ejpmr, 2021,8(8), 72-79.

SJIF Impact Factor 6.222

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

ASSOCIATION OF ABO BLOOD GROUP AND BREAST CANCER IN CASABLANCA

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Article Received on 07/06/2021 **Article Revised on 28/06/2021** **Article Accepted on 18/07/2021**

ABSTRACT

The role of ABO blood group in cancer biology has been intensively studied by several researchers, and it is now widely recognized that ABH antigens are associated with the risk of developing several types of tumors. In order to elucidate this association with breast cancer, our objective is to verify the existence of a relationship between ABO blood groups, pathological data and prognostic factors of breast cancer. This is a retrospective, cross-sectional and monocentric study, carried out by a descriptive reading of the statistics of the ABO phenotypic, clinical and anatomopathological characteristics of the patients with breast cancer, having been followed in the service of Gynecology of the Mohammed VI Center of the University Hospital of Casablanca. The percentages of blood groups found in this sample were compared to the average phenotypic frequencies of 344,954 blood donors listed in 14 Regional Blood Transfusion Centers of Morocco. This study involved 538 cases. The comparison of blood group frequencies between blood donors and patients with breast carcinoma shows that those with groups B and O are respectively the most (15.68% vs 25.8%) and least (46.05% vs 38.3%) affected. Presence of positive correlations between blood type and different histological characteristics of breast tumors: SBR, estrogen receptors, HER2... Despite all the statistical evidence regarding the involvement of the ABO system in human physiology and pathophysiology, the mechanisms by which it may interact with cancer development and progression, are still poorly understood. The findings of this work open new research perspectives to be explored.

KEYWORDS: ABO; Blood group; Breast cancer.

1. INTRODUCTION

Breast cancer is a worldwide malignant disease, affecting more than one million new cases each year. In Morocco, it is the first cancer in women and the third of all recorded cancer cases.[1], [2]

Breast cancer is a malignant process, linked to several risk factors, including family history, age of first menstruation, age of first birth, duration of lactation, parity, age of menopause, diet and hormonal levels.... Its prognosis depends on clinical, histological and biological features.[3]

After the first clinical observations linking ABO polymorphism to diseases, including infections, cardiovascular pathologies and diabetes, the role of ABO blood group in cancer biology has been intensively studied by several investigators, and it is now widely recognized that ABH antigens are associated with the risk of developing several types of tumors.[4],[5]

ABH antigens are complex carbohydrate structures covalently bound to glycoproteins or glycosphingolipids, with important roles in cell recognition, proliferation, adhesion and motility.[6] In addition to their expression on red blood cells, A and B antigens are present on several tissues in the human body, including the surface of ductal cells in the normal breast and are weakly expressed on lobular cells. The expression of ABH antigens is lost or varied on some breast tumors.[7], [8] These advances suggest a possible role of ABO blood group antigens in breast carcinogenesis.

Older studies on blood group and breast cancer risk have generally not reported any association. However, recent studies suggest that there are associations between ABO blood type and specific subtypes of breast cancer that have not been detected in previous studies of all breast cancers.[9], [10]

In light of these contradictions, our objective is the verification of the existence of a relationship between

ABO blood types, pathological data and prognostic factors in breast cancer.

An approval from the Ethics Committee for Biomedical Research of Rabat (CERBR) - Faculty of Sciences Rabat, Mohammed V University, was granted for the realization of this study.

1. MATERIAL AND METHODS

This retrospective, cross-sectional, single-center study, performed by descriptive reading of statistics of ABO phenotypic, clinical and anatomopathological characteristics of the study population of breast cancer patients.

1.1. Study population

The inclusion criteria of this study concern patients operated on for breast cancer in 2016, at the Gynecology Department of the Mohammed VI Centre of the CHU Ibn Rochd of Casablanca, whose surgical parts were studied at the Pathological Anatomy Laboratory of the CHU Ibn Rochd of Casablanca. Clinical information was collected from the patients' files, archived in the Gynecology Department of the Mohammed VI Centre. Medical records that did not contain information about blood grouping were removed from the study. Anatomical pathology data were collected from pathology reports recorded on the computerized system of the laboratory "Kalisil", in the laboratory of Pathological Anatomy.

