

# Association of ABO Blood Group and Risk of Breast Cancer

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## Abstract

ABO blood type has been observed in previous studies to be associated with the risk of certain malignancies, including pancreatic and gastric cancer. Our aim is to explore the possible relationships between blood groups and characteristics of patients and whether it is associated with the risk of breast cancer. Our study consisted of 160 breast cancer patients with serologically confirmed ABO blood group. A group of 92 healthy blood donors was identified as a control group. Overall distribution of ABO blood groups was comparable between patients (53.1% A, 21.8% O, 17.5% B and 7.5% AB) and controls (39.1% A, 32.6% O, 18.4% B and 9.7% AB). There were no significant differences in clinicopathologic characteristics among patients with different ABO blood groups. We found that patients with A blood group was positively associated with the risk of breast cancer (adjusted Odds Ratio=2.13, 95% Confidence Interval=1.04-2.96, P=0.03). We conclude that A blood type was associated with increased the risk of breast cancer and it might increase the probability to generate high-risk individuals if further studies confirm the present preliminary findings.

**Keywords:** ABO; Breast cancer; Risk

## Introduction

A high number of breast cancer cases are diagnosed every year [1]. Family history of breast cancer, age of menarche, duration of lactation, parity, age of menopause, diet and hormonal levels are known risk factors for the development of breast cancer [2,3]. One of the major antigens in humans is the blood group antigens that are present on the surface of red blood cells and different epithelial cells and alteration of these blood group antigens is associated with cancer [4,5]. An association between the ABO blood group and cancer risk was reported in an old previous study, where blood group A was associated with increased risk of stomach cancer [6]. Other recent studies have reported the association between blood groups O and A individuals with increased incidence of duodenal ulcers and gastric carcinoma [7,8] as well as, the association of B group type and pancreatic cancer, Hodgkin's lymphomas and cardiac cancer [9-11]. Therefore, blood group antigens on the surface of cancer cells can be used as useful prognostic and diagnostic markers in different types of human cancers [12,13]. Blood group A is associated with increased risk of various tumors, including neurologic tumors, salivary gland, colon, uterus, ovary, pancreas, kidney, bladder and cervix [14]. O blood group is also involved in skin cancer and melanoma [15]. The ABO gene on chromosome 9q34 encodes glycosyltransferases that catalyze the transfer of nucleotide donor sugars to the H antigen to form the ABO blood group antigens [16].

Numerous reports have documented a relation between blood types and breast cancer incidence and prognosis. However other studies have not found any relation between susceptibility to cancer breast. The association between blood group antigen expression and prognostic factors among breast cancer patients has been suggested by previous studies [17,18]. The A antigen was associated with increased risk of developing invasive ductal carcinoma in Greek women [19]. However, the evidence of an association between blood type and breast cancer is inconsistent as some studies found no association between blood group and breast cancer risk [20-22]. So our aim is to evaluate the possible relationships between blood groups and risk of breast cancer.

Blood samples were collected from 160 women with breast cancer during their preoperative control and follow-up, following mastectomy, in Mansoura University Hospital. The data of age, gender, ABO blood

group type of breast cancer patients were collected. The control sample has collected from the 92 healthy female blood donors with no history of cardiovascular disease, cancer, chronic degenerative neurologic disease, chronic obstructive pulmonary disease or hepatitis. Gel cards (Diamed AG, Switzerland) were used for ABO typing. The following information was obtained for the purpose of the present analysis: age, family history of breast cancer, menopausal status, tumor size, lymph node number, tumor grade, estrogen receptor status (ER), progesterone receptor status (PR). The study was approved by the Institutional Review Board at the Mansoura University Hospital.

## Statistical Analysis

Analyses were performed using SPSS (statistical package for social science) program (SPSS, Inc, Chicago, IL) version 16. Frequency or median values were given as descriptive statistics. Chi-square test was used to determine differences in proportions. Mann-Whitney U test was used to compare two independent groups in terms of metric variables. Odds ratios (ORs) were calculated using unconditional logistic regression, and were given within 95% confidence intervals (CI). P value of less than 0.05 was considered as statistically significant.

## Results

Table 1 shows that the mean age at diagnosis for the 160 female patients with breast cancer was 62.0 ± 4 years and 89 cases (55.6%) were postmenopausal at diagnosis. Majority of patients were ER positive (56.2%), and PR positive (75.0%). Thirty cases (48.1%) were early stage

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of tumor, being stage I-II but 51.8% of patients were in stage III. Of patients studied 38.1% did not show lymph nodes involvement and 61.8% had lymph nodes involvement. The tumor size was less than 3 cm in 45.6% of patients and more than 3 cm in 54.3% percent of patients.

