

Histopathological Spectrum of Breast Carcinoma in a Tertiary Care Centre and its Association with ABO Blood Grouping and Rh Typing

ABSTRACT

Background: Globally, breast cancer contributes to 27.7% of the newly diagnosed cases of cancer among women. Early screening and timely diagnosis of the lesions of breast help in alleviating the anxiety among patients. Histopathology is the gold standard in diagnosing the lesions, assessing the adequacy of treatment, and in disease prognosis. Studies have shown that ABO blood type has been associated with risk and survival for several malignancies. However, data for an association with breast cancer are inconsistent.

Aim: To study the histopathological spectrum breast carcinomas and to investigate the presence of a possible association between breast cancer in women and ABO blood group and Rh factor.

Material and methods: This retrospective descriptive study was done for a period of 4 years on 110 mastectomy specimens histopathologically diagnosed as breast cancers, and clinico-pathological data collected and analysed with records from the Department of Pathology, Saveetha Medical College. Association of breast cancer with ABO blood grouping and Rh typing was studied.

Results: Left breast was involved in most cases (96.4%). The mean age was 50.86 years, with 41-50 years age group showing peak incidence. Infiltrating breast carcinoma, no special type (89.6%) was the most common histological type. ER and PR positivity was seen in 46.4% and 41.8% of cases respectively. A statistically significant association was seen between hormone receptor status and histological grade. 39.1% cases belonged to O blood group, and Rh positivity was seen in 96.4% of the cases. No association was found between breast cancer and ABO/Rh blood grouping.

Keywords: breast cancer, histopathological spectrum, blood group, Rh type, hormone receptor

1. INTRODUCTION

Breast cancer is one of the most frequently occurring cancers among women and an important cause of morbidity and mortality worldwide, especially in developing countries like India. According to GLOBOCON 2018, it is the most common cancer, contributing to about 14% of all the newly diagnosed cancer cases, and 27.7% of newly diagnosed cancers among women.[1] Breast lesions show a broad spectrum with respect to benign, malignant, and non-neoplastic disease patterns. With palpable lump being the most common presentation, early evaluation of the lesion with timely and accurate diagnosis is crucial to alleviate the anxiety of patients and can be lifesaving.[2] Though clinical and radiological examinations are important screening tools, histopathological examination remains the gold standard in accurately diagnosing the breast lesions, assessing the hormonal status for therapy, treatment adequacy and prognosis of the disease.[3]

Studies have shown that several malignancies have been associated with ABO blood group type. [4,5] However this association was not made in breast carcinoma in older studies. [6,7] But recent studies suggest a possible association between blood group and ductal carcinoma of breast, with blood groups A and B being the most common. [8 -10]

This study was aimed to evaluate the spectrum of breast carcinomas and their correlation with clinico-pathological parameters, and to look for a possible association between breast cancer and ABO blood groups and Rh types.

2. MATERIAL AND METHODS

This retrospective descriptive study was done for a period of 4 years from June 2016 to May 2020 on breast carcinomas in the tertiary care centre. 186 cases were diagnosed to have breast cancer histologically during the study period, of which 110 cases were mastectomy specimens. The details of all the mastectomy specimens which had malignant lesions during the study period were collected from the tumor register. The demographic details, blood grouping, and Rh typing, histopathological and immunohistochemical data were collected from the hospital records and analysed.