1.2. Control population of ABO phenotypic distribution

In order to analyze the percentages of blood groups found in our sample, they were compared to the average phenotypic frequencies of 344,954 blood donors listed in 14 Regional Blood Transfusion Centers of Morocco. The individuals in this control group are aged between 18 and 60 years, with a sex ratio of 1:1.[11] The blood donors were treated as a control group representing the general Moroccan population. According to the conditions of recruitment of voluntary blood donors and volunteers, and the requirements of transfusion safety, they are considered healthy.

1.3. Bivariate statistical analysis

The comparison between the frequencies of blood types among patients with breast cancer and those of the blood donor population, as well as the association between blood types and other prognostic factors, was done by the parametric Chi-square test using the Statistical Package for the Social Sciences (SPSS, version 22.0).

For all statistical tests used in this research, a two-tailed value of $p < 0.05$ was considered significant.

2. RESULTS

2.1. Description of the study population

This study involved 538 cases, of which 376 (69.88%) met the inclusion criteria concerning the blood group of each patient confirmed by her blood grouping card, and the malignancy of the tumor confirmed on the conclusion of the last pathology report.

Table 1 shows the clinical and anatomic-pathological characteristics of the study population according to ABO blood types. Data for unavailable characteristics marked "not specified" were counted in the first censuses. These cases were not considered in the statistical analyses of the associations.

The mean age at diagnosis for the study population was 50.39 years, with a minimum age of 19 years and a maximum age of 82 years. The frequency of breast carcinoma ranged from 11% to 16.8% in women aged 40 to 65 years, with a maximum between 40 and 54 years and minimums at young age, less than 30 years, and at old age, more than 70 years.

Non-specific infiltrating carcinoma is the predominant histological type in our series, with a percentage of 69.70%, followed by infiltrating lobular carcinoma with 9.30%, and 21% of the patients are affected by eight other types of carcinomas: ductal in situ, with medullary aspect, mucinous, infiltrating micropapillary, metaplastic of non-specific type, lobular in situ, infiltrating papillary, and with apocrine differentiation (Table 1).

Table 1 shows that tumor size was not specified in 59 patients in the series studied. The mean tumor size was 4.22 cm [0.5 - 19 cm]. 23.35% (74/317) of women had tumors of size T1 (≤2cm), 42.58% (135/317) of size T2 (2<t<5 cm), and 34.07% had tumors of size T3 (≥5 cm) (108/317).

According to the "Scarff Bloom and Richardson (SBR)" grade classification, SBR grade I was present in 16.81% (58/345) of the breast tumors in the study sample, SBR grade II accounted for 39.42% (136/345) and SBR grade III accounted for 43.77% (151/345). 31 patient reports did not provide information on histoprognostic grade (Table I).

Hormone receptor status was not provided for 71 tumors. Estrogen receptor was positive in 73.44% (224/305) of the tumors, whereas progesterone receptor was positive in 57.70% (176/305).

The status of HER2 membrane receptors was not known in 81 patients of the study population. They were overexpressed in 29.84% (77/258) of the tumors, and 37 patients had a labeling score of 2+, corresponding to a doubtful labeling (Table 1).

Table 1: ABO phenotypic, clinical and pathological characteristics of patients.

