Section: Pathology

Original Research Article

CLINICOPATHOLOGICAL CORRELATION OF CYCLOOXYGENASE-2 (COX-2) EXPRESSION IN INVASIVE BREAST CARCINOMA AND ASSOCIATED DUCTAL CARCINOMA IN SITU: AN IMMUNOHISTOCHEMICAL STUDY

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ABSTRACT

Background: The aim of this study is to analyze the prognostic expression of COX-2 in breast carcinomas and to correlate with clinicopathological factors. Breast carcinoma is the most prevalent malignant tumor and the main cause of carcinoma mortality in women. Cyclooxygenases are enzymes that regulate prostaglandin synthesis and play an important role in inflammation.

Materials and Methods: This Descriptive study was conducted in the Department of Pathology, Meenakshi Medical College Hospital and Research Institute from June 2021 to June 2022 after approval from the Institutional Ethical Committee. Study group includes 40 female patients diagnosed with breast cancer who has undergone radical or modified radical mastectomy in the age group of 30 to 70 years during the year 2019 to 2022 are taken. Expression of COX-2, ER, PR and HER2neu was studied for all the selected cases using immunohistochemistry.

Results: Out of 40 cases, tumor with Ductal carcinoma insitu (DCIS) component was observed in 12 cases. Immunohistochemical expression of COX-2 was observed in 32 (80%) cases and negative expression was observed in 8 (20%) cases. All the 40 cases of adjacent normal breast tissue and 12 cases of tumor with DCIS component showed moderate expression.

Conclusion: In conclusion, the present study suggests that COX-2 up-regulation can predict an unfavorable prognosis of BC patients. Most of the invasive breast carcinomas are alleged to arise from DCIS so early detection and treatment at appropriate time may result in favorable prognosis. Since COX-2 Over expression is associated with reduced apoptosis and increased cell survival, studies have suggested inhibition of COX-2 may serve as a target therapy in breast cancer tumorigenesis and to prevent recurrence.

Keywords: Breast cancer, Ductal carcinoma insitu, COX-2 expression.

INTRODUCTION

With more than 16, 00,000 new cases being identified globally each year, breast carcinoma is the most prevalent malignant tumor and the main cause of carcinoma mortality in women. In India, it is the most prevalent cancer among women, with a yearly incidence of about 1, 45, 000 cases and 70,000 fatalities.[1] The modern lifestyle (early menarche, later menopause, delayed pregnancy, diminished breastfeeding, obesity due to junk foods, and increased consumption of alcohol, oral

contraceptives and hormone replacement therapy) in the western world has contributed to a considerable rise in breast cancer death rates throughout the world. Men account for about 1 % of all breast cancer occurrences, and their risk is increased by hormone imbalance, radiation exposure, and a familial susceptibility.

Malignant progression of breast cancer involves different processes regulating epithelial-mesenchymal transition, hypoxia, desmoplasia, angiogenesis, dysregulation of proliferative - signaling and growth- inhibitory factors, activation of oncogenes, and loss of tumor suppressor genes, all of which result in suppression of apoptosis and senescence.[2,3] New molecular tools, enhanced risk assessment, targeted therapy, and tailored treatment are all related to the pathophysiological background of breast cancer's rising trends. Breast cancer is treatable if found in its early stages. Gene expression profiling might offer predictive and prognostic gene signatures that could aid in tumor characterization and make it possible for more specialized treatments. In industrialized nations, the predicted five- year survival rate is over 85%; however, in underdeveloped nations, it is lower, ranging from 64.8 to 68.7%.[4]

Traditional prognostic indicators include histological subtype, axillary lymph nodes, and the size of the tumor and the staging of the disease. Molecular expression pattern of prognostic parameters like estrogen , progesterone and HER-2 neu receptors help in targeted therapy for patients with breast cancer.[5] Since patients with similar prognostic features may have different clinical outcome, researchers focus on identification of new prognostic factors which plays an important role in breast cancer treatment and prognosis. Receptors like retinoid X receptor (RXR), thyroid hormone receptors, vitamin D receptor, increased levels of urokinase type plasminogen activator (uPA) and plasminogen activator inhibitor (PAI - 1) are important in the pathophysiology of breast cancer and are associated with a poor prognosis. Prostaglandin E2 (PGE2) and associated proteins in the cyclooxygenase (COX) pathway have been identified as new biomarkers associated with a poor prognosis. As a result, the COX system's role in breast cancer is being extensively studied.[6]