In Table 2, the distribution of ABO blood groups in patients and control groups is presented. No positive correlation between age, menopausal status, nodal status, size of the tumor, stage of malignancy or presence of progesterone/estrogen receptors and ABO blood groups was found ( $P>0.05$ ).

Table 3 shows that the frequency of ABO groups of 64 breast cancer patients and healthy control subjects were shown in Table 3. In breast cancer, high frequency of the blood group A (53.1%) followed by O (21.8%), B (17.5%) and AB (7.5%), in control group A (39.1%) followed by O (32.6%), B (18.4%) and AB (9.7%) was seen. The frequency of Cancer incidence was significantly high in blood group A, while Blood Group AB had lower incidence of cancer as compared to controlled

| Characteristic        | %        | No. |
|-----------------------|----------|-----|
| <b>Age</b>            | 62.0 ± 4 |     |
| <b>Family history</b> | 23.7     | 38  |
| <b>Postmenopausal</b> | 55.6     | 89  |
| <b>Lymph node</b>     |          |     |
| Positive              | 61.8     | 99  |
| Negative              | 38.1     | 61  |
| <b>Tumor size</b>     |          |     |
| >3                    | 54.3     | 87  |
| <3                    | 45.6     | 73  |
| <b>Tumor grade</b>    |          |     |
| I&II                  | 48.1     | 77  |
| III                   | 51.8     | 83  |
| <b>ER status</b>      |          |     |
| Positive              | 56.2     | 90  |
| Negative              | 43.7     | 70  |
| <b>PR status</b>      |          |     |
| Positive              | 75.0     | 120 |
| Negative              | 25.0     | 40  |

Table 1: Baseline characteristics of patients with Breast cancer.

| Blood group                   | A         | B         | O         | AB       | P    |
|-------------------------------|-----------|-----------|-----------|----------|------|
| NO.                           | 85        | 28        | 35        | 12       |      |
| <b>Age</b>                    |           |           |           |          |      |
| >60                           | 44(51.7%) | 15(53.5%) | 19(54.2%) | 7(58.3%) | 0.24 |
| <60                           | 41(48.2%) | 13(46.4%) | 16(45.7%) | 5(41.6%) |      |
| <b>Family history</b>         |           |           |           |          |      |
| Yes                           | 20(23.5%) | 6(21.4%)  | 9(25.7%)  | 3(25.0%) | 0.45 |
| No                            | 70(76.4%) | 22(78.5%) | 26(74.2%) | 9(75.0%) |      |
| <b>Menopausal status</b>      |           |           |           |          |      |
| Premenopausal                 | 36(42.3%) | 13(46.4%) | 17(48.5%) | 5(41.6%) | 0.16 |
| Postmenopausal                | 49(57.6%) | 15(53.5%) | 18(51.4%) | 7(58.3%) |      |
| <b>Lymph node involvement</b> |           |           |           |          |      |
| Yes                           | 52(61.1%) | 17(60.7%) | 22(62.8%) | 8(66.6%) | 0.37 |
| No                            | 33(38.8%) | 11(39.2%) | 13(37.1%) | 2(33.3%) |      |
| <b>Tumor size</b>             |           |           |           |          |      |
| >3                            | 47(55.2%) | 15(53.5%) | 18(51.4%) | 7(58.3%) | 0.30 |
| <3                            | 38(44.7%) | 13(46.4%) | 17(48.5%) | 5(41.6%) |      |
| <b>Tumor stage</b>            |           |           |           |          |      |
| I&II                          | 42(49.4%) | 13(53.5%) | 17(48.5%) | 5(41.6%) | 0.19 |
| III                           | 43(50.5%) | 15(46.4%) | 18(51.4%) | 7(58.3%) |      |
| <b>ER status</b>              |           |           |           |          |      |
| Positive                      | 45(52.9%) | 17(60.7%) | 21(60.0%) | 7(58.3%) | 0.32 |
| Negative                      | 40(47.0%) | 11(39.2%) | 14(40.0%) | 5(41.6%) |      |
| <b>PR status</b>              |           |           |           |          |      |
| Positive                      | 62(72.9)  | 21(75.0%) | 28(80.0%) | 9(75.0%) | 0.28 |
| Negative                      | 23(27.0%) | 7(25.2%)  | 7(20.0%)  | 3(25.0%) |      |

