



EPIDEMIOLOGICAL STUDY OF BREAST CANCER PATIENTS AND THEIR ASSOCIATION WITH ABO BLOOD GROUP

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Abstract – Objective: ABO Blood groups play an important biological role in the immunological system. Studies have reported a strong relationship between ABO and Rhesus (Rh) blood types with various cancers; however, results are contrasting. This study encompasses epidemiology of breast cancer patients in north-eastern Uttar Pradesh region and also investigates the distribution of ABO and Rh blood antigens among breast cancer patients.

Patients and Methods: A total of 187 breast cancer patients and 209 controls were enrolled in the study. Blood group, Rh factor, histological type, and different clinicopathological parameters were recorded. The frequencies of the ABO blood group among both the groups were evaluated and compared with different clinical parameters.

Results: Frequency of blood group B (40.6%) was comparatively higher in breast cancer patients than other groups (A – 22.5%, AB – 6.4%, O – 30.5%), and the distribution of blood group among cases and controls did not differ significantly. Blood group B (n=53; 69.7%) has been found to be higher in grade II differentiation of breast cancer, but the difference was not significant. Moreover, we did not find any association of blood group with any of the receptor status.

Conclusions: Results suggested that blood group B was found to be higher in breast cancer patients, but it did not show any significant role. In addition, we did not find any association between Rh factor and breast cancer. Study findings have shown that breast cancer type, grade, stage, age of menarche (AOM), and hormonal status showed no significant associations with ABO blood group. However, further studies with larger number of patients are needed to clearly establish the role of ABO/Rh blood groups as a prognostic factor in breast cancer patients.

KEYWORDS: Breast Cancer, ABO blood type, Rh Factor.

LIST OF ABBREVIATIONS: ER - Estrogen receptor, PR - Progesterone receptor, AOM - Age of Menarche, IDCB - Infiltrating Ductal Carcinoma of Breast, DCB - Ductal Carcinoma of Breast, MCB - Medullary Carcinoma of Breast, ADC - Adenocarcinoma of Carcinoma of the Breast.

INTRODUCTION

Breast cancer remains a major public health problem and is the most common cancer among women worldwide, with nearly one million new cases occurring each year¹. It has been reported that approximately 230,480 new cases of invasive breast

cancer and 39,520 breast cancer deaths occurred among US women in 2011². The age-standardized incidence rate for breast cancer in India is 22.9 per 100,000, one-third that of Western countries and the mortality rates are considerably higher³.

After the discovery of an association between stomach cancer and blood type A by Arid and Ben-



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tall in 1953, there have been several studies on possible relationship of blood types to certain diseases⁴. The ABO blood group distribution varies in different geographical and ethnic groups^{5,6}. ABO blood group genes are mapped at 9q34.2 region in which genetic alteration is common in many cancers. Thus, blood group antigen expression may be affected by genetic change of tumor. A correlation of blood group antigen expression in tumor with metastasis and prognosis has been reported for various human malignancies, such as, colon, breast and prostate cancer as the blood group carbohydrates expressed on cell surface of metastatic cancer cells function as cell adhesion molecules. The loss or presence of blood group antigens can increase cellular motility or facilitate the interaction between tumor cells and endothelial cells of distant organs⁷⁻¹⁰. Previous studies suggested a possible association between ABO blood group and risk of certain malignancies¹, including an increased risk of breast cancer. There is ample evidence that the ABO blood group system can play a role in the etiology of diseases. However, those findings are inconsistent and contradictory in relation to breast cancer.

The relationship with blood groups and incidence, clinicopathologic parameter and prognosis had been studied in many cancers such as esophagus, cardiac, gastric, lung, laryngeal, hypopharyngeal, salivary gland, gynecologic, colorectal, pancreatic, bone, urinary bladder, ureter, renal, breast, prostate, testicular tumors and uveal melanoma¹²⁻²⁶. This study encompasses epidemiology of breast cancer patients in north-eastern Uttar Pradesh region, the distribution of ABO blood groups in breast cancer patients and compare with different clinical parameters.

PATIENTS AND METHODS

Study Population

The demographic, clinical details, ABO blood type and pathological status of breast cancer patients were collected from the Surgical Unit of Department of General Surgery, Sir Sunderlal Hospital, Banaras Hindu University, Varanasi (India). A total of 187 breast cancer patients and 209 controls were assessed for the association with ABO blood groups.

Sample Collection

Blood samples were collected from 187 women with breast cancer during their preoperative control and follow-up, following mastectomy, in Sir Sunderlal Hospital, Banaras Hindu University, Varanasi (India). These patients had similar demographic, clinical,

surgical, immunohistochemical, laboratory, and follow up data. Factors like clinical/surgical findings, blood group and histological/ immunohistochemical findings (including type of cancer, degree of malignancy, and hormone receptor status), were investigated. Two hundred nine healthy controls were collected from blood bank to allow statistical analysis. This control group is a representative group at national level in regard to the ABO blood group system and Rh status distribution.