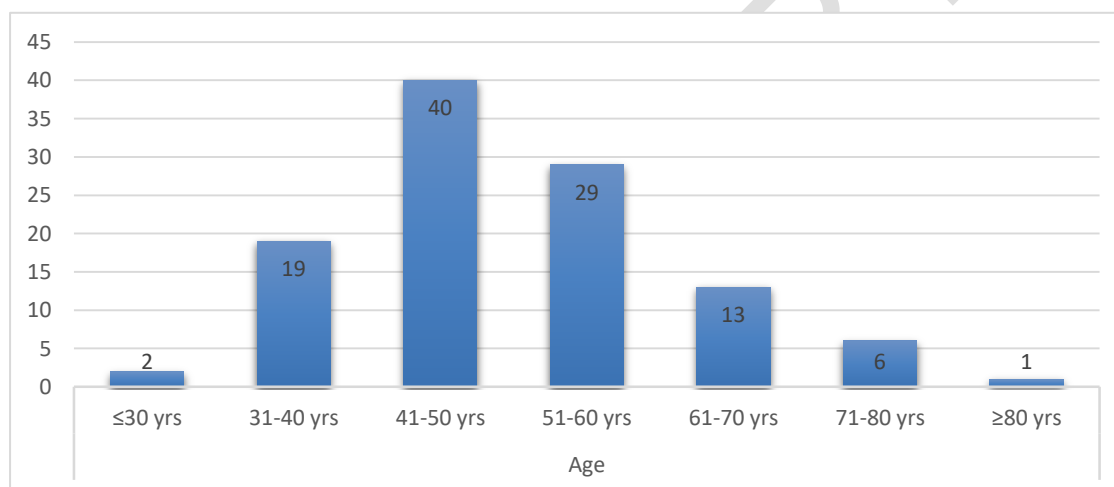
All mastectomy specimens of patients with known blood group and Rh type, diagnosed histopathologically to have breast carcinoma were included in the study. Patients with benign breast lesions, trucut biopsy specimens, and cases with no details about blood group and Rh type were excluded from the study. Complete enumeration sampling method was used. Analyses were done using IBM SPSS version 23. Frequency or median values were given as descriptive statistics. Chi-square test was used to determine differences in proportions. p value of less than 0.05 was considered as statistically significant.

The data collection was started following ethical approval.

3. RESULTS AND DISCUSSION

The mean age of our study population was 50.86 years \pm 11.33 years (range 30-81 years), with 41-50 years being the most common age group. The age distribution of the study population is shown in Fig 1.

Fig 1: Age frequency distribution of the cases of Breast carcinoma.



Left breast showed a higher incidence of carcinoma (56.4%). Upper outer was the most common quadrant involved (34.5%) among both sides, followed by central quadrant (25.5%). The most common presenting symptom was lump in the breast (91%), followed by pain and nipple discharge. Infiltrating ductal carcinoma was the most common histological type (96.36% of cases). Metaplastic, Mucinous and Adenoid cystic carcinoma were the other histological types identified. Invasive breast carcinoma - no special type was the most common subtype (89.6%). The mean tumor size was 4.04 cm, with majority of tumors in the range of 2 -5cm. 54.5% of the cases had grade II histology. 56.4% cases had positive lymph node metastasis. ER and PR positivity was seen in 46.4% and 41.8% of cases respectively. HER2 was over-expressed in 31.8% cases. Hormone receptor positivity was noted in 35.46% of cases. The relationship of hormone receptor status with histological grade is tabulated in Table 1.

Fig 2: A) Pie chart showing the distribution of various histological types of breast carcinoma