Features	Blood type				Total
	O	A	B	AB	
Number of patients	144 (38.3 %)	115 (30.6 %)	97 (25.8 %)	20 (5.3 %)	376 (100 %)
Average age (years)	50.43 [19-80]	50.81 [20-78]	50.36 [19-82]	49.94 [29-69]	50.39 [19-82]
Histological type					
Non-specific infiltrating carcinoma	101 (70.1 %)	84 (73 %)	64 (66 %)	13 (65 %)	262 (69.7)
Invasive lobular carcinoma	12 (8.3 %)	11 (9.6 %)	10 (10.3 %)	2 (10 %)	35 (9.3 %)
Ductal carcinoma in situ	6 (4.2 %)	5 (4.3 %)	5 (5.2 %)	2 (10 %)	18 (4.8 %)
Carcinoma with medullary aspect	6 (4.2 %)	3 (2.6 %)	5 (5.2 %)	1 (5 %)	15 (4 %)
Mucinous carcinoma	4 (2.8 %)	4 (3.5 %)	4 (4.1 %)	1 (5 %)	13 (3.5 %)
Invasive micropapillary carcinoma	4 (2.8 %)	3 (2.6 %)	3 (3.1 %)	0 (0 %)	10 (2.7 %)
Metaplastic carcinoma of non-specific type	4 (2.8 %)	2 (1.7 %)	2 (2.1 %)	1 (5 %)	9 (2.4 %)
Lobular carcinoma in situ	3 (2.1 %)	2 (1.7 %)	2 (2.1 %)	0 (0 %)	7 (1.9 %)
Invasive papillary carcinoma	2 (1.4 %)	1 (0.9 %)	1 (1 %)	0 (0 %)	4 (1.1 %)
Carcinoma with apocrine differentiation	2 (1.4 %)	0 (0 %)	1 (1 %)	0 (0 %)	3 (0.8 %)
Tumor size					
Average tumor size (cm)	4.57 [0.5-19]	4.21 [0.6-12]	3.9 [0.6-12.3]	3,25 [1-8.6]	4.22 [0.5-19]
T1 : ≤2 cm	24 (16.7 %)	22 (19.1 %)	23 (23.7 %)	5 (25 %)	74 (19.7 %)
T2 : 2 cm <t<5 cm	51 (35.4 %)	41 (35.7 %)	35 (36.1 %)	8 (40 %)	135 (35.9 %)
T3 : ≥5 cm	49 (34 %)	31 (27.0 %)	25 (25.8 %)	3 (15 %)	108 (28.7 %)
Not specified	20 (13.9 %)	21 (18.3 %)	14 (14.4 %)	4 (20 %)	59 (15.7 %)
Histo-pronostic grade					
SBR I	17 (11.8 %)	24 (20.9 %)	13 (13.4 %)	4 (20 %)	58 (15.4 %)
SBR II	63 (43.8 %)	27 (23.5 %)	36 (37.1 %)	10 (50 %)	136 (36.2 %)
SBR III	53 (36.8 %)	55 (47.8 %)	39 (40.2 %)	4 (20 %)	151 (40.2 %)
Non precise	11 (7.6 %)	9 (7.8 %)	9 (9.3 %)	2 (10 %)	31 (8.2 %)
Estrogen receptor status					
Positive	101 (70.1 %)	63 (54.8 %)	48 (49.5 %)	12 (60 %)	224 (59.6 %)
Negative	24 (16.7 %)	25 (21.7 %)	27 (27.8 %)	5 (25 %)	81 (21.5 %)
Not specified	19 (13.2 %)	27 (23.5 %)	22 (22.7 %)	3 (15 %)	71 (18.9 %)
Status of progesterone receptor					
Positive	72 (50 %)	52 (45.2 %)	43 (44.3 %)	9 (45 %)	176 (46.8 %)
Negative	53 (36.8 %)	36 (31.3 %)	32 (33.0 %)	8 (40 %)	129 (34.3 %)
Not specified	19 (13.2 %)	27 (23.5 %)	22 (22.7 %)	3 (15 %)	71 (18.9 %)
HER 2 status					
Positive	28 (19.4 %)	18 (15.7 %)	29 (29.9 %)	2 (10 %)	77 (20.5 %)
Doubtful	19 (13.2 %)	8 (7 %)	6 (6.2 %)	4 (20 %)	37 (9.8 %)
Negative	76 (52.8 %)	58 (50.4 %)	38 (39.2 %)	9 (45 %)	181 (48.1 %)
Not specified	21 (14.6 %)	31 (27 %)	24 (24.7 %)	5 (25 %)	81 (21.5 %)
Status of lymph node metastases					
Positive	62 (43.1 %)	65 (56.5 %)	40 (41.2 %)	13 (65 %)	180 (47.9 %)
Negative	32 (22.2 %)	13 (11.3 %)	29 (29.9 %)	3 (15 %)	77 (20.5 %)
Not specified	50 (34.7 %)	37 (32.2 %)	28 (28.9 %)	4 (20 %)	119 (31.6 %)
Status of vascular emboli					
Presence	56 (38.9 %)	60 (52.2 %)	34 (35.1 %)	11 (55 %)	161 (42.8 %)
Absence	40 (27.8 %)	25 (21.7 %)	41 (42.3 %)	5 (25 %)	111 (29.5 %)
Not specified	48 (33.3 %)	30 (26.1 %)	22 (22.7 %)	4 (20 %)	104 7.7 %)

