IJHOSCR

Original Article

International Journal of Hematology-Oncology and Stem Cell Research

Study of the Relationship between ABO Blood Group Types and Breast Cancer and Cervix Cancer in Khuzestan Province, Iran

Nazanin Joudaki[1,2,3], Ali Khodadadi[1,4], Abdolhassan Talaiezadeh[4,5], Hosein Jodat[,2], Javad Jodat[2], Ali Asadirad[1]

[1]Department of Immunology, Faculty of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
[2]Student Research Committee, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
[3]Department of Immunology, School of Medicine, Mazandaran University of Medical Sciences, Sari, Iran
[4]Cancer, Petroleum and Environmental Pollutants Research Center, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
[5] Department of Surgery, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

Corresponding Author: Ali Asadirad, Department of Immunology, Faculty of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
E-mail: ali.asadirad@gmail.com

Received: 13, Dec, 2021
Accepted: 18, Oct, 2022

ABSTRACT

Background: Breast cancer and cervix cancer are the prevalent and deadly types of solid tumors around the world. According to the importance of cancer, it is necessary to understand predisposing factors that affect cancer risk. In this regard, previous studies suggest that blood types particularly ABO and Rh-Hr Blood-Group System could play roles in the risk and different features of cancers. In the present study, we aimed to evaluate the potential of ABO and Rh blood groups as risk factors for breast cancer and cervix cancer.

Materials and Methods: A retrospective study included 109 and 14 patients diagnosed with breast cancer and cervix cancer, respectively with known ABO and Rh blood types, between 2018 and 2020 in Khuzestan province, Iran. For compression of ABO blood groups distribution between the cancer patients group and the healthy population, we used data from a large-scale study that report the distribution of ABO blood groups in 29,922 blood donors in Khuzestan province.

Results: Based on obtained results the most frequent blood group is O followed by B, A, and AB in breast cancer and followed by A, B, and AB in cervix cancer. Results showed no significant association between ABO and Rh and the risk of breast and cervix cancer. Moreover, there is no relationship between blood types and clinic pathological features of breast cancer.

Conclusion: Based on our data, ABO and in this regard, previous studies suggest that blood types particularly ABO and Rh-Hr Blood-Group System could play roles in the risk and different features of cancers. In the present study, we aimed to evaluate the potential of ABO and Rh blood groups as risk factors for breast cancer and cervix cancer do have not any association with the risk of breast and cervix cancer and their characteristics.

Keywords: ABO blood-group system; Rh-Hr bood-group system; Breast neoplasms; Cervix neoplasms

INTRODUCTION

Cancer is one of the most health-threatening and complicated diseases around the world. It involves a greater population each year and affects the quality of life depending on different types, stages, and personal factors. Solid tumors such as breast cancer and cervix cancer are the prevalent malignancy in many countries and due to their progression rate can cause considerable death annually. Therefore, it is necessary to find out valuable factors that can give some information for accounting for risk, predicting progression, response to treatment, and outcome of cancer, and help us in better disease management. Breast cancer is the most common cancer in women and a common cause of cancer death[1]. Breast cancer

is a heterogeneous disease on the molecular level and includes molecular features such as activation of human epidermal growth factor receptor 2 (HER2), estrogen receptor, progesterone receptor, and/or BRCA mutations. It is mostly curable in the early stages but can metastases to a distant organ in advanced form [1.] Different biological factors such as molecular and gene associations and hormonal balance can predispose to breast cancer and play a role in malignancy development. Cervix cancer is second the most common cancer in females that mainly occurs in developing countries[2]. Studies show that control and prevention are crucial for this deadly cancer[3]. Among different demographical and biological factors, patient blood type could play an essential role as a predisposing factor in many diseases.

Previous studies demonstrate that having each of the different blood types of the ABO system or Rh blood group could affect the risk and outcome of diseases, particularly cancers. Many studies have reported the relationship between different blood groups of patients and the risk, prognosis, and outcome of various cancers such as thyroid cancer, ovarian and vulvar cancer, skin cancers, cervix carcinoma, gastrointestinal cancers, and breast cancer [2, 4-9]. Hence the association of ABO and Rh blood group with breast cancer and cervix cancer risk is under debate [10-12].