The immune system plays a significant role in tumorigenesis. Cancer can be initiated and progressed by inflammation. Studies focused on the relationship between chronic in flammation within the local tissue environment and cancer, leading to the concept of cancer -related inflammation as an emerging hallmark of cancer. Cyclooxygenases are enzymes that regulate prostaglandin synthesis and play an important role in inflammation. There are two types of isoforms: Cyclooxygenase -1 (COX-1) is constitutively expressed, whereas COX- 2 (COX-2) is induced by growth factors, cytokines and chemokines which are present both in inflammation and malignancies.[7]

Over expression of COX-2 has been demonstrated in a variety of solid tumors, e. g. breast, ovarian, colon, gastric, oesophageal, prostate, lung, hepatic and pancreatic cancer. COX- 2 promotes aromatase gene CYP19 transcription which increases local estrogen production and thus promotes enlargement of tumor cells in oestrogen - responsive breast cancer. Elevated levels of COX-2 in tumor are associated with reduced apoptosis (due to elevated anti-apoptotic protein BCL2), increased tumor proliferation, neoangiogenesis (due to increased expression of vascular endothelial growth factor), tumor invasion, migration, and also exhibit chemoresistance.[8] Since Non-steroidal anti-inflammatory drugs can suppress the COX system non-selectively or selectively, epidemiological studies are conducted to know the effects of NSAIDS in reducing the risk of breast cancer.[9] Concurrent usage of both COX-2 inhibitors and aromatase inhibitors may contribute therapeutic strategy. Data on COX - 2 expression in DCIS are few. But COX - 2 is over expressed in preinvasive lesions. Women with increased expression of COX - 2 in DCIS have increased risk of developing invasive cancer.[10] Hence this study aims to analyze the prognostic expression of COX -2 in adjacent normal breast tissue, tumor with Ductal carcinoma in situ (DCIS) and invasive breast carcinoma.

MATERIALS AND METHODS

This is descriptive study was conducted in the department of pathology at Meenakshi Medical College Hospital and Research Institute after approval from the Institutional Ethical Committee. Totally 40 female patients were diagnosed with breast carcinoma that has undergone radical or modified radical mastectomies during the year 2019 to 2022 are taken. This study was based upon on the inclusion and exclusion criteria. Inclusion criteria includes women with primary breast cancer who have undergone radical or modified radical mastectomy in the age between 30 to 70 years are included in the study. The study also includes tumors with ductal carcinoma in situ cases. Patients with breast carcinoma other than primary adenocarcinoma such as lymphoma, sarcoma, stromal tumor and metastasis are excluded. Cases of Modified Radical Mastectomy were selected for our study which was first fixed overnight in 10% neutral buffered formalin in room temperature. Following that, sections were taken according to CAP guidelines and embedded in paraffin wax. For micros copic evaluation, sections were deparaffinized and then put for Hematoxylin and Eosin (H&E) staining. The tumor staging was done based on gross findings along with the histopathological examination of the primary tumor area, the nodal status, adjacent skin and associated structures (wherever applicable) and other relevant

clinical data available on lymph nodes and distant organ metastasis.

These findings were studied and staged according to the TNM classification of breast carcinomas. Following pathological staging, the tumors were graded as per the Nottingham histologic grading system into Grade I, Grade II and Grade III. All the sections were then subjected to immunohistochemical analysis for markers like COX-2, EstrogenReceptor(ER, Progesterone Receptor (PR) and HER-2 neu.

Statistical Analysis: All the data`s were Analyzed by using Chi-square test and student t test on SPSS software for significance.

RESULTS

Age wise Distribution of patients: [Table1] represents that the age wise distribution of patients, a total of 40 patients with invasive breast carcinoma were included. The mean age of the study group is 49.85 years and most of the patients are in the age group of 41 – 60 years (75%). Out of 40 cases, 16 women are of postmenopausal age.

Table 1: Age wise distribution of patients

Age group (Years)	Frequency	Percentage
30- 40	6	15%
41- 50	16	40%
51- 60	14	35%
>60	4	10%
Total	40	100%

Tumor Location distribution:[Table2] indicates that the majority of the lesions were distributed in the upper inner quadrant 13 cases (32.5 %), followed by central quadrant 11 cases(27. 5%), upper outer quadrant 9 cases(22.5%), nipple areolar complex 5 cases (12.5 %) and lower inner quadrant 2 cases (5%).

Table 2: Tumor location distribution

Location	Frequency	Percentage
Central	11	27.5%
Upper - outer- inner	913	22.5%32.5%
Lower- outer- inner	02	0%5%
Nipple Areolar Complex	5	12.5%
Total	40	100%

Distribution of Tumor size: In this present study, most of the cases (n=29) (72.5%) had tumor size ranging from 2 – 5 c.m. [Table 3] Among 40 cases, tumor with DCIS component was observed in 12 cases (30%). Majority of the patients presented with nipple discharge and breast mass.