B) Bar chart showing the tumor size-based distribution of cases

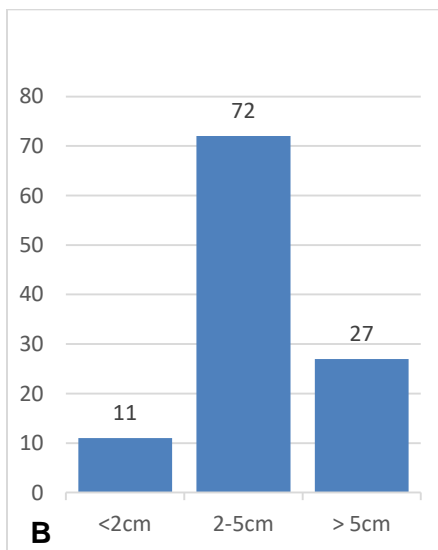
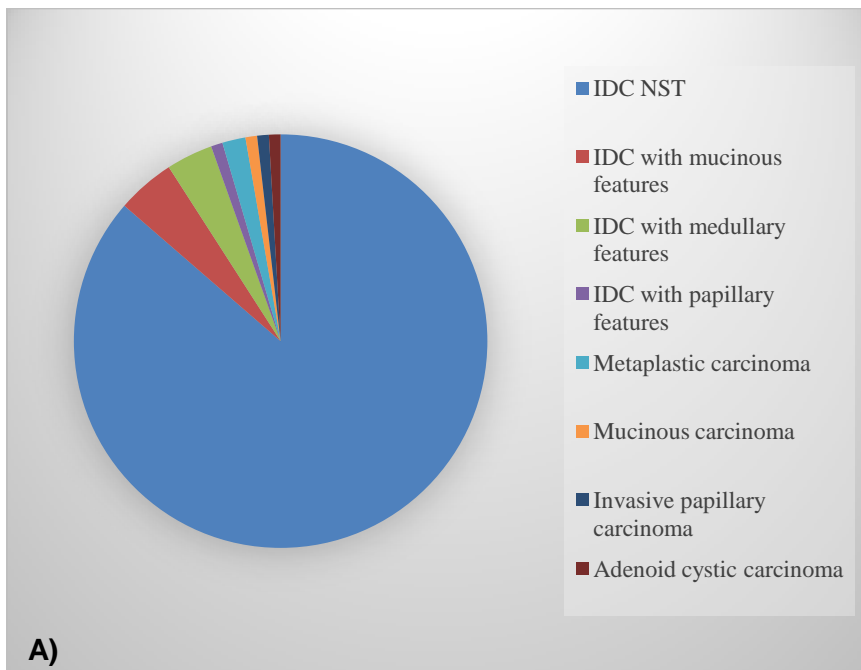


Table 1: Relationship between Hormone receptor status and Histological grade

Hormone receptor status	Histological grade			Total
	1	2	3	
ER+PR+	7 (17.94%)	26 (66.67%)	6 (15.39%)	39 (35.46%)

ER+PR-	4 (33.33%)	5 (41.67%)	3 (25%)	12 (10.90%)
ER-PR+	1 (14.29%)	5 (71.42%)	1 (14.29%)	7 (6.36%)
ER-PR-	5 (9.61%)	24 (46.16%)	23 (44.23%)	52 (47.28%)
Total	17 (15.45%)	60 (54.55%)	33 (30%)	110 (100%)

There is statistical significance among the grades when compared with different hormone receptor statuses. (P=0.04)

Table 2: Relationship of blood grouping and typing with various clinico-pathological parameters

Characteristics of Breast carcinoma patients according to ABO blood group									
Blood groups		A	AB	B	O	P value	Rh -ve	Rh +ve	P value
Number of Patients[n, (%)]		32	8	27	43		4	106	
Age	≤50yrs	14	6	18	23	0.22	1	60	0.21
	>50yrs	18	2	9	20		3	46	
Quadrant	Central	12	1	10	5	0.22	0	28	0.16
	LIQ	5	3	4	7		2	17	
	LOQ	4	1	2	3		1	9	
	UIQ	4	0	3	8		1	14	
	UOQ	7	3	8	20		0	38	
Tumor size	≤2cm	3	1	2	4	0.98	0	10	0.52
	>2cm	29	7	25	39		4	96	
Lymph node involvement	Yes	14	3	19	26	0.13	4	58	0.07
	No	18	5	8	17		0	48	
Histological grade	1	6	1	4	6	0.97	1	16	0.48
	2	17	5	16	22		1	59	
	3	9	2	7	15		2	31	
LVI	NO	10	2	13	13	0.39	1	37	0.68
	YES	22	6	14	30		3	69	
PNI	NO	24	6	23	39	0.28	4	88	0.37
	YES	8	2	4	4		0	18	
ER	Negative	18	5	16	20	0.67	3	56	0.38
	Positive	14	3	11	23		1	50	
PR	Negative	20	7	15	22	0.26	3	61	0.49
	Positive	12	1	12	21		1	45	
Her2	Negative	22	4	11	26	0.29	2	61	0.63
	Equivocal	2	0	5	5		0	12	

