prognostic factors.

Material and methods: The present study was performed in the Department of Surgery, MMIMSR, Mullana, Ambala, from 2013 to 2014, at a rural centre. The study group comprised 40 patients with carcinoma of the breast who underwent surgery and the control group included 10 patients who underwent surgery for reasons other than carcinoma of the breast. Apart from routine tests, special investigations like estimation of serum lipids and prolactin levels were carried out in each patient to assess the general health status and detect any potential evidence of distance metastasis.

Results: Most patients were in the fourth and fifth decade of life. The mean value of serum total cholesterol in the study group (190.77 mg/dL) was higher than that of the control group (166.22 mg/dL), which was statistically significant. The mean value of LDL in the study group was 153.8 mg/dL, as compared to 118.4 mg/dL in the control group; therefore, the difference in LDL cholesterol levels between the two groups was statistically significant. The VLDL level was also higher in breast cancer patients, with a mean value of 35.25 mg/dL, as compared to 22.6 mg/dL in the control group. Serum triglycerides showed higher trends in the study group than in controls. The correlation coefficient of total lipids and prolactin was 0.428, which was significant (p value 0.002), and pointed to a positive relation between prolactin and total lipids, meaning that an elevation in total lipids would lead to an increase in prolactin levels.

Address for correspondence:
Gautam Mendiratta,
Department of Surgery, M.M. Institute of Medical Sciences and Research, Mullana (Distt-Ambala), Haryana, India
Mobile phone: 07404371155, Fax: 01731304550
Email: muzzafarzaman@yahoo.com

Article received on the 29th of June 2017 and accepted for publication on the 14th of December 2017.

Conclusion: It was observed that significantly increased prolactin levels were found among patients with breast cancer. Serum lipids in carcinoma of the breast had higher levels of VLDL and LDL cholesterol and elevated triglyceride concentrations. Serum prolactin showed a statistically significant elevation in premenopausal patients as compared to postmenopausal subjects with breast cancer. Prolactin level may be also one of the risk factors for breast cancer, which points to its diagnostic significance.

Keywords: breast, carcinoma, serum prolactin, lipid profile.

Abbreviations:
BC=Breast Cancer
PRL=Prolactin
GGT=Gamma Glutamyl Transferase
TC=Total Cholesterol
TG=Triglycerides
HDL=High Density Lipoprotein
LDL=Low Density Lipoprotein
VLDL=Very Low Density Lipoprotein
ELISA=Enzyme Linked Immunosorbent Assay
OCP=Oral Contraceptives Pills

INTRODUCTION

Elevated body mass index (BMI) has been linked to an increased relative risk for receptor-positive breast cancer (BC). Epidemiologic evidence has long suggested that estrogen-progestin use is associated with a higher risk for BC (1). The ranges of age at diagnosis as well as the clinical symptoms do not differ from those of conventional invasive ductal BC (2). The incidence of the disease is less than 4% in females below the age of 35, and approximately 7% of all breast malignancies are diagnosed in women under 40, which is broadly similar to the 13% of the subjects in the current series who had ductal carcinoma *in situ* (3).

Both low fat and high fibre diets may be weakly protective against BC. Breast cancer risk factors can be broadly classified into two categories: non-modifiable risk factors, including age, race/ethnicity, genetics/family history, and age at menarche; and modifiable risk factors, including diet, alcohol consumption, overweight, smoking and physical exercise (4). Given the differences in epidemiology and management options, as well as the unique issues surrounding fertility, sexuality and pregnancy, the multidisciplinary approach to treatment for these women may often incorporate other areas of expertise (5). Serum lipids, low HDL and high serum triglycerides (TG) were found to be positively associated with the risk of BC in female patients. No association was found between fasting serum glucose level and risk of breast cancer (6). Cholesterol is a structural component of the cell membrane, mainly localized in lipid rafts – membrane micro domains that assemble the signal transduction machinery and associate to proteins implicated in key cellular signalling pathways. Many of these pathways closely associate with malignant transformation due to their influence in the organization of cytoskeleton, cell polarity and angiogenesis (7, 8).