Table3: Distribution of Tumor size

Size	Frequency	Percentage
< 2 c.m	3	7.5%
2-5 c.m	29	72.5%
> 5 c.m	8	20%
Total	40	100%

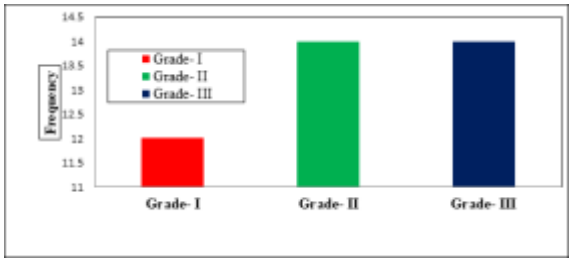


Figure 1: Histopathological Grading

Distribution of Histopathological grading:

[Figure 1] indicates that According to Nottingham histological grading, 14 (35%) of cases fall into grade II and grade III whereas grade I tumors are seen among 30% of cases.

Lymph node Status: [Figure2] represents that the Out of 40 cases included in the study, 21 cases (52. 5%) were lymph node negative and 19 cases (47.5%) were lymph node positive.

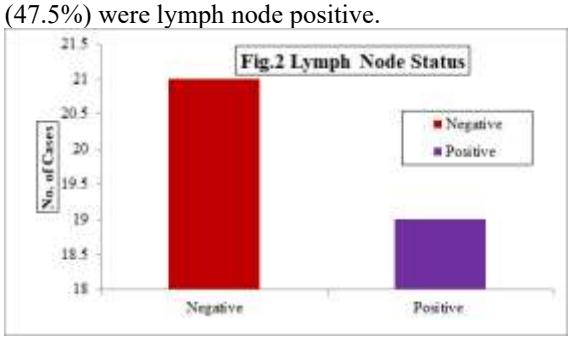


Figure 2: Lymph Node Status

Distribution of Lymph nodes among study group: [Table4] indicates that the present study, lymph nodes are categorized based on the number of lymph nodes of which 21 cases (52.5%) fall under

stage - I, 8 cases (20 %) fall under stage- II and 11 cases (27.5%) fall into stage - III.

Table4: Distribution of Lymph nodes

Lymph nodes	Frequency	Percentage
Stage- I(0 lymph nodes)	21	52.5
Stage- II (1 -3 lymph nodes)	8	20
Stage- III (> 4 lymph nodes)	11	27.5
Total	40	100

Distribution of ER and PR positivity among study group: [Table5] indicates that among 40 cases, ER positive was observed in 16 cases and PR positive was observed in 10 cases.

Table5: Distribution of ER and PR positivity among study group

Positivity	ER	PR
Positive	16	10
Negative	24	30
Total	40	40

Distribution of HER2NEU positivity among study group: Among 40 cases HER2NEU expression was observed in 14 cases (35%). Out of 40 cases, 12 cases are triple negative. [Table 6]

Table6: Distribution of HER2NEU positivity among study group

HER2 NEU	Frequency	Percentage
Positive	14	35%
Negative	26	65%
Total	40	100%

Distribution of COX- 2 Expression in tumor: In this present study, strong expression of COX - 2 was not observed in any cases. 32 cases of tumor (80%) were positive and showed moderate expression while 8 cases (20%) were negative for COX -2 expression [Table 7]. Mean age of the patients with positive expression was 52. 03 years while in patients with negative cox -2 expression had mean age of 47.75 years. Among 40 cases, tumor with DCIS component was observed in 12 cases (30 %). Moderate expression of COX -2 was seen in 12 cases of tumor with DCIS component. The adjacent tumor in all the 12 cases showed moderate expression of COX- 2. All the 40 cases of adjacent normal breast tissue showed moderate expression of COX- 2 expression.

Table7: Distribution of COX- 2 Expression in tumor

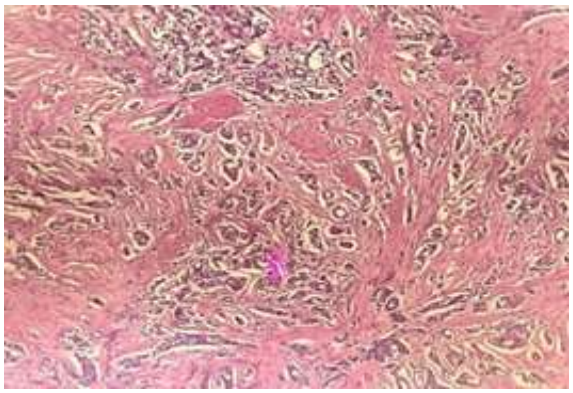
COX-2 expression	Frequency	Percentage
Strong	0	0%
Moderate	32	80%
Negative	8	20%
Total	40	100