	Positive	8	4	11	12		2	33	
--	----------	---	---	----	----	--	---	----	--

Table 3: Relationship of ABO blood grouping and Rh typing with histological type

Histological type	A	B	AB	O	Rh -ve	Rh +ve
Adenoid cystic carcinoma	1	0	0	0	0	1
IDC NOS	29	7	25	34	3	92
IDC with medullary features	1	0	0	3	0	4
IDC with mucinous features	1	0	2	2	0	5
IDC with papillary	0	1	0	0	0	1

features						
Invasive papillary carcinoma	0	0	0	1	1	0
Metaplastic carcinoma	0	0	0	2	0	2
Mucinous carcinoma	0	0	0	1	0	1

Among the study population, 39.1% of cases belonged to O blood group, with AB blood group being the least common (7.3%). 96.4% of cases were Rh positive. Blood group and Rh type were compared with various clinico-pathological parameters in the study population. (Table 2) Also, comparison was made with histological type. (Table 5)

3.1 DISCUSSION:

In our present study, we studied the relationship of ER, PR, HER2 expression, blood group and Rh typing with various clinico-pathological parameters among breast carcinoma cases.

In our study, the peak incidence was seen in the age group 41-50 years (36.4%), which was similar to the studies by Yogalakshmi et al [11], Nandam et al [12] and Jangid et al [13]. The most common quadrant involved was upper outer, which included 34.5% of the carcinomas, followed by central quadrant (25.5%), which was comparable to the studies by Anushree et al [14] (upper outer 30% and central 17%), and Jangid et al [13] (upper outer 30.19%). Among the various histological types, the most common in our study was IDC NST (86.4%), which corresponds with studies by Anushree et al [14] (60%), Yogalakshmi et al [11] (77%), Eke et al [15] (88.6%) and Nandam et al [12]. 90.9% cases showed tumor size more than 2 cm, which was close to Ambroise et al study (91.5%) [16]. Lymph node involvement was seen in 56.4% of the cases in our study, which corresponds to studies by Ambroise et al [16] (58.19%) and Aly et al [17] (61.8%). Ahadi et al study [18] showed lymphovascular and perineural invasion in 54.2% and 16.5% cases, which were similar to our study (65.5% and 16.4% respectively). Histological grading (Modified Blood Richardson score) was done in all the cases and grade II was found to be the most common (54.5% cases), which was like that noted in studies done by S. Siddiqui Aziz study [19] (2003) and Vanisha Dhaka et al [20] Sulhyan K R et al [21]. However, Imam Mohammed Ibrahim et al [22] reported Grade I tumors to be the most common.

In our study, the number of tumors positive for both ER and PR was 35.45% which is higher than the study by Thakral et al (25.64%) (2016) [23]. In our study, the number of tumors which were ER positive and PR negative was 10.91%, which is higher than the Thakral et al 2016 study (5.98%) [23]. In our study, the number of tumors negative for both ER and PR was 47.28%, which is less compared to the Thakral et al 2016 study (63.25%) [23]. In the present study, significant correlation was established between ER/PR hormone receptor status and grading of tumor.

The most common blood group observed in our study was O group (39.1%), followed by A group (29.1%). In our study there was no positive correlation between age, size of tumor, stage of malignancy, nodal metastases or presence of progesterone/estrogen receptors and ABO and Rh blood group system. This was also observed by Stamatakis et al [24], who found no correlation between the patients' clinical characteristics and blood group [19]. Similar to studies by Manzarovuet al [25], Gates et al [26] and Jayant K et al [27], we did not find any association blood group and breast carcinoma.

But this observation contrasted with the study by Amini et al [28] who found a significant relationship between the size of tumor, axillary lymph nodes involvement and ABO blood groups system. Also, Guleria et al [29] and Morurali et al [30] studies have shown a positive association of breast carcinoma with blood group A. Surekha et al [31] have reported a higher incidence of breast carcinoma among blood group B individuals.

Although the sample size is a major limitation of this study, the results are well comparable with the previous studies in the literature.