Table 2: Characterization of breast cancer patients by blood group.

subjects. The calculation of the risk that inheritance of a specific phenotype may be associated with breast cancer is laid out in Table 3. Women with blood type A appeared to be significantly associated with breast cancer (odds ratio (OR)=2.13, 95% confidence interval (CI) 1.04-2.96,  $P=0.03$ ). However, patients with other phenotypes of the ABO blood group system were not associated with the risk of breast cancer [B (OR=0.93, 95% CI 0.48-1.82) O (OR=0.57, 95% CI 0.32-1.02) and AB (OR=0.74, 95% CI 0.30-1.84)].

## Discussion

The role of inheritance in breast tumor development has been clearly established, especially after the description of many genes [19]. The association between ABO blood group antigens and malignancy was made a long time ago, yet the role of the ABO blood group in cancer risk remains controversial [23].

In our study, high frequency of blood group A and low frequency of AB blood type had been observed in breast cancer patients. This was also reported by previous studies [24,25]. No positive correlation between age, family history, size of tumor, stage of malignancy, nodal metastases or presence of progesterone/estrogen receptors and ABO blood groups system, was found. This was also observed by Stamatakos et al., who found no correlation between the patient's clinical characteristics and blood [19]. But Amini et al. found that there was a significant relationship between the size of tumor, axillary lymph nodes involvement and ABO blood groups system [26].

The association of breast cancer and the blood type had different degrees in various studies. Our study showed that the presence of A-Antigen is related to the risk of developing breast cancer. On the other hand, other studies observed no association with ABO blood group [27-29]. Results achieved from a study performed by Manzarovu et al. reported no relation between the blood groups and breast cancer [30]. While another study reported a positive association between type O and breast cancer risks [31]. Other studies observed positive associations with type A or B among women with a family history of breast cancer [32]. Other studies support the significant associations

|           | Patients (n=160) |        | Control (n=92) |        | 95% CI    | Odds Ratio | P    |
|-----------|------------------|--------|----------------|--------|-----------|------------|------|
|           | NO.              | (%)    | NO.            | %      |           |            |      |
| <b>A</b>  | 85               | (53.1) | 36             | (39.1) | 1.04-2.96 | 2.13       | 0.03 |
| <b>B</b>  | 28               | (17.5) | 17             | (18.4) | 0.48-1.82 | 0.93       | 0.84 |
| <b>O</b>  | 35               | (21.8) | 30             | (32.6) | 0.32-1.02 | 0.57       | 0.06 |
| <b>AB</b> | 12               | (7.5)  | 9              | (9.7)  | 0.30-1.84 | 0.74       | 0.52 |

**Table 3:** Association of ABO blood group with breast cancer risk.

between the blood type and breast cancer risk [19,33-35]. Previous studies reported positive associations between type A and risk of breast carcinoma [36,37]. Moreover, a study performed By Guleria et al. showed that group A was significantly associated with breast cancer when compared to control [24]. Different studies suggested that blood type A group was a risk factor for development of cancer due to observed over-representation rates of blood type A group compared to control populations [38]. The blood groups may have a connection with other diseases. Blood type A had been proved to be a risk factor for stomach cancer [6] and blood type O may protect people from pancreas cancer [8]. The possible reasons for the heterogeneity across studies include the use of retrospective cases, hospital-based controls, or other differences in population characteristics.

Blood group antigens are expressed on the surface of red blood cells and malignant breast ductal cells [16,39]. Alterations in ABO antigen expression on the surface of malignant cells have been seen for a variety of tumor types, including breast cancer [40,41]. The expression of blood group A has been reported to increase resistance to apoptosis and facilitate escape from immune control in rat colon carcinoma cells [42]. In addition, modified expression of blood group antigens on the surface of cancer cells may also alter cell motility with important implications for malignant progression [43].

Previous studies reported that blood group A may influence the systemic inflammatory response as they found associations between the genotype of the A blood group antigen and circulating levels of soluble intercellular adhesion molecule 1, E-selection and P Selection suggesting that [44,45]. These may resulted in the increased incidence of breast cancer in blood type A cases. In conclusion, in our study the people with blood type A may have a higher risk of developing breast cancer than other blood groups among patients. However, further prospective studies are necessary to define the mechanisms by which ABO blood type may influence the breast cancer risk.

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