Statistical correlation of COX-2 expression in tumor and DCIS with clinicopathological parameters: In our study, COX-2 expression among tumor and DCIS had no statistically significant correlation between the Clinicopathological factors such as age, tumor size, nodal status, histological grade, hormone receptor status. [Table 8]

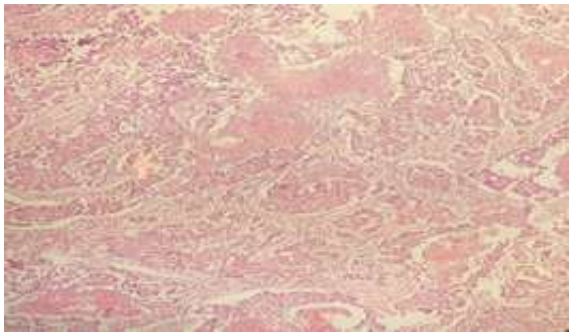
Table8: Statistical correlation of COX-2 expression in tumor and DCIS

Clinicopathologic parameters		COX-2 expression		P value
		Tumor (40)	DCIS (12)	
		%	%	
Tumor size	<2 cm	7.5	8.3	0.453
	2-5 cm	72.5	75	0.428
	>5 cm	20	16.7	0.406
Histologic grade	Grade- I	30	33.3	0.407
	Grade- II	35	16.7	0.070
	Grade- III	35	50	0..176
Lymph node status	Stage- I	52.5	58.3	0.354
	Stage- II	20	16.7	0.407
	Stage- III	27.5	25	0.437
NPI	Good	15	25	0.222
	Moderate	52.5	33.3	0.107
	Poor	32.5	41.7	0.274
ER	Positive	40	50	0.263
	Negative	60	50	0.275
PR	Positive	25	33.3	0.281

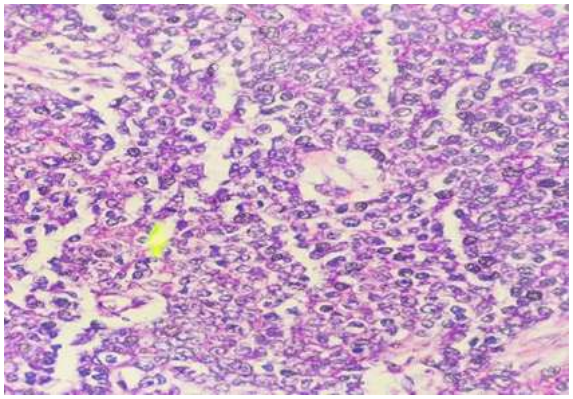
	Negative	75	66.7	0.296
HER2/Neu	Positive	35	16.7	0.070
	Negative	65	83.3	0.087



Invasive ductal carcinoma (NOS) of grade- I showing well formed glands.

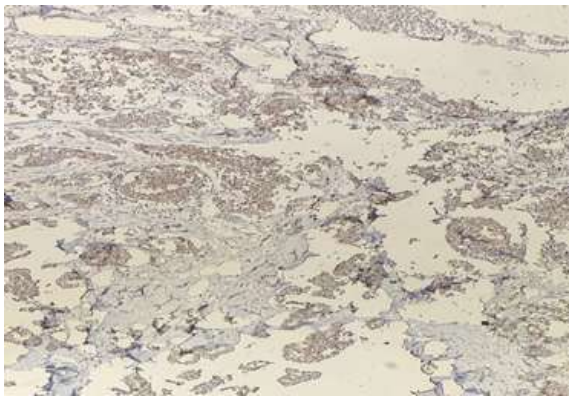


Invasive ductal carcinoma (NOS) of grade- II showing infiltrating tumor cells arranged in cords.

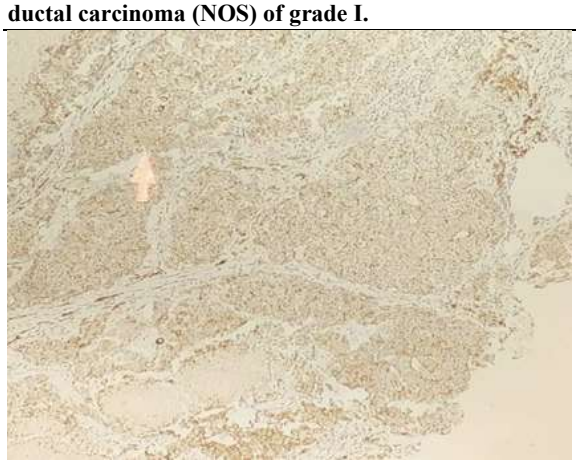


Invasive ductal carcinoma (NOS) of grade – III showing infiltratingtumorarranged in solid sheets.

