DOI: 10.7860/JCDR/2024/66137.19208

Original Article

Pathology Section

Clinicopathological Study of CD34 Antigen Expression in Benign and Malignant Breast Lesions: A Cross-sectional Study

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ABSTRACT

Introduction: Breast cancer is the most frequent cancer among women. The CD34 immunohistochemical antigen serves as a tool in differentiating between benign and malignant breast lesions. It has been suggested that CD34 may be related to invasive potential.

Aim: To evaluate the expression of the CD34 antigen in the stroma of benign and malignant breast lesions using the Immunohistochemistry (IHC) method.

Materials and Methods: This cross-sectional study was conducted in the Department of Pathology in collaboration with the Department of Surgery at Sarojini Naidu Medical College, Agra, Uttar Pradesh, India over a period of 18 months (from January 2021 to June 2022), involving a total of 50 histopathologically confirmed cases of benign and malignant breast lesions. Postsurgical specimens, including biopsies and mastectomies, were fixed in 10% neutral buffered formalin. The initial diagnosis was made by Haematoxylin and Eosin (H&E)-stained tissue sections. Sections from the same block were subjected to IHC staining using a monoclonal antibody to the CD34 antigen, and the intensity of expression in stromal cells was graded from 0 to 3+ based on nuclear positivity: up to 5% stromal cells immunoreactive (grade-0), >5% and up to 25% (grade-1), >25% and up to 50% (grade-2), and > 50% (grade-3). The data was entered into Microsoft Excel 2007 and analysed using Statistical Package for Social Sciences (SPSS) statistical software version 19.0. The inferential statistics included the use of the Chi-square test.

Results: Out of the total 50 cases evaluated, 25 (50%) were categorised as benign, and rest 25 (50%) were categorised as malignant lesions. Among the benign lesions, the most common lesion was fibroadenoma, accounting for 9 (36%) cases, followed by benign phyllode tumour, with 6 (24%) cases. Among malignant lesions, the most common lesion was Invasive Ductal Carcinoma (IDC), accounting for 23 (92%) cases. The intensity of CD34 expression was found to be significantly higher in benign as compared to malignant breast lesions. Out of the 25 benign breast cases, the maximum number of cases (19) showed Grade-3+ positivity, 5 cases showed Grade-2+, and 1 case showed Grade-0 positivity. However, among malignant lesions, maximum cases (23, 92%) showed Grade-0 on CD34 immunostaining.

Conclusion: This study was undertaken to evaluate the CD34 expression in benign and malignant breast lesions which might be able to distinguish between the benign and malignant breast lesions. The most benign breast lesions express CD34 in the stroma, while it is almost totally lost in all malignant neoplasms. Loss of CD34 is associated with the tumour's capacity for invasion. However, to determine its function as a therapeutic target in cases of breast cancer, additional research can also be done.

Keywords: Breast cancer, Immunohistochemistry, Lactating adenoma, Squamous papilloma

INTRODUCTION

The most frequent cancer among women in the world today is breast cancer. For women between the ages of 35 and 55 years, it is the main cause of cancer-associated death. Breast carcinoma is the second most prevalent cause of cancer death, after lung carcinoma [1,2]. The higher rate of early-stage disease diagnosis is responsible for the current trend towards improvement in the death rate for breast cancer, although our therapeutic choices for advanced stage breast carcinomas are still restricted. The development of targeted and molecular-based therapies will therefore require a deeper understanding of the cellular and molecular mechanisms underlying the onset and progression of breast cancer [3]. Although histopathology is the gold standard for the identification of breast lesions, IHC study also plays a significant role when histological diagnosis is equivocal, particularly when distinguishing invasive carcinomas from in-situ carcinomas. Myoepithelial cells, fibroblasts, and leukocytes, among other stromal cells, tightly control the breast tumour's development, differentiation, and invasiveness [4]. The transmembrane glycoprotein CD34 is expressed by mesenchymal cells in numerous places such as the prostate, urinary bladder, fallopian tube, etc., including the normal mammary stroma, and it functions as a modulator of cell adhesion and signal transmission. Mesenchymal cells have been shown to lose CD34 in several contexts, including when the mesenchymal population undergoes malignant transformation. Malignant breast phyllodes tumours have lower CD34 levels than benign phyllodes tumours or fibroadenomas [5,6]. Therefore, the study was conducted to compare the expression of the CD34 antigen in benign and malignant breast lesions and to establish its diagnostic efficacy for benign and malignant breast lesions as a diagnostic tool.

MATERIALS AND METHODS

The cross-sectional study was conducted in collaboration between the Department of Pathology and the Department of Surgery at Sarojini Naidu Medical College, Agra, Uttar Pradesh, India. The study was conducted over a period of 18 months, from January 2021 to June 2022. Ethical approval was obtained from the institutional ethical committee (IEC/2021/40).

Inclusion criteria: Histopathologically confirmed cases of benign and malignant breast lesions, adequate tissue for further processing for CD34, cases with detailed clinical examination for clinicopathological correlation were included in the study.

Exclusion criteria: Inadequate and autolysed tissue, patients with metastatic tumours from systemic malignancies were excluded from the study.

A total of 50 cases (25 cases of benign lesions and 25 cases of malignant lesions) of surgically resected mastectomy and lumpectomy breast specimens, including biopsies, were included in the present study. After receiving the samples, gross inspection was done and the size and appearance of the tumour were documented. After incising (bread loafing), the specimens were fixed in 10% formal saline for 12 to 24 hours. Tissue sections from the representative areas were then submitted for further processing, and paraffin wax blocks were made. Sections of 3-4 µm were made from the paraffin wax blocks and stained by routine H&E dye, then examined under a light microscope. A histological diagnosis was made, including modified Bloom-Richardson histological grading. Another section of 3-4 µm was used for IHC for CD34 and stained using the Thermo Scientific CD34 (Clone QBEnd/10) kit. The representative sections from all the cases were studied. Each section was examined, and the number of terminal duct/lobular units was identified. The sections were evaluated at high power (400X microscopic field; objective 40X, eyepiece 10X), considering a high-power microscopic field harboured 100 stromal cells.