The presence of lymph node metastases was mentioned in 70.04% (180/257) of patients. The status of lymph node metastases was not available for 119 patients, because the surgical procedure performed was just a mastectomy or a simple lumpectomy, without lymph node dissection.

Vascular emboli were present in 59.19% (161/272) of tumors. The status of vascular emboli was not mentioned on the report of 104 patients in our sample.

2.2. Bivariate statistical analysis

The bivariate statistical study concerned the analysis of ABO blood group frequencies of patients with breast carcinoma with blood donor blood group frequencies and

prognostic factors for breast cancer. A summary of the results of the analysis is presented in Table 2.

Table 2: Summary of associations between ABO blood type and different prognostic factors.

Features	Blood type				p-value
	O	A	B	AB	
Number of patients (Incidence)	144 (38.3 %)	115 (30.6 %)	97 (25.8 %)	20 (5.3 %)	
Age					
≤ 35 ans	14 (9.7 %)	8 (7 %)	13 (13.4 %)	2 (10 %)	>0.05
35-70 ans	116 (80.6 %)	103 (89.6 %)	80 (82.5 %)	18 (90 %)	
≥ 70 ans	14 (9.7 %)	4 (3.5 %)	4 (4.1 %)	0 (0%)	
Histological type					
Non-specific infiltrating carcinoma	101 (70.1 %)	84 (73 %)	64 (66 %)	13 (65 %)	>0.05
Invasive lobular carcinoma	12 (8.3 %)	11 (9.6 %)	10 (10.3 %)	2 (10 %)	
Ductal carcinoma in situ	6 (4.2 %)	5 (4.3 %)	5 (5.2 %)	2 (10 %)	
Carcinoma with medullary aspect	6 (4.2 %)	3 (2.6 %)	5 (5.2 %)	1 (5 %)	
Mucinous carcinoma	4 (2.8 %)	4 (3.5 %)	4 (4.1 %)	1 (5 %)	
Invasive micropapillary carcinoma	4 (2.8 %)	3 (2.6 %)	3 (3.1 %)	0 (0 %)	
Metaplastic carcinoma of non-specific type	4 (2.8 %)	2 (1.7 %)	2 (2.1 %)	1 (5 %)	
Lobular carcinoma in situ	3 (2.1 %)	2 (1.7 %)	2 (2.1 %)	0 (0 %)	
Invasive papillary carcinoma	2 (1.4 %)	1 (0.9 %)	1 (1 %)	0 (0 %)	
Carcinoma with apocrine differentiation	2 (1.4 %)	0 (0 %)	1 (1 %)	0 (0 %)	
Tumor size					
T1 : ≤2 cm	24 (19.4 %)	22 (23.4 %)	23 (27.7 %)	5 (31.3 %)	>0.05
T2 : 2 cm <t<5 cm	51 (41.1 %)	41 (43.6 %)	35 (42.2 %)	8 (50 %)	
T3 : ≥5 cm	49 (39.5 %)	31 (33 %)	25 (30.1 %)	3 (18.8 %)	
Histo-pronostic grade					
SBR I	17 (12.8 %)	24 (22.6 %)	13 (14.8 %)	4 (22.2 %)	0.011
SBR II	63 (47.4 %)	27 (25.5 %)	36 (40.9 %)	10 (55.6 %)	
SBR III	53 (39.8 %)	55 (51.9 %)	39 (44.3 %)	4 (22.2 %)	
Estrogen receptor status					
Positive	101 (80.8 %)	63 (71.6 %)	48 (64 %)	12 (70.6 %)	0.015
Negative	24 (19.2 %)	25 (28.4 %)	27 (36 %)	5 (29.4 %)	
Status of progesterone receptors					
Positive	72 (57.6 %)	52 (59.1 %)	43 (57.3 %)	9 (52.9 %)	>0.05
Negative	53 (42.4 %)	36 (40.9 %)	32 (42.7 %)	8 (47.1 %)	
HER 2 status					
Positive	28 (26.9 %)	18 (23.7 %)	29 (43.3 %)	2 (18.2 %)	0.04
Negative	76 (73.1 %)	58 (76.3 %)	38 (56.7 %)	9 (81.8 %)	
Status of lymph node metastases					
Positive	62 (66 %)	65 (83.3 %)	40 (58 %)	13 (81.3 %)	0.005
Negative	32 (34 %)	13 (16.7 %)	29 (42 %)	3 (18.8 %)	
Status of vascular emboli					
Presence	56 (58.3 %)	60 (70.6 %)	34 (45.3 %)	11 (68.8 %)	0.011
Absence	40 (41.7 %)	25 (29.4 %)	41 (54.7 %)	5 (31.3 %)	