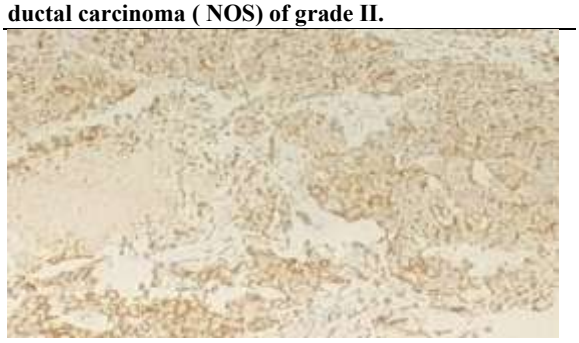
Figure3: Histological image of Invasive ductal carcinoma



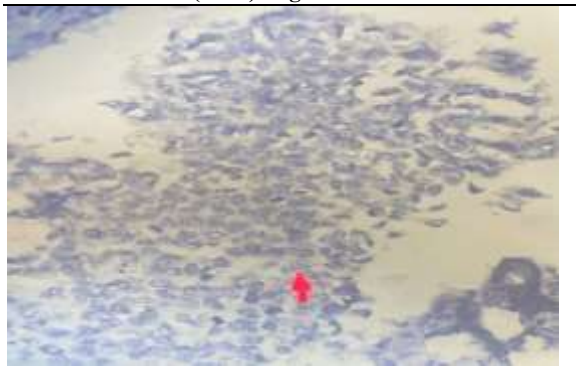
Moderate cytoplasmic staining of COX-2 in Invasive ductal carcinoma (NOS) of grade I.



Moderate cytoplasmic staining of COX-2 in Invasive ductal carcinoma (NOS) of grade II.



Moderate cytoplasmic staining of COX-2 in Invasive ductal carcinoma (NOS) of grade III.



Loss of COX-2 expression in Invasive ductal carcinoma (NOS) of grade III

Figure4: COX-2 Expression in Invasive ductal carcinoma.

DISCUSSION

In this current study, a total of 40 patients with invasive breast carcinoma were included. The mean age of the study group was 49. 85 years and most of the patients are in the age group of 41 – 60 years (75%).

Heer E et al,[10] reported, about 80 % of patients with breast carcinoma are individuals aged >50 years while 40% of patients are >65 years. The risk of developing breast cancer increases as follows- 1.5 % risk at age 40, 3% at age 50, and more than 4% at age 70. Ranjana Solanki et al,[11] reported in his study a total of 50 patients who were diagnosed with breast carcinoma with age ranging from 25 to 80 years and a median age of 51. 49 years. Most of the cases (56%) were in the age group of 35 to 44 years and 55 to 64 years with the lowest number (6 %) being in the age group of 25. Generally, the occurrence of cancer in increasing age is due to the accumulation of a vast number of cellular alterations and exposure to potential carcinogens that results in an increase of carcinogenesis with time.

In our study, most of the lesions (n=13) (32.5%) are seen in upper inner quadrant followed by 11 (27.5%) cases in central quadrant, 9 (22. 5%) cases in upper outer quadrant, 5 (12.5%) cases in nipple areolar complex and 2 (5 %) cases in lower inner quadrant. Studies done by A.Shah et al,[12] reported majority of the breast tumor in the upper outer quadrant which is associated with better prognosis when compared to tumors arising from upper inner quadrant which has been associated with aggressive behaviour and poor prognosis.

In our study, the tumors were categorized based on three sizes i.e. <2cm, 2 -5 cm and >5cm. In this present study, 72.5% of the cases (n=29) had tumor size ranging from 2 – 5 c.m. Tumor size and nodal status are the most important prognostic factors, it is believed that nodal status outperforms tumor size as a prognostic factor. When patients have a nodal stage greater than N2 (more than nine positive.[l]ymph nodes), it is well accepted that tumor size does not retain its prognostic value. Studies reported Tumor size as a strong predictor of 15 - year survival in both the node- positive and node- negative cancer subgroups. In our study, lymph nodes are categorised based on the number of lymph nodes of which 21 cases (52. 5%) fall under stage- I, 8 cases (20%) fall under stage- II and 11 cases (27 .5 %) fall into stage- III. S.A. Naro et al,[13] reported 1. 0 cm decline of size was associated with reduction of 15 - year mortality.