In the present study, a comparative evaluation of serum lipids and serum prolactin in BC patients was done. This can be valuable in understanding the aetiological basis of breast malignancy and its association with the socio-economic status in patients undergoing surgery for reasons other than malignant disease were also taken as consideration. Serum TG had more elevated levels in the study group than in controls. Similarly, serum prolactin level showed a statistically significant elevation in BC patients as compared to controls. The aim of the study was to evaluate serum lipids and prolactin levels and explore their correlation in female patients suffering from BC. ❑

MATERIAL AND METHODS

The present study was conducted on a group of 40 diagnosed cases of BC patients undergoing surgical treatment in the Department of Surgery, MMIMSR, Mullana, Ambala. The study group consisted of 40 BC patients who underwent surgery and the control group of ten women with comparable age and socio-economic status who underwent surgery for reasons other than malignant disease of the breast. Diagnosis of carcinoma of the breast was established on the basis of clinical features, fine needle aspiration cytology and tissue histopathology in operated

specimens for each patient apart from a detailed history, and clinical examination records were maintained as *per* performa attached, with special emphasis on the history of oral contraceptive use, menstrual history, parity and lactation. Routine and special investigations were carried out for each patient to judge the general health status and any potential evidence of distant metastasis.

For the estimation of serum prolactin, a sample of peripheral venous blood (5 cc) was taken pre-operatively in the morning, 1-2 days before surgery. The blood sample was then centrifuged for 10 minutes at 3000 r.p.m. and the supernatant was analysed for serum prolactin levels by ELISA method (Kit provided by DiaMetra). Results were read on an ELISA reader.

The prolactin EIA test is based on simultaneous binding of human prolactin to two monoclonal antibodies, one immobilized on microwell plates and the other conjugated with horseradish peroxidase (HPR). After incubation, the bound/free separation was performed by simple solid phase washing, and then the TMB-substrate solution (TMB) was added. After 10 minutes, necessary for maximum colour development, the enzyme reaction was stopped and absorbance was measured. Prolactin concentration in the sample was calculated based on a series of standards. Colour intensity was proportional to prolactin concentration in the sample.

Procedure

In each well, 25 microliters of standard/sample were put and then 50 microliters of ready conjugate was added. After incubation at room temperature for half an hour, decantation and washing twice with distilled water was done. Afterwards, 100 microliters of TMB substrate were added to each well. After incubation at room temperature for 10 minutes in dark, 100 microliters of stop solution were added. Absorbance was read at 450 nm against blank on the ELISA reader. The results obtained were statistically analysed and an association pattern in serum prolactin levels was looked for premenopausal (1.2-22.0 ng/mL) and postmenopausal women (0.7-17.0 ng/mL).

Serum lipid levels were estimated by the following methods: 5 mL of blood sample was collected from each subject and the following parameters were estimated:

- triglycerides (normal range 40-165 mg/dL) by the glycerol phosphate oxidase (GPO-Trinder) method;
- total cholesterol (TC) (normal range 150-200 mg/dL) by the cholesterol oxidase (CHOD-PAP) method;
- HDL cholesterol (normal range 30-70 mg/dL) by the turbidometric method;
- LDL cholesterol (normal range 95-190 mg/dL) by calculation: LDL = TC-HDL.

Serum triglycerides were measured enzymatically, based on their hydrolysis by lipase to generate glycerol that reacted enzymatically to give a coloured quinoneimine dye with an absorbance maximum at 505 nm. The intensity of the colour is directly proportional to the concentration of triglycerides in the sample. One mL of solution No 1 provided in the kit was incubated at 37°C for three minutes; 0.04 mL of serum were put in the test tube labelled T (test), and 0.04 mL of the standard (labelled as solution No 2 in the kit) were added in the test tube labelled S (standard); after incubating the mixture at 37°C for 10 minutes, 2.5 mL of distilled water were added; then, the optical density was read at 505 nm. Triglyceride concentration (mg/mL) was calculated as follows: Abs. of Test/Abs. of standard x Concentration of Standard (mg/mL).