Statistical Analysis

The SPSS version 16.0 statistical software (Statistical Package for Social Sciences, SPSS version 16.0, Chicago, IL, USA) was used for the statistical analysis of the data. Demographic data of the patients were demonstrated as a number, percentage and mean value. The blood group frequencies were compared using Chi-square test. The ABO blood group was also compared with different clinical parameters. $p < 0.05$ was deemed as the statistically significant.

RESULTS

Demographic Data

The distribution of characteristics of breast cancer patients and control has been summarized in Table 1. Mean age of breast cancer patients was 47.04 years (range 21–75 yrs). Out of total 187 breast cancer patients, 34.2% belongs to the category of age more than 50 years. On the other hand, control group participants were of age group less than 35 years. Age of menarche (AOM) of 81.3% cases belong to more than 12 age group. The most common type of breast cancer was Infiltrating Ductal Carcinoma of Breast (IDCB) (n = 86), followed by Ductal Carcinoma of Breast (DCB) (n = 85), Adenocarcinoma of Carcinoma of the breast (ADC) (n= 14) and Medullary Carcinoma of Breast (MCB) (n = 2). 33.2% of breast cancer patients were of stage II. 21.4% and 26.7% of patients were of stage IIIA and IIIB, respectively. Most of the breast cancer patients were of grade 2 (69.5%) differentiation followed by grade 3 (25.1%) and grade 1 (5.3%). Of all 187 patients of the study, only 99 patients had known receptor status. Out of 99 breast cancer patients, 27 were progesterone receptors positive (PR +), 28 estrogen receptors positive (ER +) and 67 patients were Her-2-neu positive (Her-2-neu +). Out of 99 breast cancer cases whose receptor status was known, 24.2% were triple negative cancer in which all the receptor (ER, PR and Her-2-neu) status was absent. 55.6% cases of breast cancer were present in left side.

TABLE 1. Distribution of characteristics of breast cancer and control group.

S. No	Variable	Breast Cancer N = 187 (%)	Control N = 209 (%)
1.	Age Group		
	Less than 35	35 (18.7)	203 (97.1)
	36-50	88 (47.1)	6 (2.9)
	More than 50	64 (34.2)	0
2.	Gender		
	Male	2 (1.1)	0
	Female	185 (98.9)	209
3.	AOM		
	Less than 12	35 (18.7)	–
	More than 12	152 (81.3)	
4.	Menopausal Status		
	Premenopausal	76 (40.6)	–
	Postmenopausal	111 (59.4)	
5.	HPE		
	IDCB	86 (46%)	–
	DCB	85 (45.5%)	
	MCB	2 (1.1%)	
	ADC	14 (7.5%)	
6.	Side		
	Left	104 (55.6%)	–
	Right	83 (44.4%)	
7.	Grade		
	G1	10 (5.3%)	–
	G2	2130 (69.5%)	
	G3	47 (25.1)	
8.	Stage		
	IIA	32 (17.1)	–
	IIB	62 (33.2)	
	IIIA	40 (21.4)	
	IIIB	50 (26.7)	
	IV	3 (1.6)	
9.	ER		
	Positive	27 (27.3)	–
	Negative	72 (72.7)	
10.	PR		
	Positive	28 (28.6)	–
	Negative	70 (71.4)	
11.	Her-2-Neu		
	Positive	67 (67.7)	–
	Negative	32 (32.3)	
12.	Triple Negative		
	Yes	24 (24.2)	–
	No	75 (75.8)	

Distribution of ABO blood group type among the groups

The frequency of ABO blood group types of 187 breast cancer patients (2 males and 185 females) and 209 control individuals is given in Table 2. The highest frequency of blood group B (40.6%), followed by blood group O (30.5%), A (22.5%) and AB (6.4%) was observed in breast cancer patients. In control group, high frequency of blood group O (40.2%), followed by B (38.3%), A (13.9%) and AB (7.6%) was seen. But the difference between the groups was not statistically significant. The prevalence

of Rh positive is higher (94.7 %) in both the groups i.e. breast cancer and control (Table 3). The distribution of Rh factor among cases and controls did not differ significantly. In this study, we could not find any significant relationship according to blood types with breast cancer group.