Grading was done from 0 to 3+ [7]:

0: ≤5% stromal cells immunoreactive

1+: >5 to 25% stromal cells immunoreactive

2+: >25 to 50% stromal cells immunoreactive

3+: > 50% stromal cells immunoreactive

The staining of endothelial cells in blood vessels was used as an internal control [7]. Grade-0 was interpreted as a complete loss of CD34. Grade-1 was interpreted as reduced expression, while Grade-2 and 3 were interpreted as retained expression of CD34. In the present study, Grade-0 and Grade-1 were considered as CD34 negative, and Grade-2 and Grade-3 were considered as CD34 positive [7]. The age of the patient and the site of lesions (right breast or left breast) were considered in clinicopathological correlation. Histological grading was done using the modified Bloom Richardson grading system based on tubule formation, nuclear pleomorphism, and mitotic figures [8].

1. **Tubule formation:**
    - Score 1: >75% of tumour has tubules
    - Score 2: 10%-75% of tumour has tubules
    - Score 3: <10% tubule formation
2. **Nuclear pleomorphism:**
    - Score 1: Tumour nuclei similar to normal ductal cell nuclei (2-3 x RBC)
    - Score 2: Intermediate size nuclei
    - Score 3: Large nuclei, usually vesicular with prominent nucleoli
3. **Mitotic count (per 10 HPF with 40X objective and field area of 0.196 mm^2)**
    - Score 1: 0-7 mitoses
    - Score 2: 8-14 mitoses
    - Score 3: 15 or more mitoses

Modified Bloom Richardson Grading:

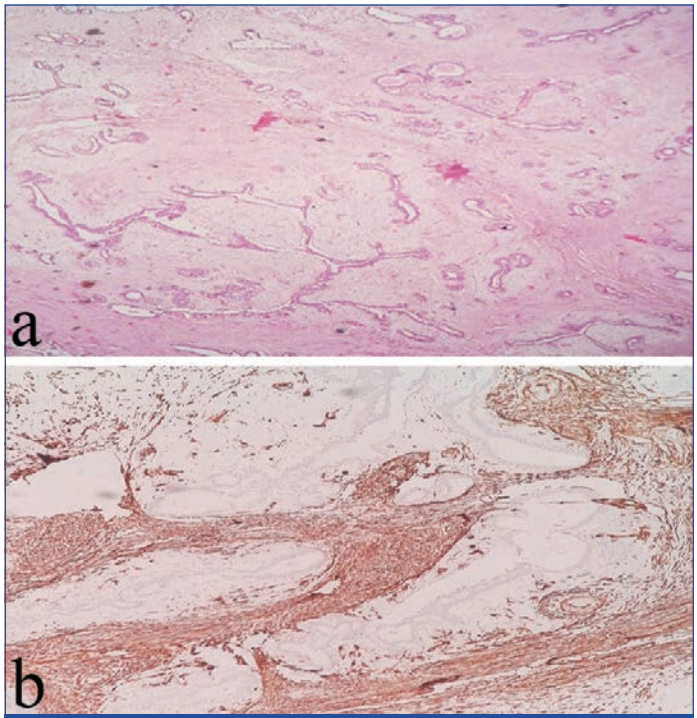
- Grade-1=Scores of 3, 4 or 5
- Grade-2=Scores of 6 or 7
- Grade-3=Scores of 8 or 9

STATISTICAL ANALYSIS

The data was entered into Microsoft Excel 2007 and analysed using SPSS statistical software version 19.0. The descriptive statistics included frequency and percentage. The inferential statistics included the use of the Chi-square test.

RESULTS

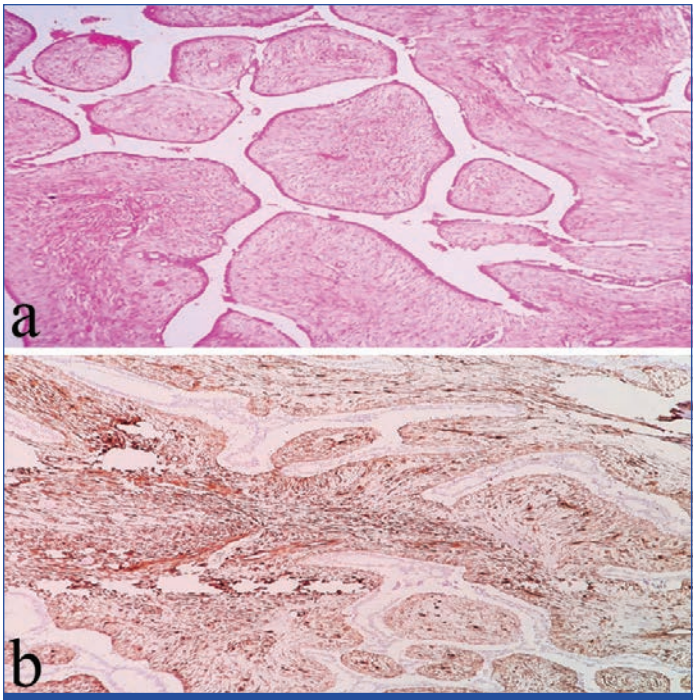
A total of 50 histopathologically confirmed cases of benign and malignant breast lesions were studied for the immunohistochemical expression of CD34. Out of the total 50 cases, only two cases were male, and the remaining 48 cases were female. Of the total 50 cases, the maximum number of cases (13 cases) was found in the 31-40 years age group, followed by the 41-50 years age group (10 cases) and the 11-20 years age group (nine cases). Out of these, 25 (50%) cases were benign, and 25 (50%) cases were malignant. Among benign lesions, the most common lesion was fibroadenoma with nine (36%) cases [Table/Fig-1a,b], followed by benign phyllode tumour with six (24%) cases [Table/Fig-2a,b], fibroadenosis with three (12%) cases, and gynecomastia with two (8%) cases [Table/Fig-3a,b], and each (4%) case of FA with epithelial hyperplasia, FA with ductal hyperplasia, and apocrine metaplasia [Table/Fig-4a,b], FA with apocrine metaplasia, Lactating adenoma [Table/Fig-5a,b], and Squamous papilloma. The most common malignant lesion was IDC with 23 (92%) cases [Table/Fig-6a,b,7a,b,8a,b], followed by one (4%) case each of malignant phyllode tumour [Table/Fig-9a,b] and Intraductal papillary carcinoma [Table/Fig-10a,b,11].