Total cholesterol was estimated by the cholesterol oxidase (CHOD-PAP) method, based on the hydrolysis of cholesterol esters by cholesterol esterase to form cholesterol and free fatty acids. This free cholesterol is further oxidized by cholesterol oxidase (CHOD) to cholest-4-en-3-one and H_2O_2. In the presence of peroxidase (POD), H_2O_2 affects the oxi-

dative coupling of phenol and 4-aminoantipyrine (4-AAP) to form a red coloured quinoneimine dye that is directly proportional to cholesterol concentration in the sample. One mL of solution No 1 provided in the kit was incubated at 37°C for 10 minutes; 0.01 mL of the serum were put in the test tube labelled (T), and 0.01 mL of the standard (labelled as solution No 2 in the kit) were added in the test tube marked as standard (S); the mixture was incubated at 37°C for 10 minutes. Blank followed by standard was aspirated and then tested. Reading of absorbance of standard and each test tube at 505 nm was done on bichromatic analysers against reagent blank.

Cholesterol concentration (mg/mL) was calculated as follows: Abs. of Test/Abs. of standard x Concentration of Standard (mg/mL).

Estimation of HDL cholesterol relies on principle that polyethylene glycol results in aggregation of the APO-B-100 containing chylomicrons of VLDL and LDL. The second reagent protected or blocked the aggregated lipoproteins with antibodies to APO-B-100 and APO-C. Cholesterol reaction enzymes were added in the third reagent, which acted only on unprotected HDL cholesterol. The fourth reagent stopped the colour reaction and solubilised the aggregates with guanidine salts clearing the reaction mixture for measurement of colour. In our experiment, two tubes labelled as calibrator (C) and sample (S) were used. In both tubes, about 375 microliters of reagent 1 (PVS & PEGME) were added; then, five microliters of calibrator (HDL/LDL) were added in tube labelled as C and five micoliters of sample were added in the tube labelled as S. Both tubes were incubated at 37°C for five minutes. Then, about 125 microliters of reagent 2 (CHOD, CHER) were added in both tubes labelled as C and S. After further incubation at 37°C for five minutes, the absorbance of calibrator and sample at 600-700 nm was read. The concentration of HDL cholesterol was calculated as follows: (Abs. Sample –Abs. of sample blank) x Conc. of Calibrator (Abs. of Cal. - Abs. Of Cal. Blank)

LDL cholesterol was estimated by the most widely used indirect method, in which cholesterol, triglyceride and HDL cholesterol are measured and LDL calculated from primary measurements using friedwald equation. All concentrations are given in mg/dL. Factor 5 is an estimate of VLDL cholesterol concentration that is based on average ratio of triglyceride to cholesterol in VLDL. (LDL cholesterol) = (Total cholesterol) – (HDL cholesterol) – (triglyceride).

Observations. A detailed clinical history and examination of each case was recorded. In all cases, serum prolactin levels and serum lipid profile were studied accordingly. Most BC patients were in the fourth and fifth decade of their life. Sixteen (40%) cases were in their fourth decade and 11 (27.5%) in their fifth decade. No case of BC was reported below the age of 20. The mean age of participants in the study group was 46.1 years and that of controls 36.9 years. All patients in the study group were married. The average age at menarche in the study group was 14.7 years as compared to 14.1 years in the control group, showing thereby BC had similar menarche to controls. The average period of parity in BC patients of the study group was 3.5, which was higher than in controls (2.7) (Table 1).

Age group (years)	Study group		Control group	
	No. of cases	% age	No. of cases	% age
0-10	-	0	-	0
11-20	-	0	1	10
21-30	2	5	3	30
31-40	16	40	1	10
41-50	11	27.5	3	30
51-60	7	17.5	2	20
>60	4	10	0	0

TABLE 1. Distribution according to age group

In the study group, 23 (57.5%) of all patients were postmenopausal and 17 (42.5%) premenopausal subjects, while in the control group there were five premenopausal and five postmenopausal women (50%). The average age at first child birth in BC patients (study group) was 19.7 years, which was marginally higher than that of the control group (average of 18.6 years).