2.3. Association between ABO blood types and incidence of breast carcinoma

The frequencies of ABO blood types of patients with breast carcinoma were compared with the frequencies of blood types of blood donors representing the general population.

Table 3: ABO blood group distribution among women with breast carcinoma and blood donors.

Blood type	Percentage of patients with breast carcinoma (n=376)		Percentage of blood donors (n=344954)(sex-ratio= 1:1)
O	38,3%	<	46,05%
A	30,6%		33,89%
B	25,8%	>	15,68%
AB	5,3%		4,33%
X^2 = 34,449	**ddl = 3**		**p <0,001**

The frequency of blood group O in the breast carcinoma population (38.3%) is lower than the frequency in blood donors (46.05%), whereas the percentage of diseased patients with blood group B (25.8%) is higher than the frequency in blood donors (15.68%) ($p < 0.001$).

2.4. Association between ABO blood types and age at diagnosis

The age range between 35 and 70 years represents the cohort of patients most affected by breast cancer. However, the association between ABO blood type and age at diagnosis was not statistically significant ($p > 0.05$).

2.5. Association between ABO blood types and histo-prognostic grade SBR

In patients with blood types A, B, O and AB, SBR grade III accounted for 51.9% (55/106), 44.3% (39/88), 39.8% (53/133) and 22.2% (4/18), respectively ($p=0.011$).

2.6. Association between ABO blood types and estrogen receptor status

Estrogen receptors were more expressed in blood group O patients with a percentage of 80.8% (101/125), than in non-O patients with a percentage of 68.3% (123/180) ($p = 0.015$).

Patients with blood group B expressed less estrogen receptor with a percentage of 64 % (48/75), than in non-B patients with a percentage of 76.5 % (176/230) ($p = 0.03$).

2.7. Association between ABO blood types and HER2 receptor status

Tumors in patients with blood type B had the highest frequency of HER2 receptor overexpression (43.30%) compared to other blood types ($p = 0.04$).

2.8. Association between ABO blood types and lymph node metastasis status

The highest percentage of positive invaded nodes was noted in blood group A (83.3%), followed by blood group AB (81.3%), then blood group O (66%), and blood group B (58%). The difference in percentages between group B and non-B groups was statistically significant ($p = 0.005$).

2.9. Association between ABO blood types and vascular emboli status

Patients with blood group A had the highest percentage of positive vascular emboli (70.6%), followed by patients with blood group AB (68.8%), then blood group O (58.3%), and blood group B (45.3%) ($p = 0.011$).

