Original Research Article

Association of female Breast carcinoma, its prognostic factors and ABO blood group: A retrospective study

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Abstract

Back ground: Association between ABO blood group antigens and cancer has been described since 1953. Association of breast carcinoma and ABO group is not clear**. Aims and objectives**: To study the association between blood group type and breast carcinoma, its prognostic factors and molecular subtypes**. Material and methods**: This is retrospective study which includes 273 breast cancer cases. Association between prognostic factors, molecular subtypes of breast carcinoma and blood group type was assessed**. Results:** Out of 273 cases of breast carcinoma, maximum number of cases were of O group (41.5%).Among grade 1 and grade 2 patients majority were having blood group O and grade 2 patients were having B group. All the blood groups showed tumor size of 2 to 5cms and were in stage 2 in maximum cases. Maximum cases with lymphnodal metastasis were seen in O group (45.1%).Her2 rich cases were commonly observed in B group (38%) where as Luminal A, Luminal B, and triple negative were commonly seen in O group (43.2%,46.3% and 39% respectively). **Conclusion:** Women with blood group O are at more risk of developing breast carcinoma followed by blood group B, A and AB. There was no statistical significance for association between the blood groups and prognostic factors of breast carcinoma. Lymph nodal metastasis was seen more in blood group O patients. Maximum number of Her2 rich cases were seen in B group whereas Luminal A, Luminal B and triple negative were seen in O group.

Key words: ABO Blood group, Female breast carcinoma, Prognostic factors, Association

Introduction

Breast carcinoma is the most common malignancy among the female population in the world with exception of West Africa, where cervical carcinoma is more common[1]. Breast carcinoma was diagnosed in 2.1 million women in 2018 (approximately for every 18 seconds one new case was diagnosed). It has highest cancer mortality rates in women across the world except in some countries like Northern Europe, South America, north and Sub-Saharan Arica, where the main causes of mortality was cervical / or lung cancer[2]. In the era of modern medicine, morphological classification, tumor grading depending upon extent of tubule formation, nuclear pleomorphism, mitotic activity, tumor size, lymph node involvement and metastasis are not sufficient to assess the behavior of breast carcinoma[3]. Hence molecular patterns of breast carcinoma were studied which assisted in management of cases[4].

Association between cancers and ABO blood group has been reported in many studies, in which stomach cancer was associated with blood group A[5] and blood group B was associated with Hodgkin lymphoma, pancreatic cancer and cardiac cancer[6,7].

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Several studies have been documented on the association between blood group type and breast carcinoma. Few studies have shown relationship between prognostic factors of breast carcinoma and blood group type[8] and few studies showed no association[9]. In our study we tried to study the association between blood group type and breast carcinoma, its molecular subtypes and prognostic factors.

Material and methods

Our study is retrospective hospital-based study carried in Department of pathology, Sri Venkateswara Institute of Medical Sciences, Tirupathi for period of 3 years from January 2019 to January 2022 after getting approval from institutional ethical committee. We studied 273 breast carcinoma cases. Medical records of these patients were reviewed. Clinicopathological data like tumor stage, tumor size, lymph node status, histological grade, ER status, PR status, HER2 status and ki67 index were collected from laboratory records. Molecular subtyping depending upon hormone receptor status and proliferation index was recorded. Molecular subtypes are Luminal A (ER, PR positive, HER2 negative and low Ki67), Luminal B (ER positive, PR positive/ negative, Her2 positive/ negative and Ki67 low/high), HER2 enriched (ER, PR negative, HER2 positive, Ki67 low/high) and basal like triple negative (ER, PR, HER2 negative and Ki67 high)[10]. Blood groups of the cases determined serologically were noted. Association between histopathological prognostic factors

in breast carcinoma like tumor size, tumor grade, lymphatic invasion, molecular subtypes and blood group typing was studied.

Inclusion criteria

All the cases of breast carcinomas with histopathological diagnosis of invasive ductal carcinoma who underwent radical mastectomy and with details of ER, PR, HER2/neu and Ki 67 were included in the study

Exclusion criteria

Breast carcinoma cases diagnosed on core biopsies, breast carcinoma cases undergone radical mastectomy but without immunohistochemistry status and benign breast lesions were excluded in our study

Statistical analysis

Collected data will be entered into Microsoft excel 2019. Quantitative variables were presented as mean and standard deviation. Qualitative variables were presented as numbers and percentages. Chi-square test was used to test the significant difference between proportions. SPSS 26th version was used for doing statistical analysis. P value less than 0.05 was considered as statistically significant.