The ABO blood group system is determined by antigen A or antigen B expression on the surface of red blood cells. Also, the ABO antigens are highly expressed on the epithelial cells of the gastrointestinal, bronchopulmonary, and urogenital tracts [6, 7]. The expression of ABO antigens on tumor cells is different from normal cells, and this is caused by loss or structural changes in their antigens [13, 14]. Changes in expression are related to escape from immune response and apoptosis. Moreover, it results in an alteration in the specificity of glycosyltransferase that affects the clearance of P-selectin, E-selectin, and ICAM-1 from blood [13-15]. On the other hand, Dysregulation of A and B glycosyltransferase which have an important role in the immune system and can result in increasing Von Willebrand factor and angiogenesis [16]. A decrease in ABO antigens is related to a decline in adhesion and metastasis potential. Additionally, tumoral A-like antigen can role in tumor escapes from the immune system. Moreover, ABO antigens can affect systemic inflammatory responses that play role in the initiation and expanse of cancer[6,7,17].

Despite extensive efforts in recent years, due to antithetical reports, our knowledge remains scant about the role of ABO and Rh blood type in the risk, prognosis, and outcome of solid tumors patients and it needs more investigation to shed more light on this subject. The present study investigates the association between the ABO Blood-Group System and Rh blood group and the risk of breast cancer and cervix cancer.

MTERIALS AND METHODS

Study design

A retrospective study included 109 and 14 patients diagnosed with breast cancer and cervix cancer respectively, with known ABO blood type, between 2018 and 2020 in Khuzestan province, Iran. Available demographic data, ABO blood groups, and pathological status of patients were collected from the Cancer research center of Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran. The mean age of breast cancer and cervix cancer patients was 48.50 years (range 30-83 years) and 45.85 years (range 13-64 years) respectively. For compression of ABO blood group distribution between the cancer patients group and the healthy population, we used data from a large-scale study that report the distribution of ABO blood groups in 29,922 blood donors in Khuzestan province[18]. Moreover, the research was approved by the Ethics Committee of Ahvaz Jundishapur University, and the ethics code of this study was IR.AJUMS.REC.1400.344.

Statistical analysis

All data were analyzed using the SPSS version 26.0 software package (IBM, Chicago, IL, USA). Chi-square ($\chi 2$) test or Fisher's exact test was used for frequency distributions of data and possible associations with ABO blood groups. Graphs were performed by the GraphPad Prism 8.0 software.

Breast cancer vs. Health population

As shown in Figure 1, the O blood group was the most frequent blood group among the breast cancer group (45.9%) and healthy population group (40.0%). The distribution of ABO blood groups was similar in the two groups (P-value = 0.728) (Table 1).

Table 1. Distribution of ABO blood groups in breast cancer and healthy population

Blood type	A	B	AB	O	P
Breast cancer (%)	22.0%	23.9%	8.2%	45.9%	0.728
Healthy population (%)	28.0%	25.0%	7.0%	40.0%	

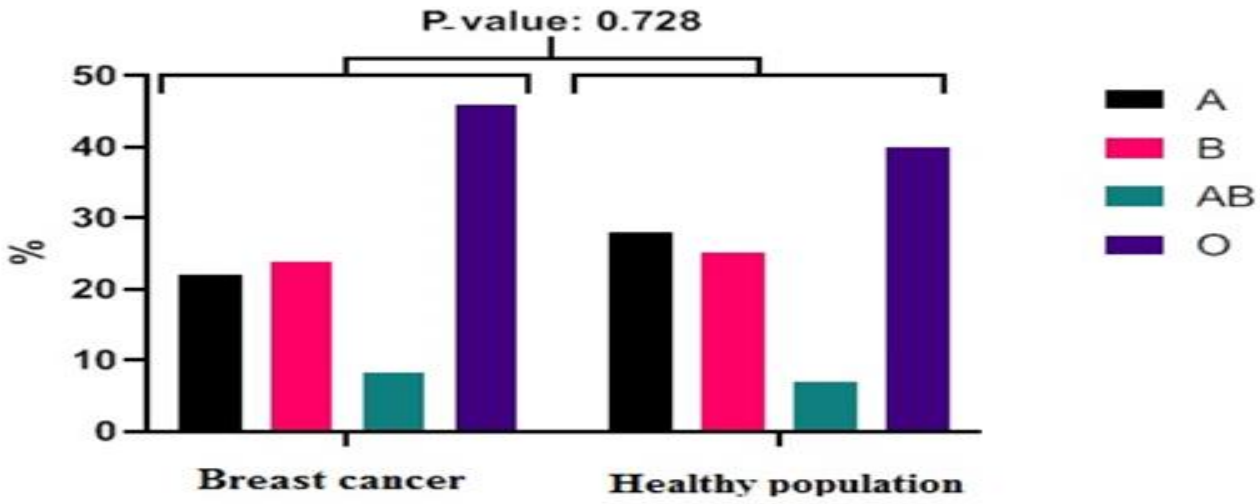

Figure 1. Frequency of different blood groups between breast cancer and healthy population. O blood group was the most frequent blood group between the two groups. P-value < 0.05 indicate statistical significance.