In the study group, 65% of patients were non-vegetarians and the rest of 35% vegetarians, while in the control group 40% were non-vegetarians and 60% vegetarians. The height of patients in the study group varied between 150-155 cm and 160-165 cm, while most patients in the control group were in the range of 145-155 cm. In the study group, 27 (67.5%) subjects were within the

normal range of weight, 11 (27.5%) were overweight and two underweight; in the control group, three (30%) patients were within the normal range of weight, six (60%) underweight, and one (10%) overweight (comparison of weight has been according to the BMI). Seventeen (42.5%) patients in the study group had used oral contraceptives for a variable period of time and only one in the control group had a history of oral contraceptives consumption. All cases in the study group reported the onset of their problems as varying between a few days to two years ago, most of them being experienced one to six months ago. The mean reporting time was 7.14 +/- 2 SD.

In the study group, mostly the right breast was involved. Twenty one (52.5%) patients had right sided involvement of breast and 19 (47.5%) left sided involvement. No cases of bilateral breast involvement were seen. Fourteen (35%) of the patients had symptoms in the form of a lump, with no other associated symptom or sign. Eleven (27.5%) cases presented with pain along with the lump. Pain and nipple discharge were present in seven (17.5%) cases, while lump and nipple discharge in six (15%) cases. Only two (5%) cases had lump with pain, tenderness and ulcer. Fifteen (37.5%) of the subjects presented with *peau d'orange* and nine (22.5%) with fixity to skin, while six (15 %) had both (fixity to skin and *peau d'orange*). But 10 (25%) of them had no such signs. No case of cancer-en-cuirasse was reported. In majority of cases, involvement of upper outer quadrant was seen, i.e., 25 (62.5%) cases. Eight (20%) cases were in the lower outer quadrant. Involvement of the upper inner quadrant was seen in four (10%) cases, and of more than one quadrant in three (7.5%) cases. No case showed lower inner quadrant involvement. In 22 (55%) cases of carcinoma of the breast, anterior axillary group of lymph nodes was involved. Ten (25%) cases involved the central group of axillary lymph nodes. Six (15%) cases involved posterior group of lymph nodes, while two (5%) cases involved the apical group of lymph nodes. No involvement of lateral and subscapular groups was noticed.

When patients were evaluated for staging at the time of their reporting according to Manchester Staging, the maximum number of cases, *i.e.* nineteen (47.5%), were in stage II, followed by 17 (42.5%) cases with stage III and two (5%) in stage I. Apparently, cases with stages II and III accounted for 90% of all cases. There were two cases belonging to stage IV in this study. On histopathology, the majority of cases [36 (90%)] were infiltrating ductal carcinoma, two (5%) were diagnosed as cystosarcoma phylloides and two (5%) as medullary carcinoma.

Most patients (42.5%) in the present study had a tumour size of T3 stage, while 27.5% of the subjects reported symptoms when they had a tumour size of T2 stage. In 20% of cases, lymph nodes were clinically not palpable. However, there was a significantly palpable mobile lymph node in the ipsilateral axilla in 57.5% of cases and fixed lymph nodes in 17.5% of cases. Clinical evidence of distant metastasis was seen in 5% of cases, while 95% of cases had no distant metastasis (Table 2).

	No. of cases	Percentage
Tumour (T)		
Tis : No Palpable tumour	0	0
Tx : Size cannot be assessed	0	0
T1 : < 2 cm	5	12.5
T2 : 2-5 cm	11	27.5
T3 : > 5 cm	17	42.5
T4: Any size invading skin or chest wall	7	17.5
Lymph nodes (N)		
N0 : No nodal metastasis	8	20
N1 : Mobile axillary nodes	23	57.5
N2 : Fixed axillary nodes	7	17.5
N3 : Supra-clavicular	2	5
Metastasis		
M0 : No distant metastasis	38	95
M1 : Distant metastasis	2	5