Results

273 breast carcinoma patients were studied. Table 1 presents the distribution of various blood groups among breast cancer patients.

Table 1: Distribution of blood groups among breast cancer patients

Type of blood group	Number (%)
A group	57 (20.9%)
B group	94 (34.4%)
AB group	9 (3.2%)
O group	113 (41.5%)
Total	273

Table 1 showed that maximum number of cases were seen among O group patients (41.4%) followed by B (34.4%),A(20.9) and AB (3.2%)group. Blood groupO had higher risk of breast carcinoma in comparison with other groups.

Prognostic factors were studied in relation to various blood groups in breast carcinoma cases

Table 2: Comparison of tumor grade, size and stage among different blood group

Grade of tumor	Type of blood group				Total (n=273)	P Value
	A No.(%) (n=57;20.9)	AB No.(%) (n=9;3.3)	B No.(%) (n=94;34.4)	O No.(%) (n=113;41.4)		
1	17 (21.5)	3 (3.8)	27 (34.2)	32 (40.5)	79	0.307
2	29 (21.4)	5 (3.7)	53 (39.9)	49 (36)	136	
3	11 (19)	1 (1.7)	14 (24.1)	32 (55.2)	58	
Size of tumor (cms)						
< 2	5 (11.6)	3 (7)	15 (34.9)	20 (46.5)	43	0.466
2 – 5	44 (21.7)	5 (2.5)	71 (35)	83 (40.9)	203	
>5	8 (29.6)	1 (3.7)	8 (29.6)	10 (37)	27	
Tumor stage						
T1	8 (16.7%)	3 (6.3)	17 (35.4)	20 (41.7)	48	0.906
T2	39 (21.4)	5 (2.7)	63 (34.6)	75 (41.2)	182	
T3	5 (17.9)	1 (3.6)	9 (32.1)	13 (46.4)	28	
T4	5 (33.3)	0 (0)	5 (33.3)	5 (33.3)	15	

In all blood groups most of the breast carcinoma cases were of grade 2. Among grade 1 and grade 3 patients majority were having blood group O (40.5% and 55.2% respectively), among grade2 patients most of the cases were having B group (39.9%).These differences were not statistically significant (Table 2).

When the tumor size was studied among different blood groups, all the blood groups showed maximum number cases with tumor size of 2 to 5cms and did not show statistical significance. Among patients with tumor size of less than 2cms, 2 to 5cms and more than 5cms majority were having blood group O compared to other groups. (Table 2).

Among the different blood groups, maximum number of breast carcinoma cases were in the stage 2 and did not show statistical significance. All stages were commonly observed among blood group O patients (Table 2)

Table 3: Comparison of lymph node metastasis among different blood groups

Lymph node metastasis)	Type of blood group				Total	P Value
	A No.(%)	AB No.(%)	B No.(%)	O No.(%)		
Present	31 (21.8)	4 (2.8)	43 (30.3)	64 (45.1)	142	0.426
Absent	26 (19.8)	5 (3.8)	51 (38.9)	49 (37.4)	131	
Total	57 (20.9)	9 (3.3)	94 (34.4)	113 (41.4)	273	

Lymph node metastasis in breast carcinoma cases were compared in different blood groups. Maximum cases with lymph node metastasis were seen in O group (45.1%)followed by B group (30.3%) patients (Table 3) however no statistical significance was seen.