Association of ABO blood group with different variables has been given in Table 4. No significant difference was observed on comparing the ABO blood group type in breast cancer patients with different clinical variables. On associating the ABO blood group with age of the breast cancer group, B group was higher in the



TABLE 2. Prevalence of ABO blood group and Rh type among Breast Cancer and Control

S. No	Variable	Breast Cancer N = 187 (%)	Control N = 209 (%)	p-value
1.	Blood Group			0.068
	A	42 (22.5)	29 (13.9)	
	B	76 (40.6)	80 (38.3)	
	O	57 (30.5)	85 (40.7)	
	AB	12 (6.4)	15 (7.1)	
	Total	187	209	
2.	Rh Factor			0.573
	Positive	177 (94.7%)	198 (94.7)	
	Negative	10 (5.3%)	11 (5.3)	
	Total	187	209	

age group 36-50 years, but the difference was not statistically significant. Similarly, blood group B (n=53; 69.7%) was found to be higher in grade II differentiation of breast cancer, but the difference was not significant. The frequency of IDCB (47.4%) and DCB (46.1%) was moderately higher in blood group B ($p>0.05$). Moreover, we did not find any association of blood group with any of the receptor status. Blood group type B was comparatively higher (28.2%) in triple negative breast cancer patients, though no significant association was observed between ABO blood type and triple negative breast cancer patients ($p>0.05$).

DISCUSSION

The ABO blood type, an easily accessible factor in the genetic makeup of the patient, has been linked to many cancers. In the present study, we look at the association of ABO blood groups with breast cancer patients in North-Eastern Uttar Pradesh region. The findings of our study do not support an association between the blood group ABO and risk of breast cancer. No significant associations

were observed between ABO type and breast cancer subtype, histopathological type, hormone status type (ER, PR, Her-2-neu).

The overall distribution of ABO blood groups was B>O>A>AB reported in this study, consistent with other North Indian studies^{27,28}. In our patients, we did not find any significant association with blood types. A recent study examined the association between ABO blood group and incidence of ovarian cancer over 10 years among 49,153 women in the Nurses’ Health Study (NHS) and suggested a possible association between the B blood group antigen and increased risk of ovarian cancer²⁹. Meo et al³⁰ suggested that the risk of breast cancer is high for ‘A’ blood group and ‘Rhesus +ve’.

Previous findings from the research were different from this study although some showed consistent results. There was no association between blood group and breast cancer as stated in one study; while in another study it was found to be correlated with blood group A as opposed to AB^{31,32}. In this study, blood group type B was found to be borderline significant with increased incidence of breast cancer. Contradictory reports are available about the association of blood group with breast

TABLE 3. Blood groups ABO/Rh distribution in Breast Cancer and Control.

Blood Group	Breast Cancer N = 187 (%)	Control N = 209 (%)	Z value
A+	40 (21.4)	29 (13.9)	0.068
B+	75 (40.1)	78 (37.3)	
O+	50 (26.7)	82 (39.2)	
AB+	12 (6.4)	0	
A-	2 (1.1)	2 (1)	
B-	3 (1.6)	4 (1.9)	
O-	5 (2.7)	4 (1.9)	
AB-	0		
Total	187	209	

TABLE 4. Association of ABO blood group with different clinical variables.

Variables	Blood Group				p-value
	A	B	O	AB	
Age Group					
Less than 35	5 (11.9%)	15 (19.7%)	14 (24.6%)	1 (8.3%)	0.704
36-50	21 (50%)	37 (48.7%)	24 (42.1%)	6 (50%)	
More than 50	16 (38.1)	24 (31.6%)	19 (33.3%)	5 (41.7%)	
Gender					
Female	42	75 (98.7%)	56 (98.2%)	12	0.830
Male	0	1 (1.3%)	1 (1.8%)	0	
AOM					
Less than 12	9 (21.4%)	17 (22.4%)	9 (15.8%)	0	0.267
More than 12	33 (78.6%)	59 (77.6%)	48 (84.2%)	12	
Menopausal Status					
Premenopausal	13 (31%)	32 (42.1%)	26 (45.6%)	5 (41.7%)	0.514
Postmenopausal	29 (69%)	44 (57.9%)	31 (54.4%)	7 (58.3%)	
Side					
Left	25 (59.5%)	39 (51.3%)	32 (56.1)	8 (66.7%)	0.699
Right	17 (40.5%)	37 (48.7%)	25 (43.9%)	4 (33.3%)	
Grade					
G1	2 (4.8%)	2 (2.6%)	3 (5.3%)	3 (25%)	0.099
G2	29 (69%)	53 (69.7%)	41 (71.9%)	7 (58.3%)	
G3	11 (26.2%)	21 (27.6%)	13 (22.8%)	2 (16.7%)	
HPE					
IDCB	23 (54.8)	36 (47.4%)	24 (42.1%)	3 (25%)	0.754
DCB	16 (38.1)	35 (46.1%)	26 (45.6%)	8 (66.7%)	
MCB	0	1 (1.3%)	1 (1.8%)	0	
ADC	3 (7.1%)	4 (5.3%)	6 (10.5%)	1 (8.3%)	
Stage					
IIA	7 (16.7%)	15 (19.7%)	10 (17.5%)	0	0.162
IIB	16 (38.1%)	19 (25%)	24 (42.1%)	3 (25%)	
IIIA	10 (23.8)	19 (25%)	9 (15.8%)	2 (16.7%)	
IIIB	8 (19)	23 (30.3%)	12 (21.1%)	7 (58.3%)	
IV	1 (2.4)	0	2 (3.5%)	0	
Rh Factor					
Positive	40 (95.2%)	73 (96.1%)	52 (91.2%)	12 (100%)	0.508
Negative	2 (4.8%)	3 (3.9%)	5 (8.8%)	0	
ER					
Positive	6 (27.3%)	10 (25.6%)	10 (30.3%)	1 (20%)	0.953
Negative	16 (72.7%)	29 (74.4%)	23 (69.7%)	4 (80%)	
PR					
Positive	5 (22.7%)	12 (30.8%)	10 (30.3%)	1 (20%)	0.876
Negative	17 (77.3%)	27 (69.2%)	23 (69.7%)	4 (80%)	
Her-2-neu					
Positive	17 (77.3%)	25 (64.1%)	21 (63.6%)	4 (80%)	0.626
Negative	5 (22.7%)	14 (35.9%)	12 (36.4%)	1 (20%)	
Triple Negative					
Yes	4 (18.2%)	11 (28.2%)	9 (27.3%)	0	0.468
No	18 (81.8%)	28 (71.8%)	24 (72.7%)	5 (100%)	