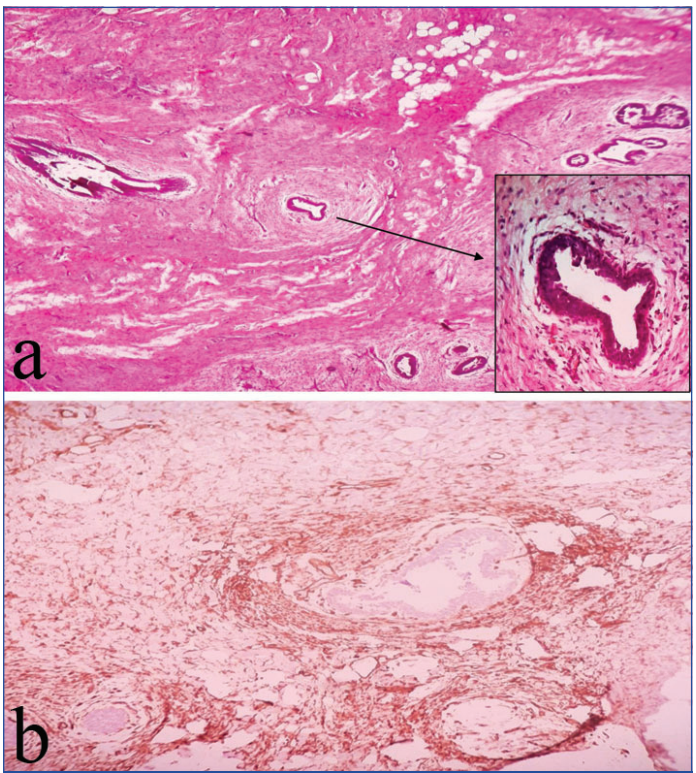
[Table/Fig-1]: a) Showing proliferation of stromal component and compressed epithelial component with elongated and slitelike appearance; Fibroadenoma (H&E, 100x). b) Showing grade-3 CD34 immunohistochemical staining in a case of Fibroadenoma (IHC, 100x).

In this study, in the benign cases, the most common age group affected was 11-20 years, with nine cases (36%), followed by the 21-30 and 31-40 years age groups, with six cases each (24%). Out of the total 25 cases of malignant lesions, the maximum cases were found to affect the 41-50 years age group, followed by the 31-40 year age group, with seven cases [Table/Fig-12].

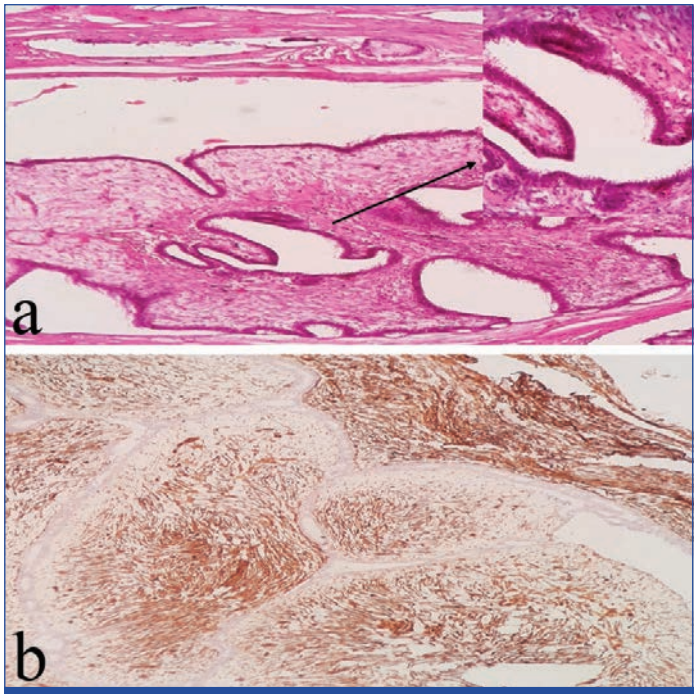
In this study, out of 25 benign breast cases, the maximum number of cases (19 cases) were found to be grade-3 positive, followed by grade-2 positivity in five cases and grade-0 in one case. Out of the nine cases of fibroadenoma, six cases showed grade-3 positivity. Out of the total six cases of benign phyllodes