Table 4: Association between molecular subtypes and different blood groups

Molecular type	Type of blood group				Total	P Value
	A No.(%)	AB No.(%)	B No.(%)	O No.(%)		
Her2 rich	13 (26)	0 (0)	19 (38)	18 (36)	50	

Luminal A	14 (18.9)	2 (2.7)	26 (35.1)	32 (43.2)	74	0.481
Luminal B	14 (20.9)	1 (1.5)	21 (31.3)	31 (46.3)	67	
Triple negative	16 (19.5)	6 (7.3)	28 (34.1)	32 (39)	82	
Total	57 (20.9)	9 (3.3)	94 (34.4)	113 (41.4)	273	

Table 4 showed that Her 2 rich was commonly observed among blood group B patients (38%). Luminal A, Luminal B and triple negative were most observed among O group patients (43.2%, 46.3% and 39% respectively). However statistical significance was not there between blood groups and molecular subtypes

Discussion

Identification of increasing forms of different morphological variants of breast carcinoma by pathologists during the last 50 years has led to discussion on breast cancer classification. However, there are doubts as to whether these variants are biologically significant or not. Breast cancer is a heterogenous disease rather than a single disease with different histological and biological properties due to genetic, epigenetic and transcriptome changes, with varying clinical findings and treatment responses. This phenotypic difference influences breast cancer diagnosis, treatment, and prognosis.

With advancement of molecular techniques such as gene expression profiling, "heterogeneity in breast cancer concept" has now become generally accepted. Thus, pathologist were introduced to the so called new era of "molecular classification" that is developed from the traditional old fashioned morphological classification. Targeted therapies and more importantly individualized treatment programme have become possible with the implementation of this classification. Perou and Sorlie proposed "molecular classification" terminology in breast carcinoma for the first time with a comprehensive study showing the differences in gene expression in 2000[11]. Clinically relevant molecular subtyping of breast cancer depends upon expression of ER (Estrogen Receptors), PR (Progesterone Receptors), HER2 (Human Epidermal Growth Factor Receptor 2) and Ki 67 (Cell proliferation regulator). Molecular subtyping helps to stratify breast cancer into different entities that require different monitoring strategies and specific treatment and also helps in understanding prognosis[10].

ABO blood group is determined by the expression of antigens which are carbohydrate moieties present on membrane of red blood cells[12]. These antigens are not only expressed on the surface of erythrocytes but also on cells like epithelium, vascular endothelia, platelets and neurons[13]. Mechanism by which ABO blood groups are related to development and progression of carcinoma is largely unknown[14]. One of the possible mechanisms is dysregulation in the ABO glycosyltransferase activity which are involved in the process of cell membrane signaling and intercellular adhesion as well as in the host immune response[15] ABO glycosyl transferases can modulate the levels of Von Willebrand factor in the plasma which has an important role in modulating apoptosis and angiogenesis, thus affecting tumorigenesis[16]. ABO antigens influence the host inflammatory state and further influence tumor progression and spread[17]. Association between polymorphism of ABO gene locus and plasma levels of p – selectin, E-selectin, soluble intercellular adhesion molecule-1 (ICAM-1) and Tumor necrosis factor has been reported in some studies[18]. The soluble ICAM -1 binds to the corresponding ligands on circulating cells and thus inhibits attachment of lymphocytes to the endothelial cells. Similar mechanism is used by cancer cells to adhere to the endothelial cells and metastasize[19]. In the blood groups other than O group, particularly in A group, soluble ICAM-1 levels are less hence chances of metastasis is more and showed decreased survival in some studies[20].

Relationship between breast cancer and ABO blood group was assessed by several investigators. Sujatha B and Sherry Jenilin G in their study observed that breast cancer had significant association with blood group A followed by O and B. In their study patients with AB blood group had minimum risk[21]. In our study O group has significant association with breast carcinoma followed by B and A. Our study also showed minimum association of breast carcinoma with AB group.

In the studies done by M Solak et alblood group O was associated with Luminal type of breast cancer which correlated with our studies[22]. But in studies done by Nadir K et al Blood group O had higher incidence of triple negative breast cancers and low rates of luminal types[23].

In our study nodal metastasis were seen in maximum cases of O and A group, but in study done by Solak et al[22] nodal metastasis was significantly less in O and A group.

Conclusion

Our study concludes that there is an association between breast cancer and blood groups. Women with blood group O are at more risk of developing breast carcinoma followed by blood group B and A. Women with blood group AB are at least risk for breast carcinoma. Though there was no statistical significance between the blood groups and staging, grading, lymphnodal metastasis and molecular subtypes of breast carcinoma,lymph nodal metastasis was seen more in blood group O patients. Her 2 rich cases were common among blood group B patients . Luminal A, Luminal B and triple negative were more common among O group patients.Further large group studies should be conducted to elucidate the relationship between breast cancer risk and prognosis with types of blood groups.

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