2.10. Association between ABO blood types and other prognostic factors

The distribution of ABO blood types in breast cancer patients in our sample is independent of carcinoma histological types, tumor size, and progesterone receptor status.

3. DISCUSSION

The results of our study showed a higher frequency of blood group B in the breast carcinoma patient population compared with the blood donor population, and a lower frequency of blood group O in the patient population compared with the control population. The frequencies of the other blood types (A and AB) showed no statistically significant difference.

These results are consistent with several previous studies that reported a high prevalence of familial breast cancer in blood group B, with poor survival and higher risk of relapse, whereas blood group O is associated with cases showing a good prognosis.[12]-[19]

The association of blood group B with other types of cancer is also reported in ovarian tumors, cervical cancer, and pancreatic cancer.[12], [20], [21]

However, several studies, including one conducted in India on 303 women, have suggested that blood group A has a relatively higher risk of developing breast cancer. This hypothesis is also the conclusion of two meta-analyses that are in contrast to numerous studies that have shown no association between breast cancer and ABO blood types.[17], [22]-[26]

These inconsistencies in results between different studies may be related to the sample sizes used, or also to ethno-dependent gene and phenotype polymorphism, hence the importance of studying the polymorphic, gene and phenotypic particularity of each population.

Our results of analysis of ABH antigen distribution and histoprognostic grade (SBR) of breast carcinomas, report a statistically significant difference, marked by a high histoprognostic grade (SBR III) in patients of blood group A, and followed by B, O and AB. These findings are the exception in the history of similar research, as no study has yet revealed a positive association in this sense.[4], [12], [13], [27], [28]

Estrogen receptors are more expressed in blood group O patients than in non-O patients, whereas they are less expressed in blood group B patients than in non-B patients. These findings corroborate the results of Zouine et al. showing a positive correlation between blood type O and estrogen receptor expression. Some authors have suggested a link between blood groups A and B and hormone receptor positivity.[12], [14], [15], [29]

It should be noted that tumors expressing estrogen receptors are generally low-grade tumors with a favorable prognosis, whereas carcinomas not expressing these receptors are high-grade, proliferating, and associated with a poor prognosis.[30]

Our analysis showed that HER2 receptor overexpression is associated with breast carcinomas in group B patients.

This statement addresses the hypothesis of Holdsworth et al. considering ABO blood groups as a prognostic factor in breast cancer, and showing a high risk of death in group B patients. This conjecture can be explained by our results, in the sense that overexpression of the HER2/neu membrane receptor protein in breast carcinoma is associated with prominent tumor growth, greater metastatic potential, and high aggressiveness. However, several literature reviews have refuted this link.[4], [14], [19], [25]

HER2 receptor status was questionable for 37 cases in our series with an equivocal 2+ score, requiring a more sensitive and specific in situ hybridization technique to conclude their status. These cases were not considered in the statistical study.

Our analysis also revealed the presence of vascular emboli and lymph node metastases with a high percentage in patients with blood group A, then successively AB, O and B. The involvement of vascular emboli as a factor favoring lymph node invasion and distant metastases has been demonstrated in several works.[14], [31], [32]

Concerning the age at diagnosis of the patients in our series, the median age was 50 years, which is in agreement with the results of the study of Pandey & al. conducted in India. However, the median age at diagnosis was 61 years according to the US National Cancer Institute research conducted between 2008 and 2012.[33], [34]

In our sample, the age range between 35 and 70 years showed a significant frequency of breast carcinoma in all 4 blood groups of the ABO system. The association between age at diagnosis and ABO blood groups was not statistically significant, confirming the findings of Prakash et al. and Aly et al. who reported no positive association between age and the ABO blood group system.[15], [27]

As for the study conducted by Zouine et al. it was observed that blood type B had a high risk of breast cancer at an age above 70 years, while blood type A was associated with a high risk in women below 35 years.[12]