4. CONCLUSION

In our study, the peak incidence of malignancy was noted among the age group 41-50 years and majority of the tumors are of T2 stage (tumor size 2cm to 5cm). Screening and awareness about breast carcinoma before 4th or 5th decade can

detect the malignancy at an early stage. Statistically significant correlation was noted between histological grade and hormone receptor status.

Though certain studies have shown a positive association between breast carcinoma and blood group, our study did not show any significant association; hence ABO/Rh blood group could not be used as a prognostic factor in breast carcinoma.

ETHICAL APPROVAL

Ethical clearance- Institutional ethics committee approval was obtained.

REFERENCES

1. World Health Organization. Global Health Observatory. Geneva: World Health Organization; 2018. who.int/gho/database/en/. Accessed June 21, 2018.
2. Manasa Reddy M, Raghu K. Histopathological Spectrum of Neoplastic and Non-neoplastic Breast Lesions: A Two Years Study. *Int J Sci Stud* 2017;4(11):158-162
3. Akrami M, Mokhtari M, Tahmasebi S, Talei A. Surgical and Clinical Pathology of Breast Diseases. <http://www.dx.doi.org/10.5772/52105>
4. Wolpin BM, Kraft P, Gross M, Helzlsouer K, Bueno-de-Mesquita HB, Steplowski E, StolzenbergSolomon RZ, Arslan AA, Jacobs EJ, Lacroix A, Petersen G, Zheng W, et al. Pancreatic cancer risk and ABO blood group alleles: results from the pancreatic cancer cohort consortium. *Cancer Res.* 2010; 70:1015–23.
5. Edgren G, Hjalgrim H, Rostgaard K, Norda R, Wikman A, Melbye M, Nyren O. Risk of Gastric Cancer and Peptic Ulcers in Relation to ABO Blood Type: A Cohort Study. *Am J Epidemiol.* 2010;172:1280–5.
6. Anderson DE, Haas C. Blood type A and familial breast cancer. *Cancer.* 1984; 54:1845–9. [PubMed: 6478419]
7. Tryggvadottir L, Tulinius H, Robertson JM. Familial and sporadic breast cancer cases in Iceland: a comparison related to ABO blood groups and risk of bilateral breast cancer. *Int J Cancer.* 1988; 42:499–501. [PubMed: 3170024]
8. Stamatakis M, Kontzoglou K, Safioleas P, Safioleas C, Manti C, Safioleas M. Breast cancer incidence in Greek women in relation to ABO blood groups and Rh factor. *Int Semin Surg Oncol.* 2009; 6:14. [PubMed: 19689811]
9. Anderson DE, Haas C. Blood type A and familial breast cancer. *Cancer.* 1984; 54:1845–9. [PubMed: 6478419]
10. Tryggvadottir L, Tulinius H, Robertson JM. Familial and sporadic breast cancer cases in Iceland: a comparison related to ABO blood groups and risk of bilateral breast cancer. *Int J Cancer.* 1988; 42:499–501. [PubMed: 3170024]
11. Yogalakshmi S, Kavitha M. A study of histopathological spectrum of breast lesions. *Int J Sci Stud.* 2019;7(1):1-5.
12. . Nandam MR, Shanthi V, Grandhi B, Byna SS, Vydehi BV, Conjeevaram J. Histopathological spectrum of breast lesions in association with Histopathological Grade versus Estrogen receptor and Progesterone receptor status in breast cancers: A Hospital based study. *Annals of Pathology and Laboratory Medicine.* 2017 Oct 25;4(5):A496-501.
13. Jangid P, Jangid MK, Pachori G. A histopathological study of malignant lesions of the female breast in a tertiary care centre. *J. Evolution Med. Dent. Sci.* 2020;9(24):1793-1797, DOI: 10.14260/jemds/2020/392
14. Anushree CN, Priyadarshini MR, Manjunatha YA. Histopathological spectrum of neoplastic and nonneoplastic lesions of breast in a tertiary care centre in Bangalore. *Indian Journal of Pathology and Oncology.* 2019 Apr;6(2):203-6.
15. Eke BA, Ojo BA, Akaa PD, Ahachi CN, Soo C, Adekwu A. The spectrum of breast diseases in Nigeria North Central: A histopathological survey. *Journal of Advances in Medical and Pharmaceutical Sciences.* 2017 May 25:1-6.