TABLE 2. Clinical staging of malignancy, according to TNM classification

The mean value of serum total cholesterol in the study group was 190.77 mg %, slightly higher than that of the control group (166.22 mg/dL), which was a statistically significant elevation. Serum triglycerides showed a higher increase in the study group than in controls, and this elevation was also statistically significant. The mean value

in the study group was 192.61 mg % as compared to 99.5 mg % in the control group. The mean value of LDL in the study group was 153.8 mg %, comparatively to 118.4 mg/dL in the control group; therefore, LDL cholesterol levels were statistically significant. Also, VLDL level was found to be higher in patients with BC, their mean value being 35.25 mg/dL as compared to 22.6 mg % in the control group, which was statistically significant (Table 3).

Patients	TC	TG	LDL	HDL	VLDL
Study group SD	190.77 70.77	192.61 54.4	153.8 49.45	52.34 24.55	35.25 14.97
Control group SD	166.22 13.024	99.5 34.4	118.4 19.6	50 11.57	22.6 5.58
t-test	2.05	6.71	3.548	0.439	4.28
P value	<0.045	<.001	<0.001	.949	<.001
SD=Standard Deviation					

TABLE 3. Variation in lipid parameters

The mean serum prolactin value in the study group was 25.82 ng/mL, with a standard deviation (SD) of 13.81, as compared to that measured in the control group (8.87 ng/mL, SD 3.56). These elevated levels of prolactin in the study group had a highly statistical significance (Table 4). The correlation coefficient of total lipids and prolactin was 0.428, which was significant (p value 0.002), indicating a positive relation between prolactin and total lipids and meaning that the increase in total lipids would lead to an elevation in prolactin levels. It was further highlighted that significantly increased prolactin levels have been found among patients with carcinoma of the breast (Table 5). In the study group, the mean value of prolactin was clearly showed to be 22.91 +/- 11.57 SD among postmenopausal women and 29.75 +/- 15.88 SD among premenopausal subjects (Figure 1), while in the control group it was 7.06 +/- 2.99 SD and 10.68 +/- 3.37, respectively (Table 6). ❑

	Study group (ng/mL)	Control group (ng/mL)
Prolactin level SD	25.82 13.81	8.87 3.56
Range	4.2 – 65.4	4.5 – 15.6
t –value	6.898	
P value	<.001	
SD=Standard Deviation		

TABLE 4. Variation in serum prolactin level

	Total lipid & prolactin	Total Cholesterol & prolactin
Correlation coefficient	0.428	0.163
P value	0.002	0.257

TABLE 5. Coefficient of correlation between lipid fractions and prolactin

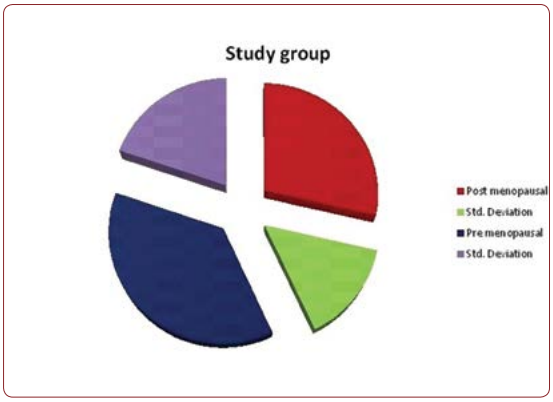

FIGURE 1. Chart showing comparasion of prolactin levels in pre- and post menopausal

Menopausal status	Study group	Control group
Postmenopausal	22.91	7.06
Standard Deviation	11.57	2.99
Premenopausal	29.75	10.68
Standard Deviation	15.88	3.37

TABLE 6. Comparison of prolactin in pre- and postmenopausal women

DISCUSSION

Breast is a modified sweat gland. From puberty to death, the female breast is subjected to constant dynamic changes related to menarche, menstrual changes, pregnancy, lactation and menopause (9). The elevated LDL-C concentration, which is more susceptible to oxidation, may result in higher lipid peroxidation in BC patients. Environmental factors, such as weight and diet, altered plasma lipids and

lipoproteins were correlated to BC risk factors, which indicated that lipids might be responsible for BC (10). It was found that LDL-C fraction has been significantly associated with BC progression, which might be helpful in understanding and medical follow-up of high-risk groups. In BC patients, LDL-C levels are useful as diagnostic and prognostic factors (11). Our study presented the mean value of LDL in the study group was 153.8 mg/dL as compared to 118.4 mg/dL in the control group, indicating that LDL cholesterol levels were statistically significant.

