

ORIGINAL ARTICLE

Blood groups type linked to breast cancer in a Greek cohort of women - a case control study

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Summary

Purpose: To investigate the possible association between ABO blood types and breast cancer in Greek women.

Methods: 202 female patients with breast cancer and 139 healthy women as control group were examined clinically and with breast ultrasound and those older than 40 years, also with bilateral digital mammography.

Results: In the case-group, 26.7% had blood group O, 5.5% had blood group B, 61.9% had blood group A and 5.9% had blood group AB. In the control-group, 47.5% had blood group O, 13.7% had blood group B, 31.6% had blood group A and 7.2% had blood group AB. Usage of diagrams with

the percentages of frequency, the average control, Pearson, Spearman, Student's t-tests analyzed with SPSS statistical software showed a significant correlation between breast cancer and blood group A ($p < 0.01$).

Conclusions: Although in the literature it is controversial whether ABO/Rh blood groups have association with breast cancer, the results of our study show a significant correlation between breast cancer and blood group A.

Key words: breast cancer, blood group, ABO, malignancy, breast cancer risk factors

Introduction

ABO blood group system was discovered by Karl Landsteiner in 1900. The blood group is determined by the presence of antigens on the surface of red blood cells and their corresponding plasma antibodies. The Rhesus system (Rh) consists of five subcategories of antigens: D, C, c, E, e. The D antigen determines whether the blood group is Rh positive (+) or Rh negative (-). When someone carries the D antigen on the surface of the red blood cells, is characterized as Rh (+). In contrast, the absence of D antigen is characterized as Rh (-). Each person belongs to one of the eight

blood groups: O-, O+, B-, B+, A-, A+, AB- or AB+. The most frequent blood group is O+ and the rarest AB-. During the last decades, several studies have shown a possible association between ABO blood type and the risk of some malignancies [1-9]. However, because of the controversial results from previous studies, the relationship between ABO blood groups and breast cancer remains unclear [10]. According to the above, the aim of this study was to search for possible relationship between blood groups and breast cancer in a cohort of our patients.

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Methods

Study design

This research was a case-control study. Between 2016 and 2019 we collected the data of the patients who consulted in breast clinics and 360 patients were enrolled in the study whereas 19 had incomplete information and were excluded. All of the patients were in two hospitals: Alexandroupolis University Hospital and Rea Hospital in Athens. The 341 participants included in the study were divided in two groups. The case-group included 202 women with breast cancer pathologically confirmed after breast surgical procedure. The control group included 139 women without breast cancer and who were examined with clinical examination, breast ultrasound and/or bilateral digital mammography in the breast clinics. The two different groups were evaluated in the same period of time. All women participated to the study after signing informed consent.

Statistics

The obtained information regarding ABO-blood group and the presence or absence of breast cancer was analyzed using IBM SPSS 20 software. The percentages, as well as the frequency of each blood group among the case and control population are given as descriptive statistics. Chi square test and crosstabulation were useful in order to find any differences between proportions and the p value. P value lower than 0.05 was considered statistical significant.

Results

Our series consisted of 341 women, of whom 202 were patients with breast cancer (59.2%) and 139 (40.8%) healthy controls (Table 1).

In the case-group, 54 women (26.7%) had blood group O, 11 (5.5%) had blood group B, 125 (61.9%) had blood group A and 12 (5.9%) had blood group AB. In the control group, 66 women (47.5%) had blood group O, 19 (13.7%) had blood group B, 44

(31.6%) had blood group A and 10 (7.2%) had blood group AB (Table 2).

Tables 2 and 3 show the crosstabulation and χ^2 between the two populations of the sample and the blood groups. Patients with a blood group A seemed to excel, which was also confirmed by the statistical analysis. The χ^2 method and Pearson analysis (Table 4) showed that there is a significant correlation between breast cancer patients and blood group A (Table 5, $p < 0.01$), revealing that women with this blood group had higher risk for breast cancer compared with women having O, B and AB blood group.

Discussion

It is widely accepted that genetic factors play an important role in the development of cancer. Especially, after the description of BRCA1 and BRCA2 genes, the role of inheritance in breast tumorigenesis has been well established [10,11].

The majority of the larger studies [9,12-15] support the view that ABO-blood group has no association with breast cancer. Nevertheless, a recent Greek study found a possible relation between ductal breast cancer and blood group A, in contrast with the other blood groups [11].

Moreover, the authors of this study concluded that blood group A has the worst prognosis of all. Furthermore, a study of Meo et al in 2017, which is the most recent, concluded that women with blood type A and Rh(+) have higher risk of breast cancer, while women with AB (-) have smaller risk [16].