In our study according to Modified Bloom Richardson histological grading, 70% of cases fall into grade II and grade III whereas grade I tumors are seen among 30% of cases. In the Study done by NamitaBhutani et al,[14] Grade II tumors constituted 54% of the cases followed by grade I (32 %) and grade III (14%) tumors using Modified Bloom Richardson grading system. The Nottingham Prognostic Index (NPI) was used to determine the prognosis of breast cancer patients. Based on the study by Rituyadav et al and Rajeev sen et al 15, Nottingham Prognostic Index (NPI) defines three prognostic groups such as good (<=3.4), moderate (>3.4 to <=5.4), and poor (> 5.4) which predicts the severity in the breast cancer patients.

In this present study, among 40 cases, ER positive was observed in 6 cases (40 %), PR positive in 10 cases (25%) and HER 2 neu expression was observed in 14 cases (35%). ER negative, PR negative and negative expression of HER2 neu was observed in 24 (60%), 30 (75%) and 26 (65%) cases respectively. Out of 40 cases, 12 cases (40%) were triple negative. The above findings are similar to the study done by Jung Ah Lee et al.[16]

COX-2 Expression and its correlation with clinicopathological parameters Many prognostic factors have been identified for breast cancer, including size, nodal status, hormone receptors, and HER 2/neu expression. Hormone therapy, HER2/neu and COX -2 inhibitors have been effective in focusing treatment and have become the standard treatment for patients with breast cancer, besides the chemotherapy and radiation therapy. Brueggemeier et al,[17] demonstrated the regulation of estrogen in relation to COX-2 and concluded that increased COX- 2 expression results in increased aromatase activity via autocrine and paracrine mechanisms that forms the basis of breast cancer pathogenesis. Many studies have revealed correlation between COX- 2 and breast cancer, but clinical relevance or prognostic values are still controversial, hence we conducted this study to determine the correlation between clinicopathologic factors and COX- 2 expression. However, In our study COX -2 expression had no statistically significant correlation between the Clinicopathological factors such as age, tumor size, nodal status, histological grade, hormone receptor status. Kelly et al,[18] also found no statistical significant correlation between Clinicopathological factors and COX -2 expression. In our study, out of 40 cases, 32 cases showed moderate expression, all the 40 cases of adjacent normal breast epithelial tissue and 12 cases of tumor with DCIS component showed moderate expression. But there was no statistical significance in COX- 2 expression among these groups. In this present study, strong expression of COX - 2 was not observed in any of the cases. 32 cases (80%) showed moderate expression and 8 cases (20 %) were negative for COX- 2 expression.

Mean age of the patients with positive expression was 52.03 years while patients with negative cox- 2 expression had mean age of 47.75 years. Ranjana Solanki et al,[19] reported mean age of the patients with positive COX-2 expression as 48.41 years while in patients with negative COX - 2 expression it was 54. 57 years.

In our study, COX- 2 expression was moderately expressed in 80% of the patients and the tumor size in most of the cases were between 2 -5 cm. There

was no statistically significant correlation between the COX -2 expression and tumor size in our study. Similar findings were found in studies done by Ashish sharmaet al.[20]

Ranjana Solanki et al,[19] reported among 50 cases, twenty one (42%) cases were negative for COX-2 expression.[15](30%) cases showed moderate expression. The DCIS component revealed strong COX -2 expression in ten cases. Moderate expression of COX- 2 was seen in four (22.2 %) cases whereas four (22. 2%) cases did not express COX -2. Our study did not show any strong COX-2 expression in any of the cases.

Another study by Boland G P et al,[21] showed Cyclooxygenase type-2 expression in DCIS (67%, P <0.001) and IBC (63%, P <0. 001) and was significantly greater than in normal breast (23%). There was no difference in COX- 2 expression level between DCIS and IBC (P=0.87). In this present study among 40 cases, tumor with DCIS component was observed in[12 cases (30%). Moderate expression of COX- 2 was seen in 12 cases of tumor with DCIS component and there was no significant correlation between cox-2 expression of DCIS and IBC.

Positive COX-2 expression was observed in both the ER/PR positive/ negative and the HER2/ neu positive/ negative groups in the current study and it was not found to be dependent on hormonal receptor status. COX-2 expression was not found to be statistically significant in relation to hormonal receptor status. Except for Perrone G et al,[22] the majority of the literature pertaining to the correlation of COX- 2 expression among tumor areas and hormonal status has found no statistical correlation. The limitations in our study were encountered because of the sample selection that included only Invasive ductal carcinoma cases. This disparity could be overcome in future by the selection of high grade cases with varying histological types.