The mechanism for an association between blood lipids and breast cancer risk is unknown. The observed lipid profile (higher HDL-C and apoA1, and lower non-HDL-C and apoB) could reflect increased levels of, or greater response to, endogenous estrogens, which increases the chances of occurrence of breast cancer, especially estrogen receptor–positive disease (12). Several studies have linked hyperprolactinemia to an increased risk of breast cancer in women (13). Mechanisms that have been suggested to explain this possible action of prolactin include the increased synthesis and expression of prolactin receptors in malignant breast tissue and a prolactin-induced increase in DNA synthesis in breast cancer cells *in vivo* (14). One of the hypothesized roles of prolactin in the development of mammary tumours is to create mammary gland conditions favourable for the action of carcinogens through its stimulation of the rate of mammary gland DNA synthesis, a measure of the frequency of mammary gland cell division (15).

Moreover, the usual features seen in breast tumours are increased cholesterol levels and inhibition of acyl-CoA: cholesterol acyltransferase 1, an enzyme involved in cholesteryl esterification which lowers proliferation and invasion rate (14). The study observed that hypercholesterolemia was not present despite cancer cells accelerating intracellular cholesterol synthesis. Some other published data support the notion that cancer cells are able to uptake cholesterol from the bloodstream. In BC tissue, LDL-C receptors are seen at higher levels than in normal tissue (16). Another study found that LDL-C fraction is significantly associated with BC progression and may actually be useful in the identification and medical follow-up of high-risk groups. Therefore, LDL-C level at diagnosis emerge as a prognostic factor in BC patients. Additionally, results support a role for systemic cholesterol in BC progression and indicate that cholesterol metabolism could be a therapeutic target in BC treatment (17).

Obesity increases the risk in postmenopausal women. Our study shows that overweight patients are at higher risk of developing carcinoma of the breast than underweight women. In the present study, the mean value of serum total cholesterol in the study group was 190.77 mg/dL, slightly higher than that measured among controls (166.22 mg/dL), which was a statistically significant elevation. Serum triglycerides showed a higher increase in the study group as compared to the control group and this elevation was also statistically significant; their mean value in the study group was 192.61 mg/dL as compared to 99.5 mg/dL in controls. The correlation coefficient of total lipids and prolactin (0.428) was significant (.002 p value), meaning that an increase in total lipids would lead to an elevation in prolactin levels. We concluded that higher prolactin levels have been found among patients with carcinoma of the breast.

Other studies showed that, in postmenopausal group, the pooled standardized mean difference (SMD) of triglycerides (TG) and high density lipoprotein cholesterol (HDL-C) were 0.94 (95% CI 0.33 to 1.55) and -0.62 (95% CI -1.11 to -0.13), respectively. No significant differences were noted for total cholesterol (TC), low density lipoprotein cholesterol (LDL-C), apolipoprotein A1 (ApoA1), and apolipoprotein B (ApoB) between premenopausal and postmenopausal cases and controls. The results in this meta-analysis suggested that TG levels were higher in both premenopausal and postmenopausal BC compared with normal controls (18). Our study observed that the higher levels of serum triglycerides in the study group compared to controls were statistically significant. The mean value of LDL in the study group was 153.8 mg/dL as compared to 118.4 mg/dL in the control group, indicating that LDL cholesterol levels were statistically significant. The mean serum prolactin value in the study group was 25.82 ng/mL (SD 13.81) as compared to the control group value of 8.87 ng/mL (SD 3.56). These elevated levels of prolactin in the study group were statistically highly significant.