Furthermore, two other studies reported a relationship between blood group A [17] or blood group B [18] and high risk of familial breast cancer. In addition, some smaller studies tended to report significant associations [19-21]. Only one study found a positive association between O blood group and

Table 1. Case/control frequency and percentages

Case/control groups	Frequency	Percent	Valid percent	Cumulative percent
0 (case group)	202	59.2	59.2	59.2
1 (control group)	139	40.8	40.8	100.0
Total	341	100.0	100.0	

Table 2. Crosstabulations

		Blood types				Total
		O	B	A	AB	
Case Control	0	54	11	125	12	202
	1	66	19	44	10	139
Total		120	30	169	22	341

Table 3. Chi square

Correlations		Patients	Blood type
Spearman's rho			
Patients	Correlation coefficient	1,000	-0,236**
	Sig. (2-tailed)	.	0,000
	N	341	341
	Bootstrap ^b		
	Bias	0,000	0,000
	Std. Error	0,000	0,000
	95% Confidence interval		
	Lower	1,000	-0,236
	Upper	1,000	-0,236
Blood type	Correlation coefficient	-0,236**	1,000
	Sig. (2-tailed)	0,000	.
	N	341	341
	Bootstrap ^b		
	Bias	0,000	0,000
	Std. Error	0,000	0,000
	95% Confidence interval		
	Lower	-0,236	1,000
	Upper	-0,236	1,000

** Correlation is significant at the 0.01 level (2-tailed). ^bUnless otherwise noted, bootstrap results are based on 1000 stratified bootstrap samples

Table 4. Pearson's correlation

Correlations		Patients	Blood type	
Patients				
	Pearson's correlation	1	-0,235	
	Sig. (2-tailed)		0,000	
	Sum of Squares and Cross-products	82,340	-39,909	
	Covariance	0,242	-0,117	
	N	341	341	
	Bootstrap ^b			
	Bias	0	0,000	
	Std. error	0	0,000	
	95% confidence interval			
	Lower	1	-0,235	
	Upper	1	-0,235	
	Blood type	Pearson's correlation	-0,235	1
		Sig. (2-tailed)	0,000	
Sum of Squares and Cross-products		-39,909	351,636	
Covariance		-0,117	1,034	
N		341	341	
Bootstrap ^b				
Bias		0,000	0	
Std. error		0,000	0	
95% confidence interval				
Lower		-0,235	1	
Upper		-0,235	1	

^bUnless otherwise noted, bootstrap results are based on 1000 stratified bootstrap samples

Table 5. Descriptive statistics

		Statistic	Bootstrap ^a			
			Bias	Std. error	95% confidence interval	
					Lower	Upper
Patients	Mean	0.41	0.00	0.00	0.41	0.41
	Std. Deviation	0.492	0.00	0.00	0.492	0.492
	N	0.341	0.00	0.00	0.341	0.341
Blood group	Mean	1.27	0.00	0.00	1.27	1.27
	Std. deviation	1.017	0.00	0.00	1.017	1.017
	N	341	0	0	341	341

^aUnless otherwise noted, bootstrap results are based on 1000 stratified bootstrap samples

breast cancer [22]. As for the association between breast cancer survival and ABO blood group, the results are also controversial. One study report absence of association [23], whereas two other studies reported a poorer survival among cases with blood group B or AB [24] or any non-O blood group [25]. The heterogeneity between studies is due to the small number of cases included in the analyses.

Also, a systematic review and meta-analysis which was conducted in 2014 reported the same conclusion regarding blood group A [26] and specifically, found that blood group A is associated with 12% risk of breast cancer. In contrast to the previous meta-analysis which found a borderline association [27], this meta-analysis had more statistical power because it found significant association between blood group A and breast cancer.

Several mechanisms might explain the associations observed. As an example, ABO gene on chromosome 9q34 encodes glycotransferases that catalyze the transfer of nucleotide donor sugars to the H antigen to form the ABO blood group antigens [9,17,28]. Blood group antigens are expressed on the surface of red blood cells and also on the surface of normal breast ductal cells [29]. Some malignant breast tumors lose ABO antigen expression. Modified expression of blood group antigens on the surface of malignant cells may affect the cancer spread and the initiation modifying the sensitivity

to cell apoptosis and the immune reaction [26,30]. Moreover, blood group antigens may influence the systemic inflammatory response, and it is generally believed that chronic inflammation is linked with cancer development [9], suggesting a possible role of ABO antigens in breast carcinogenesis.

Conclusion

Despite genetic breast cancer related to mutations of BRCA1, BRCA2 and other minor genes constitute 5-10% of all breast cancers, it seems that other genetic factors such as blood group are involved also in inherited cancers. In our series of 341 Greek patients who consulted in the two breast clinics, patients with breast cancer were more frequently (about 2-fold) with blood group A in contrast with patients without breast cancer were group O was the predominant group.

Further studies with larger number of patients are necessary in order to clarify the real role of ABO-blood groups as a risk factor of breast cancer and to explore the mechanisms of the aforementioned association.

Conflict of interests

The authors declare no conflict of interests.

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