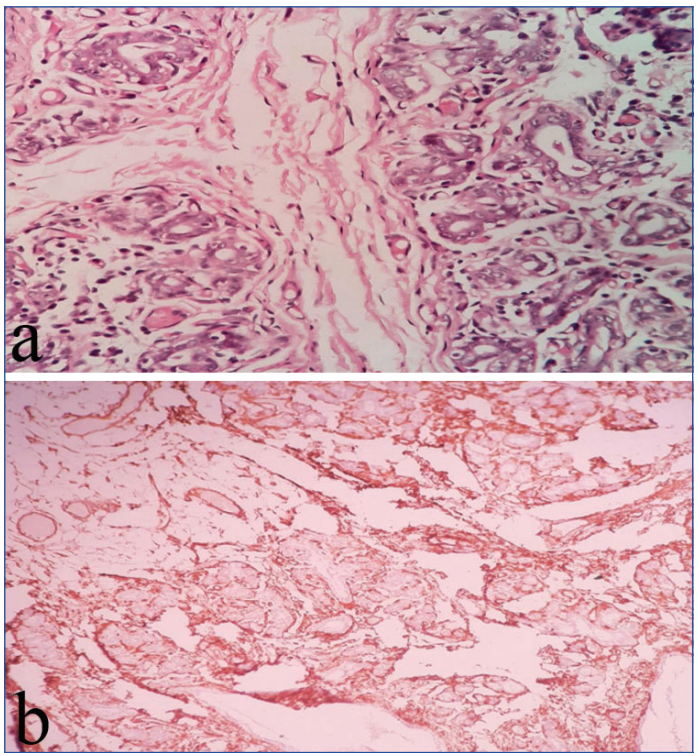
[Table/Fig-2]: a) Showing intracanalicular growth pattern with increased stromal cellularity and ductal epithelial cells; Benign phyllode tumour (H&E, 100x). b) Showing grade-3 CD34 immunohistochemical staining in a case of benign phyllode tumour (IHC, 100x).



[Table/Fig-3]: a) Showing proliferation of ducts (inset showing benign ductal epithelium, 400x) without lobule formation with loose periductal stroma; Gynaecomastia (H&E, 100x). b) Showing grade-3 CD34 immunohistochemical staining in a case of gynaecomastia (IHC, 100x).



[Table/Fig-4]: a) Showing proliferation of stromal component and ductal hyperplasia with apocrine metaplasia (Inset, 400x); Fibroadenoma with ductal hyperplasia and apocrine metaplasia (H&E, 100x). b) Showing grade-3 CD34 immunohistochemical staining in a case of fibroadenoma with ductal hyperplasia and apocrine metaplasia (IHC, 100x).



[Table/Fig-5]: a) Showing proliferation of epithelial component and closely packed tubules in back-to-back arrangement with supporting stroma and prominent lactational changes; lactating adenoma (H&E, 100x). b) Showing grade-3 CD34 immunohistochemical staining in a case of lactating adenoma (IHC, 100x).

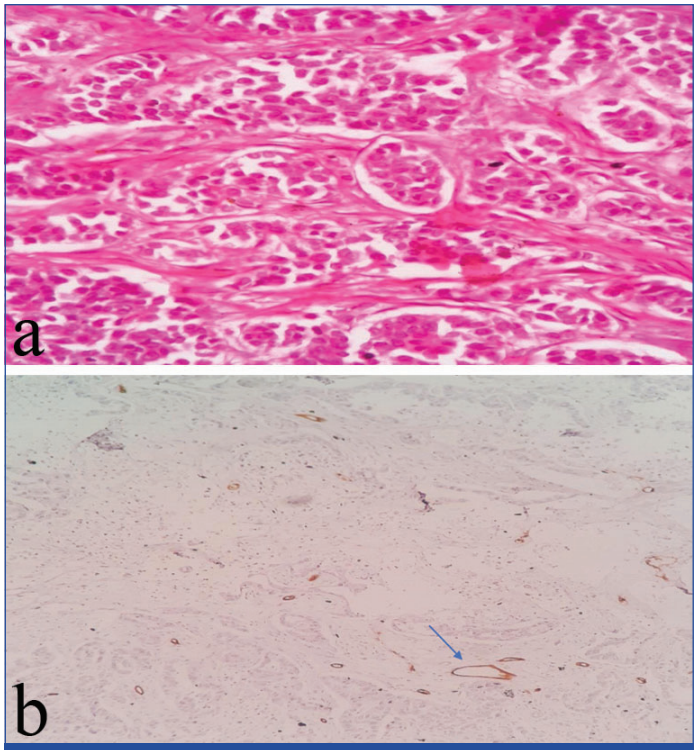
tumour, the maximum cases (04 cases, 66.7%) showed grade-3 positivity [Table/Fig-2b]. The difference was statistically significant (p-value=0.025) when analysed using the Chi-square test [Table/Fig-13].

In this study, out of 23 cases of IDC, the maximum cases of IDC showed Grade-0 positivity (21 cases, 91.3%), followed by 2 (8.7%) cases of Grade-1+; while each case of malignant phyllode tumour and intraductal papillary carcinoma were found to be Grade-0 positive. The difference was statistically non-significant when analysed using the Chi-square test (p-value=0.934) [Table/Fig-14].

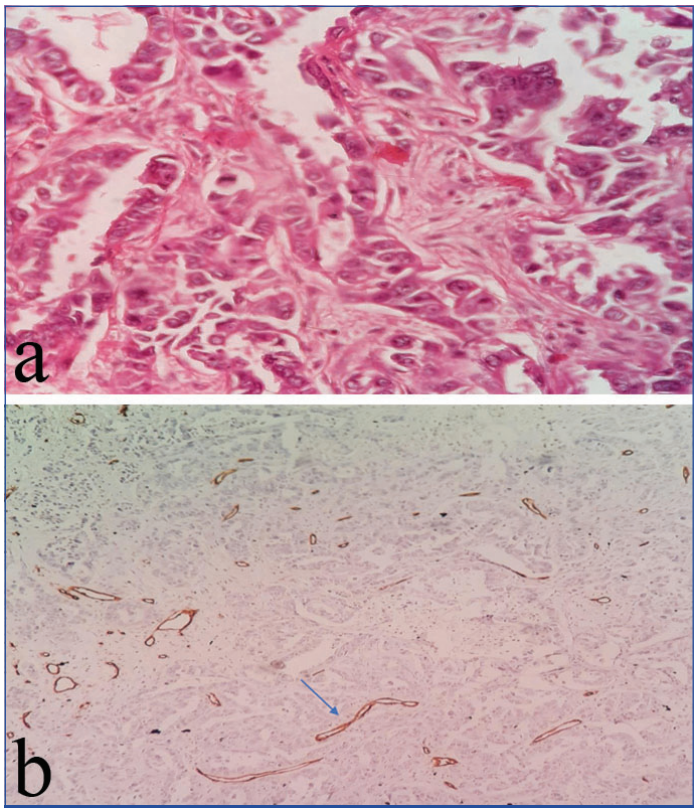
In this study, based on the association of the histological grade of IDC with CD34 expression, the maximum cases of IDC Grade-1 (09 cases, 81.81%) showed Grade-0 positivity, and 02 cases (18.11%) showed Grade-1 positivity with CD34 immunostaining. All cases of IDC with histological Grade-2 (05 cases) and Grade-3 (07 cases) showed Grade-0 positivity with CD34 immunostaining [Table/Fig-15].