In our study, among 32 COX- 2 positive cases, 13 cases (40. 7%) fall into grade- II, 12 cases (37.5%) fall into grade I and 7 cases (21.8%) belong to grade III. Out of 8 COX- 2 negative cases, 6 cases (75%) fall into grade III and 2 cases (25%) under grade II. Ranjana Solanki et al 11 reported in his study, among the COX -2 positive group, 14 (48.3%) cases belonged to grade 2, nine (31%) cases belonged to grade 1 and six (20. 7%) cases belonged to grade 3. In cases with negative COX - 2 expression, 12 (57.1 %), 7 (33.4 %) and 2 (9. 5%) cases fell in the category of histological grade 2, 1 and 3, respectively.

Carraro DM et al,[23] has stated that Ductal carcinoma in situ of the breast is characterised by the proliferation of abnormal epithelial cells with morphological features of malignancy within the basement membrane of the mammary ductal system, without the presence of stromal invasion. It is clear that DCIS is a lesion capable of progressing to form an invasive malignancy.

In an effort to understand the biology of the disease, and factors which may predict conversion into invasive ductal cancer, much attention has focused on clarifying patterns of protein expression. Surprisingly few studies have addressed the issue of COX-2 expression in DCIS, with varying conclusions. The presence of COX- 2 expression in preinvasive breast cancer is an important finding. It suggests that COX - 2 may play a role in the development of these lesions, or even in their transition into invasive cancers. In our study, all the 12 cases of tumor with DCIS component showed moderate expression of COX- 2. However, there was no statistically significant correlation between COX-2 expression and clinicopathological factors such as age, tumor size, nodal status, histological grade, hormone receptor status. But there are studies which report correlations with HER2 positivity and hormone receptor negativity indicating the existence of a subgroup of DCIS lesions with more aggressive biological potential.

Studies in COX-2 expression in breast cancer have produced varied results. Experimental studies have been done to investigate the correlation between COX-2 expression and prognostic factors. Few studies have been carried out to correlate the COX-2 expression with clinicopathological factors. The results of the studies show both significant correlation or did not find any relationship with prognostic factors or clinico pathological factors. Variation could be due to differences in the scoring system and cut offs used for COX- 2 expression. In our study, among 40 cases of tumor, COX-2 expression was observed in 32 cases and there was no statistical significant correlation with clinicopathological factors. Since COX -2 expression leads to increased synthesis of prostaglandins which result in reduced apoptosis and increased survival. COX -2 suppression can be used as a therapeutic and preventive step in breast cancer. NSAIDS Selectively or non selectively suppress the COX system thereby preventing the tumor development. Studies with large sample numbers and adequate follow -up are required to clarify why there is disparity between studies, and to give an insight into the mechanisms of this disease process.

CONCLUSION

In conclusion, the present study suggests that COX-2 up- regulation can predict an unfavorable prognosis of BC patients. Our results showed no statistically significant correlation of COX - 2 over expression with clinicopathological and prognostic features. Earlier studies have proposed an association of COX-2 expression to the factors associated with poor prognosis in breast cancer, such as larger tumor size, positive lymph node status, higher T stage and N stage. There was a moderate COX - 2 expression in the tumor, tumor

with DCIS component and the adjoining breast epithelium in our study. Most of the invasive breast carcinomas are alleged to arise from DCIS so early detection and treatment at appropriate time may result in favourable prognosis. Since COX - 2 Over expression is associated with reduced apoptosis and increased cell survival, studies have suggested inhibition of COX- 2 may serve as a target therapy in breast cancer tumorigenesis and to prevent recurrence.