Breast cancer vs. Healthy population

The findings of this study showed that the distribution of the Rh blood group was similar in the two groups (P-value = 0.471) (Table 2) (Figure 2).

Table 2: Distribution of Rh blood groups in breast cancer and healthy population

Blood type	Positive	Negative	P
Breast cancer (%)	94.5%	5.5%	0.471
Healthy population (%)	92.38%	7.62%	

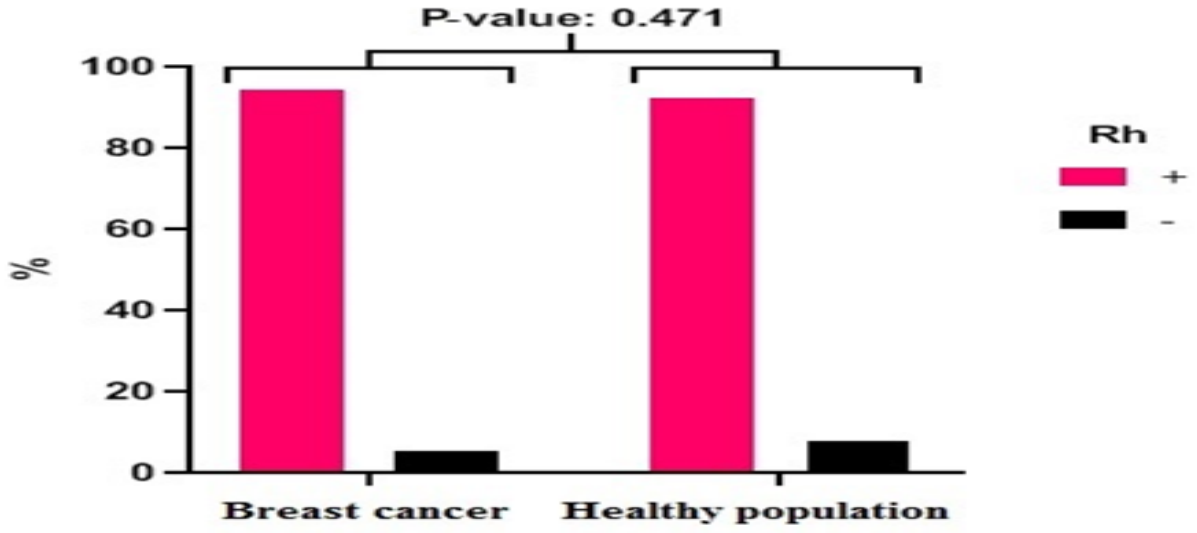

Figure 2. Frequency of different blood groups between breast cancer and healthy population, P-value < 0.05 indicate statistical significance.

ABO blood groups and Clinico-pathological characteristics

According to the obtained results (Table 3), Histopathological features such as the site of the tumor, tumor type, and grade were similar in all ABO blood groups.

The percentage of all ABO blood groups was similar in Histopathological features such as the site of the tumor, tumor type, and grade.

Table 3: Clinico-pathological characteristics and ABO blood type

Blood type		A	B	AB	O	P
Total [N, (%)]		24 (22.0)	26 (23.9)	9 (8.3)	50 (45.9)	
Site [N, (%)]	Left	9 (17.3)	15 (28.8)	7 (13.5)	21 (40.4)	0.119
	Right	15 (26.3)	11 (19.3)	2 (3.5)	29 (50.9)	
Tumor type [N, (%)]	IDC	17 (23.0)	19 (25.7)	6 (8.1)	32 (43.2)	0.741
	ILC	0 (0.0)	1 (16.7)	2 (33.3)	3 (50.0)	
	Others*	6 (25.0)	5 (20.8)	1 (4.2)	12 (50.0)	
	Missing	1 (20.0%)	1 (20.0)	0 (0.0)	3 (60.0)	
Grade [N, (%)]	Ⅰ	1 (5.9)	4 (23.5)	2 (11.8)	10 (58.8)	0.560
	Ⅱ	13 (28.9)	12 (26.7)	2 (4.4)	18 (40.0)	
	Ⅲ	3 (30.0)	2 (20.0)	0 (0.0)	5 (50.0)	
	Missing	7 (18.9)	8 (21.6)	9 (13.5)	17 (46.0)	

Rh blood groups and Clinico-pathological characteristics

As shown in Table 4, the distribution of the Rh blood group in terms of Histopathological features such as site of the tumor (P-value = 1.000), tumor type (P-value = 1.000), and grade (P-value = 0.137) was similar.