16. Ambroise M, Ghosh M, Mallikarjuna VS, Kurian A. Immunohistochemical profile of breast cancer patients at a tertiary care hospital in South India. *Asian Pac J Cancer Prev*. 2011 Jan 1;12(3):625-9.
17. Aly R, Yousef A, Elbably O. Association of ABO blood group and risk of breast cancer. *J Blood Disorders Transf*. 2014;5:241.
18. Ahadi M, Heibatollahi M, Zahedifard S. Comparison of ER, PR, Ki67 and HER-2/neu Reactivity Pattern with Patients' Age, Histologic Grade, Tumor Size and Lymph Node Status in Invasive Ductal Breast Cancer. *International Journal of Cancer Management*. 2020 Jun 1;13(6).
19. Siddiqui MS, Kayani N, Pervez S, Aziz SA, Muzaffar S, Setna Z, Israr M, Hasan SH, Gill MS. Breast diseases: a histopathological analysis of 3279 cases at a tertiary care center in Pakistan. *Journal of Pakistan Medical Association*. 2003;53(3):94.
20. Dhaka V, Mane VP, Pawar VR, Mote DG, Mohite SV. Clinicopathological study of mastectomy specimens in tertiary hospital. *Indian Journal of Pathology and Oncology*. 2016 Jul;3(3):446-9.
21. Sulhyan KR, Anvikar AR, Mujawar IM, et al. Histopathological study of breast lesions. *Int J Med Res Rev* 2017;5(1):32-41.
22. Ibrahim IM, Iliyasu Y, Mohammed AZ. Histopathological review of breast tumors in Kano, northern Nigeria. *Sub Saharan African J Med* 2015;2(1):47-51. *Research Analysis* 2018;7(6):65-7.
23. Thakral A, Daveswar M. Histomorphological study of a spectrum of breast diseases n association with immunohistochemistry in Vododara, Gujarat, India. *Int J Sci stud* 2016;4(9):44-54.
24. Stamatakis M, Kontzoglou K, Safioleas P, Safioleas C, Manti C, et al. (2009) Breast cancer incidence in Greek women in relation to ABO blood groups and
25. Rh factor. *Int Semin Surg Oncol* 6: 14.
26. Munzarová M, Kovarik J, Hlávková J (1986) A, B, O blood groups and the course of breast cancer disease. *Czech Med* 9: 44-50.
27. Gates MA, Xu M, Chen WY, Kraft P, Hankinson SE, Wolpin BM. ABO blood group and breast cancer incidence and survival. *Int J Cancer* 2011;130:2129-37.
28. Jayant K. Relationship of ABO blood group to certain types of cancer common in Western India. *Ind J Cancer* 1971; 8: 185–188.
29. Amini M, Fatah SH, Kalantari M (2010) ABO blood groups and prognosis of breast cancer: a case-control study in Arak/Iran. *IJBC* 1: 155-159
30. Guleria K, Singh HP, Kuar H, Sambyal V. ABO blood group in gastrointestinal tract (GIT) and Breast Carcinoma Patients. *Anthropologist* 2005; 7: 189–192.
31. Mourali, N, Muenz LR, Tabbane F, Belhassen S, BahiJ, Levine PH. Epidemiologic features of rapidly progressing breast cancer in Tunisia. *Cancer* 1980; 46: 2741–2746.
32. Surekha D, Shrinivasan A, Sailaja K, Rao D. Association of esterase D and ABO blood group in breast cancer. In: *Trends in Human Genetics, Biotechnology and Bioinformatics: Next 5 years*. 29th Annual conference of Indian Society of Human Genetics, Bangalore. 2004; 122– 123.