DISCUSSION

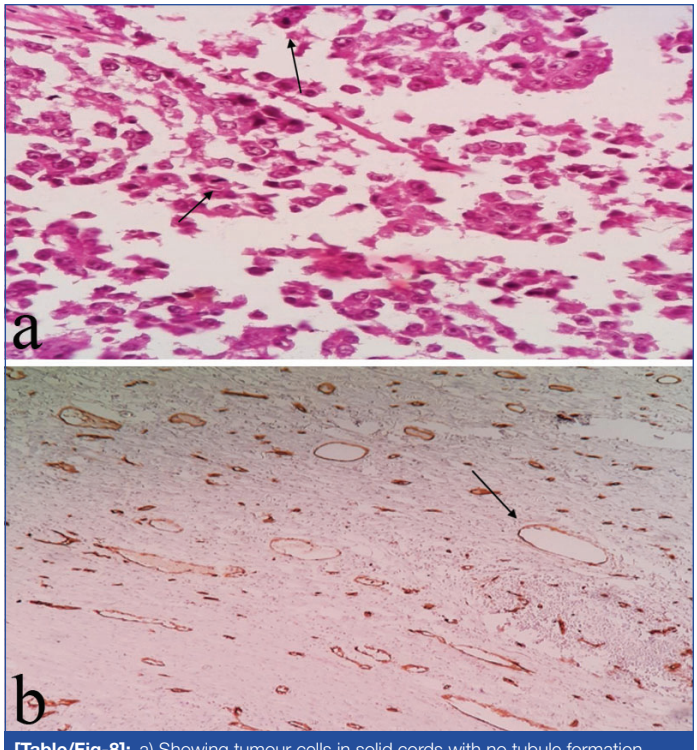
Breast cancer is still one of the most common diseases in India and throughout the world, continuing to take a high toll on



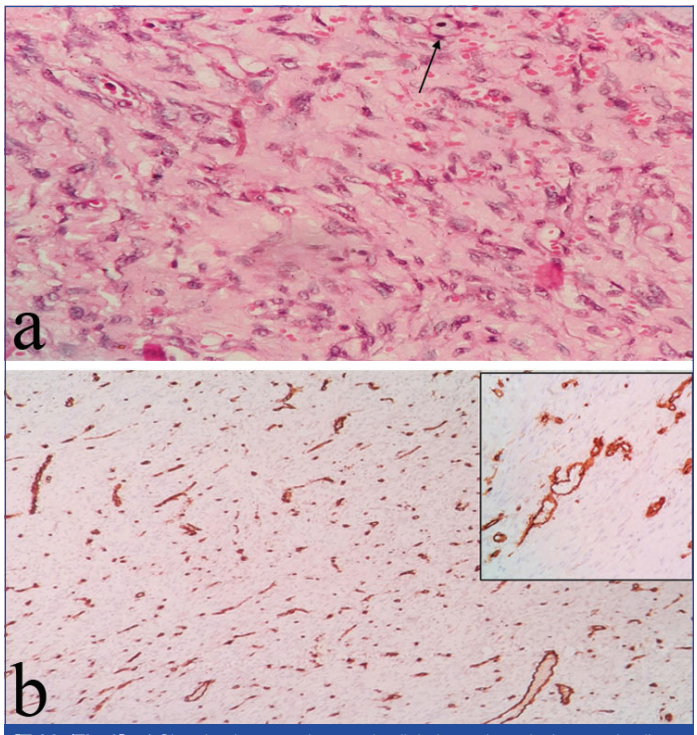
[Table/Fig-6]: a) Showing >75% tubule formation with mild nuclear pleomorphism; Invasive Ductal Carcinoma (IDC) Grade-1 (H&E, 400x). b) Showing grade-0 CD34 immunohistochemical staining of stromal cells and CD34 positive blood vessels in background (Arrow); Invasive Ductal Carcinoma (IDC) Grade-1 (IHC, 100x).



[Table/Fig-7]: a) Showing tumour cells arranged in cords and 10-75% tubule formation with moderate nuclear pleomorphism; Invasive Ductal Carcinoma (IDC) Grade-2 (H&E, 400x). b) Showing grade-0 CD34 immunohistochemical staining of stromal cells and CD34 positive blood vessels in background (Arrow); Invasive Ductal Carcinoma (IDC) Grade-2 (IHC, 100x).