REFERENCES

1. Dent R, Hanna WM, Trudeau M, Rawlinson E, Sun P, Narod SA. Time to disease recurrence in basal -type breast cancers: effects of tumor size and lymph node status. Cancer 2009; 115:4917 – 23.
2. Carter CL, Allen C, Henson DE. Relation of tumor size, lymph node status, and survival in 24,740 breast cancer cases. Cancer 1989; 63: 181 –7.
3. Takeshita E, Osanai T, Higuchi T, Soumaoro LT, Sugihara K. Elevated cyclooxygenase-2 expression is associated with histological grade in invasive ductal breast carcinoma. J Med Dent Sci. 2005; 52: 189 -93.
4. Ristimaki A, Sivula A, Lundin J, Lundin M, Salminen T, Haglund C, et al. Prognostic significance of elevated cyclooxygenase-2 expression in breast cancer. Cancer Res. 2002; 62: 632 -5.
5. Half E, Tang XM, Gwyn K, Sahin A, Wathen K, Sinicrope FA, et al. Cyclooxygenase- 2 expression in human breast cancers and adjacent ductal carcinoma in situ. Cancer Res. 2002;62:1676 -81.
6. Murakami M. Naraba H, Tanioka T, Semmyo N, Nakatani Y, Kojima F, Ikeda T, Fueki M, Ueno A, Oh S, and Kudo I. Regulation of prostaglandin E 2 biosynthesis by inducible membrane – associated prostaglandin E 2 synthase that acts in concert with cyclooxygenase - 2. J Biol Chem. 2000;275(32): 783 -32.
7. Shapiro S, Venet W, Strax P, Venet L, Roeser R. Ten - to fourteen- year effect of screening on breast cancer mortality. J Natl Cancer Inst1982;69:349 – 55
8. Fitzpatrick FA, Soberman R. Regulated formation of eicosanoids. The Journal of clinical investigation. 2001 Jun 1; 107(11): 1347 -51.
9. Hoellen F, Kelling K, Dittmer C, Diedrich K, Friedrich M, Thill M. Impact of cyclooxygenase-2 in breast cancer. Anticancer research. 2011 Dec 1; 31 (12): 4359 -67.
10. Heer E, Harper A, Escandor N, Sung H, McCormack V, Fidler - Benaoudia MM. Global burden and trends in premenopausal and postmenopausal breast cancer: a population - based study. The Lancet Global Health. 2020 Aug 1;8(8): e1027 -37.
11. Solanki R, Agrawal N, Ansari M, Jain S, Jindal A. COX - 2 expression in breast carcinoma with correlation to clinicopathologic al parameters. Asian Pacific Journal of Cancer Prevention: APJCP. 2018; 19 (7):1971 .
12. Shah A, Haider G, Abro N, Hashmat S, Chandio S, Shaikh A, Abbas K. Correlation Between Site and Stage of Breast Cancer in Women. Cureus. 2022 Feb 27 ;14(2).
13. Narod SA. Breast cancer in young women. Nature reviews Clinical oncology. 2012 Aug; 9(8):460 -70.
14. Bhutani N, Moga S, Poswal P, Sharma B, Arora S, Singla S. COX -2 Expression in Carcinoma of the Breast and Surrounding Non - neoplastic Breast Tissue. Archives of Breast Cancer. 2021 Jan 28:29 - 36.
15. Yadav R, Sen R, Chauhan P. Calculation of NPI score: prognosis of breast cancer. Executive Editor. 2013 Oct;4(4): 205.
16. Lee JA, Bae JW, Woo SU, Kim H, Kim CH. Correlation between COX-2 expression and hormone receptors in invasive ductal breast cancer. Journal of the Korean Surgical Society. 2010 Mar 1;78 (3):140 -8.
17. Brueggemeier RW, Díaz-Cruz ES, Li PK, Sugimoto Y, Lin YC, Shapiro CL. Translational studies on aromatase, cyclooxygenases, and enzyme inhibitors in breast cancer. The Journal of Steroid Biochemistry and Molecular Biology. 2005 May 1;95(1 - 5):129-36.
18. Kelly LM, Hill AD, Kennedy S, Connolly EM, Ramanath R, Teh S, Dijkstra B, Purcell R, McDermott EW, O'Higgins N. Lack of prognostic effect of Cox-2 expression in primary breast cancer on short-term follow-up. European Journal of Surgical Oncology (EJSO). 2003 Nov 1; 29(9): 707 -10.
19. Solanki R, Agrawal N, Ansari M, Jain S, Jindal A. COX - 2 expression in breast carcinoma with correlation to clinicopathologic al parameters. Asian Pacific Journal of Cancer Prevention: APJCP. 2018; 19 (7):1971 .
20. Sharma A, Marwah N, Parmar P, Sen R. Expression of COX-2 in carcinoma Breast. Journal of Clinical &Diagnostic Research. 2018 Mar 1;12(3).
21. Boland GP, Butt IS, Prasad R, Knox WF, Bundred NJ. COX -2 expression is associated with an aggressive phenotype in ductal carcinoma in situ.British Journal of Cancer. 2004 Jan;90(2):423 - 9.
22. Rosenberg L, Palmer JR, Zauber AG, Warshauer ME, Stolley PD, Shapiro S. A hypothesis: nonsteroidal anti - inflammatory drugs reduce the incidence of large bowel cancer. J Natl Cancer Inst. 1991; 83(5): 355 –358.
23. Carraro DM, Elias EV, Andrade VP. Ductal carcinoma in situ of the breast: morphological and molecular features implicated in progression. Bioscience reports. 2014 Feb 1;34(1).