Furthermore, other studies have demonstrated a poor prognosis of breast cancer in young women, with a high incidence of hormone receptor-negative, and a higher histoprognostic grade (SBR III).[35], [36]

The distribution of ABO blood types in breast cancer patients in our sample is independent of the histological types of carcinomas, confirming the findings of previous studies. Nevertheless, Stamatakos et al. reported a positive association between type A and ductal carcinoma.[14], [17]

The histological types of tumors and their relationships with the ABO blood group system have been analyzed in different researches dealing with cancers in general, or a cancer other than breast cancer, such as the prospective study conducted in Shanghai and published in 2017 that showed a link between B and AB blood groups and tumors of carcinoma and adenocarcinoma types. Also, it has been reported that non-O blood groups were associated with an increased risk of exocrine pancreatic cancer.[25], [37]

Our reading of the medical records did not reveal any relationship between tumor size of breast carcinomas and ABO blood types in the patients of our series. This confirms the research of Zouine et al, Urun et al, and Aly et al, and is in contrast to the studies of Amini et al. in 134 patients and Yu et al. in 424 patients, who reported positive correlations between AB blood type and large tumor size.[4], [12], [38]

Despite all the statistical associations implicating the ABO system in the tumor process of breast carcinomas, the mechanisms of its interaction with cancer progression are still poorly understood. One hypothesis proposes that the enzymatic activity of ABO glycosyltransferases is closely related to intercellular adhesion processes, membrane signaling and the immune response. Alteration of these surface molecules may promote the process of malignancy, by a mechanism similar to the role played by ABO glycosyltransferases in the modulation of circulating plasma levels of von Willebrand factor (vWF), thus inducing an increased risk of venous thromboembolism. This association is particularly suspicious, also considering that vWF is a plasma glycoprotein, which acts as an adhesive molecule, binds between platelets and endothelial cells and plays a critical role in angiogenesis and apoptosis. Indeed, it has been detected at high levels in sera of non-O blood type cancer patients, explaining their poor prognosis.[16], [39]

Alterations in the inflammatory state due to ABO blood group antigens, is another potential mechanism, by which blood group may influence the progression and spread of malignancy. Studies have reported an association between polymorphisms at the ABO gene locus and the systemic inflammatory response strongly related to carcinogenesis by regulating serum levels of several pro-inflammatory and adhesion molecules, including: tumor necrosis factor-alpha (TNF-α), and soluble intercellular adhesion molecule-1 (sICAM-1). These molecules are important mediators of chronic inflammation and immune cell recruitment.[16], [40]-[43]

Tumor necrosis factor-α (TNF-α) is a key mediator of apoptosis. At low serum levels, its apoptotic and antitumor actions are decreased, but its angiogenic action is increased. This marker of inflammation is found at low levels in the serum of blood group A and B patients.[42], [44]

Plasma sICAM-1 concentration was associated with multiple variations in nucleotide polymorphism in the ABO locus and in the ICAM gene. Expression of sICAM-1, which inhibits lymphocyte attachment to endothelial cells by binding to ICAM ligands on circulating cells, is significantly reduced in patients with non-ABO blood groups (especially group A). Cancer cells use similar mechanisms for adhesion to endothelial cells, the decrease in sICAM-1 levels in patients with non-O blood groups, may promote the metastatic spread of tumors.[14], [45]

4. CONCLUSION

According to the results of our study, there is a strong association between ABO blood group system and breast carcinoma, with a high incidence in patients with blood group B, and low in group O.

Despite all the statistical evidence regarding the involvement of the ABO system in human physiology and pathophysiology, the mechanisms by which it may interact with cancer development and progression are still poorly understood.

Further studies on blood types in large series are needed to elucidate the mechanisms of the relationship between blood type and disease.

Also, the findings of this work open new research perspectives, since the association of ABH, HER2 and estrogen receptor expression has been statistically proven, it would be interesting to explore the signaling pathways of these markers, by molecular biological methods in in vitro models.

CONFLICT OF INTEREST

The authors declare that they haven't known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

FUNDING SOURCES

The research has not been externally funded.

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