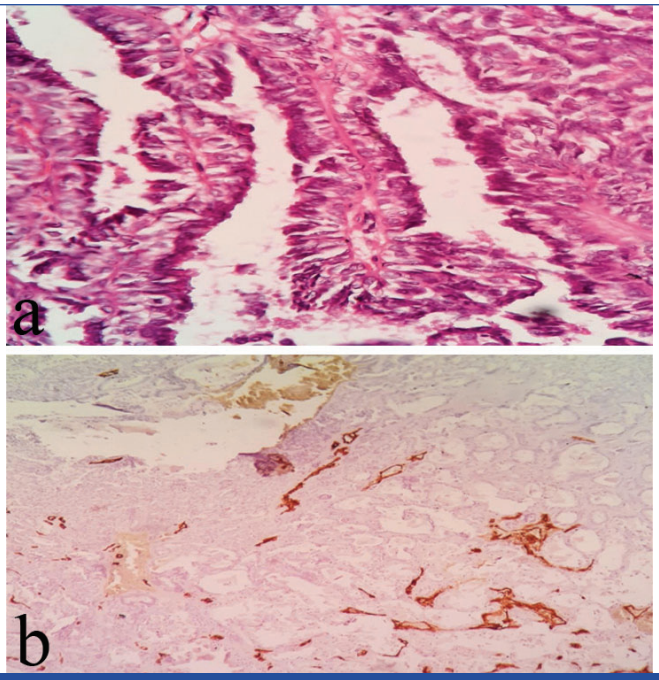


[Table/Fig-8]: a) Showing tumour cells in solid cords with no tubule formation and moderate nuclear pleomorphism with mitotic figures (Arrow); Invasive Ductal Carcinoma (IDC) Grade-3 (H&E, 400x). b) Showing grade-0 CD34 immunohistochemical staining of stromal cells and CD34 positive blood vessels in background (as control); Invasive Ductal Carcinoma (IDC) Grade-3 (IHC, 100x).



[Table/Fig-9]: a) Showing increased stromal cellularity and atypical stromal cells with hyperchromatic pleomorphic nuclei and mitotic figure (Arrow); Malignant Phyllodes Tumour (H&E, 400x). b) Showing grade-0 CD34 immunohistochemical staining of stromal cells and CD34 positive blood vessels in background (Inset); Malignant Phyllodes Tumour (IHC, 100x).

human life despite recent improvements and numerous studies conducted in this field. Studies on newer techniques for breast cancer treatment and quick and accurate diagnosis of cancer are desperately required [9]. The stroma surrounding the tumour is significantly different from normal stroma due to changes in protein synthesis, which also controls the proliferation of the tumour's epithelial component [10]. Mesenchymal cells expressed CD34, a transmembrane glycoprotein, at various places, including the normal mammary stroma. It was thought to be involved in the control of cell adhesion and signal transmission. Mesenchymal cells have been shown to lose CD34 in several circumstances when there has been a malignant change in the mesenchymal population [11]. The function of the stromal microenvironment in the development of different tumours has long been debated. The stroma surrounding the tumour is significantly different from normal stroma due to changes in protein synthesis, which also controls the proliferation of the tumour's epithelial component [7,10]. Mesenchymal cells express CD34, a transmembrane glycoprotein, at various places,



[Table/Fig-10]: a) Showing tumour with papillary architecture with delicate fibrovascular core lined by malignant epithelial cells without myoepithelial layer; Intraductal papillary carcinoma (H&E, 400x). b) Showing grade-0 CD34 immunohistochemical staining in a case of Intraductal papillary carcinoma (IHC, 100x).

Type of lesions	n (%)
1. Benign lesions (N=25)	**25**
Fibroadenoma (FA)	09 (36)
FA with epithelial hyperplasia	01 (4)
FA with ductal hyperplasia and apocrine metaplasia	01 (4)
FA with apocrine metaplasia	01 (4)
Gynaecomastia	02 (8)
Lactating adenoma	01 (4)
Fibroadenosis	03 (12)
Benign phyllodes tumour	06 (24)
Squamous papilloma	01 (4)
2. Malignant lesions (N=25)	**25**
Malignant phyllodes tumour	01 (4)
Intraductal papillary carcinoma	01 (4)
Invasive Ductal Carcinoma (IDC)	23 (92)

[Table/Fig-11]: Distribution of study subjects based on type of lesions.

Type of lesions	Grade-0	Grade-2+	Grade-3+
Fibroadenoma	0	3 (33.3%)	6 (66.7%)
FA with epithelial hyperplasia	0	0	1 (100%)
FA with ductal hyperplasia and apocrine metaplasia	0	0	1 (100%)
FA with apocrine metaplasia	0	0	1 (100%)
Gynaecomastia	0	0	2 (100%)
Lactating adenoma	0	0	1 (100%)
Fibroadenosis	0	0	3 (100%)
Benign phyllodes tumour	0	2 (33.3%)	4 (66.7%)
Squamous papilloma	1 (100%)	0(0%)	0
Total	**01**	**05**	**19**

[Table/Fig-13]: Showing association of CD34 stain grading with different types of benign lesions.
Chi-square test at p-value of 0.025 is significant, There was no single cases of grade-1

Type of lesions	Grade-0	Grade-1+
Malignant phyllodes tumour	1 (100%)	0
Intraductal papillary carcinoma	1 (100%)	0
Invasive ductal carcinoma	21 (91.3%)	2 (8.7%)
Total	**23**	**02**

[Table/Fig-14]: Association of CD34 stain grading with different types of malignant lesion.
Chi-square test at p-value of 0.934 is non-significant

Histological grade of IDC	CD34 expression grade			
	0	1+	2+	3+
Grade-1	09 (81.81%)	02 (18.11%)	00	00
Grade-2	05 (100%)	00	00	00
Grade-3	07 (100%)	00	00	00
Total	**21**	**02**	**00**	**00**

[Table/Fig-15]: Showing CD34 expression in different histological grade of Invasive Ductal Carcinoma (IDC).
Chi-square test at p-value of 0.932 is non-significant

including the normal mammary stroma [11]. Improved knowledge of the molecular and cellular mechanisms behind tumour progression can help in the early diagnosis of breast carcinomas as well as the development of specific therapies. The function of the stromal microenvironment in the development of different tumours has long been debated [7].