A study concluded that prolactin levels were associated with nulliparity in premenopausal (P=0.05) but not in postmenopausal women. As-

sociations in postmenopausal women included an inverse association with increasing body mass index (P=0.0008) and a direct association with the use of recent/current hormone therapy (P=0.0006). We saw that higher prolactin levels were more strongly associated with lobular compared with ductal carcinoma among postmenopausal women (P=0.02) (19). The present study clearly shows that in the study group, the mean value for prolactin among premenopausal and in postmenopausal women was 29.75 +/- 15.88 SD and 22.91 +/- 11.57 SD, respectively, whereas in controls, it was 10.68 +/- 3.37 and 7.06 +/- 2.99 SD, respectively. Another study stated that increased circulating levels of prolactin may be associated with a higher risk of *in situ* carcinoma breast. It was observed that up to 50% of non-treated *in situ* breast lesions would lead to invasive disease (20).

A study revealed that positive associations between prolactin and *in situ* breast cancer risk were similar to those observed for invasive BC. Prior analyses limited to invasive cases found modest significant associations between circulating prolactin and risk of invasive breast cancer, with up to a 50% increase in risk contrasting top *versus* bottom quartiles (21, 22). Our study showed that in the study group, the mean serum prolactin value was 25.82 ng/mL (SD 13.81), while in controls it was 8.87 ng/mL (SD 3.56). The correlation coefficient of total lipids and prolactin (0.428) was significant (p value 0.002), meaning that an increase in total lipids would lead to an elevation in prolactin levels. It was further highlighted that significantly increased prolactin levels have been found among patients with carcinoma of the breast.

The following findings have been recorded in our study:

- Serum lipids in carcinoma of the breast showed distinct statistical significant alterations
- Serum prolactin showed a statistically significant elevation in patients with carcinoma of the breast as compared to normal healthy controls
- Serum prolactin showed a statistically significant elevation in premenopausal patients comparatively to postmenopausal patients with carcinoma of the breast.
- The study showed that serum prolactin was directly proportional to serum lipid level. ❑

CONCLUSION

Serum lipids in carcinoma of the breast showed distinct statistical significant alterations such as elevated triglycerides, HDL cholesterol, and VLDL levels. Serum prolactin showed a statistically significant increase in patients with carcinoma of the breast as compared normal healthy control. Therefore, prolactin could also be considered to be a major risk factor in patients with carcinoma of the breast. Further research with larger size samples is still required to provide better factors. ❑

Conflicts of interest: none declared.
Financial support: none declared.

References

1. **Munsell MF, Sprague BL, Berry DA, Chisholm G, Trentham-Dietz A.** Body Mass Index and Breast Cancer Risk According to Postmenopausal Estrogen-Progestin Use and Hormone Receptor Status. *Epidemiol Rev* 2014;1:114-136. doi: 10.1093/epirev/mxt010.
2. **Singal R, Singh P, Sahu P, Mittal A, Naredi B, Gupta S.** Metaplastic carcinoma of the breast with high grade spindle cell component with osteoid formation – a rare case report. *Acta Chir Belg* 2011;4:243-245.
3. **Singal R, Gupta S.** Operable breast cancer in a young female: A rare presentation. *Clin Cancer Investig J* 2012; 1:109-110.
4. **Peltzer K, Pengpid S.** Awareness of Breast Cancer Risk among Female University Students from 24 Low, Middle Income and Emerging Economy Countries. *Asian Pac J Cancer Prev* 2014;15:7875-7878.
5. **Singal R, Narang D, Dang R, Bakshish K, Garg P.** Awareness and Follow up of Breast Cancer in a Young Female. *J Health Med Informat* 2015;6:181.
6. **Haritwal AK, Chourasia RK, Ojha S.** A comparative study of serum lipid profile and glucose level between breast cancer patients and controls at tertiary care hospital in India. *Inter J Medical Sci Res Prac* 2015;1:16-19.
7. **Lingwood D, Simons K.** Lipid rafts as a membrane-organizing principle. *Science* 2010; 5961:46-50.
8. **Babina IS DS, Nabi IR, Hopkins AM.** Lipid rafts as master regulators of breast cancer cell function. In: *Breast Cancer – Carcinogenesis, Cell Growth and Signalling Pathways*. Edited by Gunduz M, Gunduz E, InTech; 2011. ISBN ISBN 978-953-307-714-7 2011.
9. **Singal R, Mehta SK, Bala J, Zaman M, Mittal A, Gupta G, et al.** A Study of Evaluation and Management of Rare Congenital Breast Diseases. *J Clin Diagn Res* 2016;10:PC18-PC24.