cancer; as increased B group or A group in breast cancer patients has been reported. Many previous studies have reported an association between ABO blood group and the risk of various cancers. Another study using the same two cohorts reported an association between ABO blood type and the risk of developing pancreatic cancer ($p = .004$; log-rank test)³³. High frequency of blood group B (~50%) was seen in genitourinary, liver, pancreatic and gallbladder cancer patients but sample size was small⁶. A meta-analysis was recently carried

out in 14 studies and concluded that the forms of ABO blood have no association with the risk of breast cancer³⁴. A recent research suggests a high association of O blood type with breast carcinoma compared to non-O blood types³⁵.

There was no strong association of breast cancers and blood group in another study, but a higher prevalence occurred in blood group B³⁶. Stamatakis et al³⁷ investigated the correlation between breast cancer in Greek women and ABO blood groups and found that blood group A was



associated with ductal breast cancer (49.6%), in contrast to the other blood groups and particularly to blood group AB (3.6%). Blood group A in our study has been found to be higher in the infiltration of breast ductal carcinoma. Pandey et al³⁸ observed an increased frequency of carcinoma of the gallbladder in blood groups A and AB. Yu et al³⁹ looked at the association of Triple Negative Breast cancer patients with ABO blood type/Rh factors and they failed to demonstrate an association between ABO blood type/Rh factor. Similarly, our results also found no significant correlation of ABO blood group with triple negative breast cancer patients. Moreover, we did not find any association between the Rh factor and the risk of breast cancer. Other studies also reported inconsistent results between Rh factor and breast cancer risk³⁷. Ronco et al⁴⁰ showed a high risk of breast cancer, while Stamatakis et al³⁷ and Dede et al⁴¹ did not observed such correlation.

Results of this study showed that the type, age, stage, and hormonal status of the breast cancer showed no significant associations with ABO blood group. Similar to our results, Akin and Altundag⁴² did not identify significant associations between ABO and Rh blood type with patient's age, tumor grade, stage, hormonal status and distant metastasis.

ABO blood group genes are map at 9q in which the genetic alteration is common in many cancers⁴³. Thus, ABO blood group antigen expression may be affected by the genetic change of tumors⁴⁴. On the other hand, it is possible the observed associations are not due to the blood group antigens themselves, but to the effects of genes closely associated with them. Therefore, the contrasting results of ABO blood group and breast cancer may be because of these genetic changes. The study has some limitations also. The sample size in this study was small, since it is a case-control, hospital-based study that limits our conclusion strength.

CONCLUSIONS

The prevalence of ABO blood group in breast cancer patients were B>O>A>AB. Moreover, the study showed no significant association of ABO blood groups and Rh factor with breast cancer. Further studies on blood group antigens in larger series are needed to elucidate the relationship between blood group antigens and breast cancer. However, further studies with larger number of patients are needed to clearly establish the role of ABO/Rh blood groups as a prognostic factor in breast cancer patients.

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ETHICAL APPROVAL:

The study was approved by the Institutional Ethical Committee of Institute of Medical Sciences, Banaras Hindu University .

INFORMED CONSENT:

Written informed consent was obtained from all individual participants included in the study.

CONFLICT OF INTEREST:

Authors declare that they have no conflict of interest

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