The present study was performed on a total of 50 cases of breast lesions; 25 cases were benign, and 25 cases were malignant. The

Type of lesions		11-20 years	21-30 years	31-40 years	41-50 years	51-60 years	Above 60 years	Total
Benign lesions	Fibroadenoma	4 (44.4%)	3 (33.3%)	2 (22.2%)	0	0	0	9 (36%)
	FA with epithelial hyperplasia	1 (100.0%)	0	0	0	0	0	1 (4%)
	FA with ductal hyperplasia and apocrine metaplasia	0	0	1 (100%)	0	0	0	1 (4%)
	FA with apocrine metaplasia	0	1 (100%)	0	0	0	0	1 (4%)
	Gynaecomastia	2 (100%)	0	0	0	0	0	2 (8%)
	Lactating adenoma	1 (100%)	0	0	0	0	0	1 (4%)
	Fibroadenosis	1 (33.3%)	1 (33.3%)	1 (33.3%)	0	0	0	3 (12%)
	Benign phyllode tumours	0	1 (16.7%)	2 (33.3%)	1 (16.7%)	2 (33.3%)	0	6 (24%)
	Squamous papilloma	0	0	0	0	0	1 (100%)	1 (4%)
	Total benign lesions	09 (36%)	06 (24%)	06 (24%)	01 (4%)	02 (8%)	01 (4%)	25 (100%)
Malignant lesions	Invasive Ductal Carcinoma	0	0	7 (30.4%)	7 (30.4%)	6 (26.1%)	3 (13.0%)	23 (92%)
	Malignant phyllodes tumour	0	0	0	1 (100%)	0	0	01 (4%)
	Intraductal papillary carcinoma	0	0	0	1 (100%)	0	0	01 (4%)
	Total malignant lesions	0	0	07 (28%)	09 (36%)	06 (24%)	03 (12%)	25 (100%)
Total cases		**09**	**06**	**13**	**10**	**08**	**04**	50

[Table/Fig-12]: Age wise distribution of benign and malignant lesions.
Chi-square test at p-value of 0.132 for benign lesions and 0.995 for malignant lesions

histopathological diagnosis was made on H&E section: thereafter IHC staining for CD34 on histological sections of breast lesions. In this study, out of a total of 50 cases, 48 patients were female and 2 patients were male. The youngest patient encountered in this study was a 15-year-old female, and the oldest patient was a 65-year-old female. Maximum number of cases were in the 4th to 6th decade of life.

Similar results were found by Bharti R and Khan AA et al., while Chakraborty AP et al., and Kuroda N et al., found the maximum number of cases in individuals older than the 5th decade of life (62%), and Chen Z et al., found the maximum number of cases in individuals older than the 4th decade of life [7,12-15]. Moreover, present study found that the maximum number of benign lesion cases occurred in the 2nd to 3rd decade of life, and the maximum number of malignant lesions were found in the 4th to 5th decade of life. Present study found that the maximum number of breast lesions were IDC, followed by fibroadenoma. Similar results were found by Cimpean AM et al., (41.00% cases of IDC), Tete A et al., (43.5% cases of IDC), and Kuroda N et al., (31.20% cases of IDC) [4,9,14], while Chakraborty AP et al., found fibroadenomas (21.70% cases) to be the most common lesion, followed by IDC (11.00% cases) [7]. Chauhan H et al., found DCIS (40.74% cases) to be the most common lesion, followed by IDC (29.60% cases), and Moore T et al., found phyllodes tumour (42.60% cases) to be the most common lesion, followed by FA (24.50% cases) [6,11].

Present study found that in the benign lesions, the maximum number of benign cases were fibroadenomas (36.00% cases), followed by benign phyllodes tumours (24% cases). Similar results were found by Khan AA et al., Elancheran M et al., and Kaçar A et al., as they found 74.69%, 84.5%, and 64.20% cases of fibroadenomas, respectively [13,16,17]. While Chauhan H et al., found radical scar lesions (66.66% cases) to be the most common benign lesion, followed by fibroadenomas (33.33% cases) [11]. Among the malignant lesions, the maximum number of malignant breast lesions were IDC (92.00% cases). Similar results were found by Elancheran M et al., Khan AA et al., and Chen Z et al., as they found that 95.65%, 88.5%, and 95.45% cases of IDC, respectively [13,15,16].

Based on the staining grading system of CD34, in this study, present study found that the maximum benign breast lesions (19 cases) showed grade-3 CD34 positivity, followed by grade-2 positivity in 05 cases, and a single case of squamous papilloma showed CD34 negativity. Similar results were found by Chakraborty AP et al., Chauhan H et al., Khan AA et al., Song JY et al., and Yazhou C et al., [7,11,13,18,19]. However, the maximum malignant lesions (23 cases, 92%) showed grade-0 positivity, followed by 02 cases (8%) with grade-1 positivity with CD34 immunostaining, which was found to be concordant with Moore T et al., Tete A et al., Chauhan H et al., Khan AA et al., and Kuroda N et al., [6,9,11,13,14].

In this study, all benign lesions were CD34 positive, except for the single case of squamous papilloma. The study was found concordant with Cimpean AM et al., Chakraborty AP et al., Tete A et al., Elancheran M et al., and Noronha Y et al., [4,7,9,16,20]. Although, all malignant lesions were found to be CD34 negative. The result was consistent with Chakraborty AP et al., Tete A et al., Chauhan H et al., Khan AA et al., Elancheran M et al., and Yazhou C et al., [7,9,11,13,16,19].

In the present study, based on the correlation of the histological grade of IDC with CD34 grading, the maximum cases (9/11 cases) of histological Grade-1 showed CD34 Grade-0 staining, and 2/11 cases showed CD34 Grade-1 staining. All cases of histological Grade-2 and Grade-3 showed CD34 Grade-0 staining. However, all cases of histological grades 1, 2, and 3 were found to be CD34 negative. Bharti R found that all cases of histological grades 1, 2, and 3 were CD34 negative, except for one case of histological Grade-1, which showed CD34 positivity [12]. Chakraborty AP et al., found that all cases of histological grades 1, 2, and 3 were CD34 negative with Grade-0 CD34 staining in all cases [7].