10. **Martin LJ, Melnichouk O, Huszti E, Connelly PW, Greenberg CV, Minkin S, et al.** Serum lipids, lipoproteins, and risk of breast cancer: a nested case-control study using multiple time points. *J Natl Cancer Inst* 2015;107:v32.
11. **Gupta A, Shridhar K, Dhillon PK.** A review of breast cancer awareness among women in India: Cancer literate or awareness deficit? *Eur J Cancer* 2015;14:2058-2066.
12. **Tamimi RM, Byrne C, Colditz GA, Hankinson SE.** Endogenous hormone levels, mammographic density, and subsequent risk of breast cancer in postmenopausal women. *J Natl Cancer Inst* 2007;15:1178-1187.
13. **Halbreich U, Kinon BJ, Gilmore JA, et al.** Elevated prolactin levels in patients with schizophrenia: mechanisms and related adverse effects. *Psychoneuroendocrinology* 2003;28 (Supp I):53-67.
14. **Nagasawa H.** Prolactin: its role in the development of mammary tumours. *Med Hypotheses* 1979;5:1117-1121.
15. **Antalis CJ, Arnold T, Rasool T, Lee B, Buhman KK, Siddiqui RA.** High ACAT1 expression in estrogen receptor negative basal-like breast cancer cells is associated with LDL-induced proliferation. *Breast Cancer Res Treat* 2010;3:661-670.
16. **Pires LA, Hegg R, Freitas ER, Tavares ER, Almeida CP, Baracat EC, et al.** Effect of neoadjuvant chemotherapy on low-density lipoprotein (LDL) receptor and LDL receptor-related protein 1 (LRP-1) receptor in locally advanced breast cancer. *Braz J Med Biol Res* 2012;6:557-564.
17. **Rodrigues Dos Santos C, Fonseca I, Dias S, Mendes de Almeida JC.** Plasma level of LDL-cholesterol at diagnosis is a predictor factor of breast tumor progression. *BMC Cancer* 2014;14:132.
18. **Zhao Y, Wang H, Pan Y, Li N, Bian C.** Association of lipid profile levels in pre menopausal and postmenopausal women with breast cancer: a meta-analysis. *Int J Clin Exp Med* 2016;2:552-563.
19. **Faupel-Badger JM, Sherman ME, Garcia-Closas M, Gaudet MM, Falk RT, Andaya A, et al.** Prolactin serum levels and breast cancer: relationships with risk factors and tumour characteristics among pre- and postmenopausal women in a population-based case–control study from Poland. *Br J Cancer* 2010;103:1097-1102.
20. **Tikk K, Sookthai D, Fortner RT, Johnson T, Rinaldi S, Romieu I, et al.** Circulating prolactin and in situ breast cancer risk in the European EPIC cohort: a case-control study. *Breast Cancer Res* 2015;17:49.
21. **Tikk K, Sookthai D, Johnson T, Rinaldi S, Romieu I, Tjønneland A, et al.** Circulating prolactin and breast cancer risk among pre- and postmenopausal women in the EPIC cohort. *Ann Oncol* 2014;25:1422-1428.
22. **Tworoger SS, Eliassen AH, Zhang X, Qian J, Sluss PM, Rosner BA, et al.** A 20-year prospective study of plasma prolactin as a risk marker of breast cancer development. *Cancer Res* 2013;73:4810-4819.