Limitation(s)

The limitation of the study was the restricted number of cases and the use of a limited marker, as many myoepithelial markers are used to differentiate between benign and malignant breast lesions.

CONCLUSION(S)

The present study was undertaken to evaluate the expression of the CD34 antigen in the stroma of benign and malignant breast lesions using IHC method. It is concluded that diffuse expression of CD34 is present in the normal breast stroma, in addition to the blood vessel wall. Most benign breast lesions express CD34 in the stroma. In all malignant neoplasms, CD34 expression in the stroma is almost totally lost. Loss of CD34 is associated with the tumour's capacity for invasion. It might be able to distinguish between benign and malignant breast lesions and act as a key diagnostic indicator. To determine its function as a therapeutic target in cases of breast cancer, additional research can also be done.

REFERENCES

[1] Köhrmann A, Kammerer U, Kapp M, Dietl J, Anacker J. Expression of Matrix Metalloproteinases (MMPs) in primary human breast cancer and breast cancer cell lines: New findings and review of the literature. BMC Cancer. 2009;9:188.
[2] Khadem R, Mahdi FC, Al-Mosawi K, AL-Janabi AA. The role of estrogen in breast cancer. Biomed Biotechnol Res J. 2020;4(4):293-96.
[3] Allinen M, Beroukhim R, Cai L, Brennan C, Lahti-Domenici J, Huang H, et al. Molecular characterization of the tumour microenvironment in breast cancer. Cancer Cell. 2004;6(1):17-32.
[4] Cimpean AM, Raica M, Narita D. Diagnostic significance of the immunoexpression of CD34 and smooth muscle cell actin in benign and malignant tumours of the breast. Rom J Morphol Embryol. 2005;46(2):123-29.
[5] Yamazaki K, Eyden BP. Ultrastructural and immunohistochemical observation on intralobular fibroblasts of human breast with observations on the CD34 antigen. J Submicrosc Cytol Pathol. 1995;27(3):309-23.
[6] Moore T, Lee AHS. Expression of CD34 and bcl-2 in phyllodes tumours, fibroadenomas and spindle cell lesions of the breast. Histopathology. 2001;38(1):62-67.
[7] Chakraborty AP, Mukhopadhyay D, Mandal A, Samaddar A, Pathak S. Clinicopathological study of breast lesions with special reference to the role of CD34 immunostaining in diagnosis a cross-sectional study from a tertiary care hospital of West Bengal, India. J Clin Diagn Res. 2022;16(4):EC36-EC40.
[8] Hoda SA. Invasive ductal carcinoma: Assessment of prognosis with morphologic and biologic markers. In Rosen PP. Rosen's Breast Pathology. 4th ed; 2014: Pp. 429.
[9] Tete A, Kumari N, Sinha AK. A study of CD34 antigen expression in benign and malignant breast lesions in patients attending RIMS, Ranchi. IOSR J Med Dent Sci. (IOSR-JDMS). 2022;21(2):37-43.
[10] Silberstein GB. Tumour-stromal interactions: Role of the stroma in mammary development. Breast Cancer Res. 2001;3(4):218-23.
[11] Chauhan H, Abraham A, Phillips JRA, Pringle JH, Walker RA, Jones JL. There is more than one kind of myofibroblast: Analysis of CD34 expression in benign, in situ, and invasive breast lesions. J Clin Pathol. 2003;56(4):271-76.
[12] Bharti R. CD34 expression as a surrogate marker for diagnosis of invasive ductal carcinoma of breast. Int J Sci Res. 2021;10(05):28-30.
[13] Khan AA, Alam K, Harris H. A clinicopathological study of CD34 antigen expression in benign and malignant breast lesions. J Clin Exp Pathol. 2017;7(4):01-09.
[14] Kuroda N, Jin YL, Hamauzu T, Toi M, Miyazaki E, Hiroi M, et al. Consistent lack of CD34-positive stromal cells in the stroma of malignant breast lesions. Histol Histopathol. 2005;20(3):707-12.
[15] Chen Z, Xu S, Xu W, Huang J, Zhang GU, Lei L, et al. Expression of cluster of differentiation 34 and vascular endothelial growth factor in breast cancer, and their prognostic significance. Oncol Lett. 2015;10(2):723-29.
[16] Elancheran, Dhivya M, Raghuveer CR, Rajkumar P. Stromal expression of CD34 immunohistochemical antigen in proliferative lesions of breast. IAIM. 2019;6(4):156-59.
[17] Kaçar A, Paker I, Akbiyik F, Arikok AT, Mambet E. CD117 and CD34 staining patterns in childhood benign mammary lesions. Turk J Pathol. 2012;28(1):31-37.
[18] Song JY, Yoon HK. Immunohistochemical phenotypes of phyllodes tumour of the breast. Korean J Pathol. 2008;42(3):151-56.

[19] Yazhou C, Wenlv S, Weidong Z, Licun W. Clinicopathological significance of stromal myofibroblasts in invasive ductal carcinoma of the breast. Tumour Biol. 2004;25(5-6):290-95.

[20] Noronha Y, Raza A, Hutchins B, Chase D, Garberoglio C, Chu P, et al. CD34, CD117, and Ki-67 Expression in Phyllodes tumour of the breast: An immunohistochemical study of 33 cases. Int J Sur Pathol. 2011;19(2):152-58.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Jun 20, 2023
- Manual Googling: Sep 19, 2023
- iThenticate Software: Jan 16, 2024 (15%)

ETYMOLOGY: Author Origin

EMENDATIONS: 6

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? Yes
- Was informed consent obtained from the subjects involved in the study? No
- For any images presented appropriate consent has been obtained from the subjects. No

Date of Submission: **Jun 19, 2023**
Date of Peer Review: **Sep 14, 2023**
Date of Acceptance: **Jan 18, 2024**
Date of Publishing: **Mar 01, 2024**