Table 4: Clinico-pathological characteristics and ABO blood type

Blood type		Positive	Negative	P
Total [N, (%)]		103 (94.5)	6 (5.5)	
Site [N, (%)]	Left	49 (94.2)	3 (5.8)	1.000
	Right	54 (94.7)	3 (5.3)	
Tumor type [N, (%)]	IDC	69 (93.2)	5 (6.8)	1.000
	ILC	6 (100.0)	0 (0.0)	
	Others*	32 (95.8)	1 (4.2)	
	Missing	5 (100.0%)	0 (0.0)	
Grade [N, (%)]	Ⅰ	14 (82.4)	3 (17.6)	0.137
	Ⅱ	44 (97.8)	1 (2.2)	
	Ⅲ	10 (100.0)	0 (0.0)	
	Missing	35 (94.6)	2 (5.4)	

Breast cancer biomarkers and ABO blood groups

The results showed that the prevalence of ABO blood groups was similar in positive and negative group of estrogen receptor (ER) (P-value = 1.000), Progesterone receptor (PR) (P-value = 0.386), HER2/neu (P value = 0.168) and in different status of Ki67 (P-value = 0.326) (Table 5).

Table 5: Hormonal biomarker and ABO blood groups

Blood type		A	B	AB	O	P
ER status	Positive	5 (17.2)	2 (6.9)	2 (6.9)	20 (69.0)	1.000
	Negative	1 (10.0)	1 (10.0)	0 (0.0)	8 (80.0)	
Total [N, (%)]		6 (15.4)	3 (7.7)	2 (5.1)	28 (71.8)	
PR status	Positive	2 (9.1)	1 (4.5)	1 (4.5)	18 (81.8)	0.386
	Negative	4 (23.5)	2 (11.8)	1 (5.9)	10 (58.8)	
Total [N, (%)]		6 (15.4)	3 (7.7)	2 (5.1)	28 (71.8)	
HER2/neu status	Positive	0 (0.0)	0 (0.0)	1 (8.3)	11 (91.7)	0.168
	Negative	3 (16.7)	3 (16.7)	1 (5.6)	11 (61.1)	
Total [N, (%)]		3 (10.0)	3 (10.0)	2 (6.7)	22 (73.3)	
Ki67 status	<10%	0 (0.0)	0 (0.0)	0 (0.0)	9 (100.0)	0.326
	10-30%	1 (20.0)	0 (0.0)	0 (0.0)	4 (80.0)	
	>30%	1 (14.3)	1 (14.3)	0 (0.0)	5 (71.4)	
Total [N, (%)]		2 (9.5)	1 (4.8)	0 (0.0)	18 (85.7)	

Breast cancer biomarkers and Rh blood groups

The results showed that the prevalence of ABO blood groups was similar in positive and negative groups of estrogen receptor (ER) (P-value = 0.400), Progesterone receptor (PR) (P-value = 0.598), HER2/neu (P-value = 0.352) and in different status of Ki67 (P-value = 0.048) (Table 6).

Table 6: Hormonal biomarker and Rh blood groups

Blood type		Positive	Negative	P
ER status	Positive	26 (89.7)	3 (10.3)	0.400
	Negative	10 (100.0)	0 (0.0)	
Total [N, (%)]		36 (92.3)	3 (7.7)	
PR status	Positive	20 (90.9)	2 (9.1)	0.598
	Negative	16 (94.1)	1 (5.9)	
Total [N, (%)]		36 (92.3)	3 (7.7)	
HER2/neu status	Positive	12 (100.0)	0 (0.0)	0.352
	Negative	16 (88.9)	2 (11.1)	
Total [N, (%)]		28 (93.3)	2 (6.7)	
Ki67 status	<10%	9 (100.0)	0 (0.0)	0.048
	10-30%	3 (60.0)	2 (40.0)	
	>30%	7 (100.0)	0 (0.0)	
Total [N, (%)]		19 (90.5)	2 (9.5)	

Cervix cancer vs Healthy population

The highest frequency of blood group O (57.2%), followed by blood group A (28.6%), B (7.1%), and AB (7.1%) was observed in cervix cancer patients (Table 7). Moreover, the distribution of blood groups among cervix cancer patients and the healthy population did not differ significantly (P-value = 0.421) (Figure 3).

Table 7: Distribution of ABO blood type of cervix cancer and healthy population

Blood type	A	B	AB	O	P
Cervix cancer (%)	28.6%	7.1%	7.1%	57.2%	0.421
Healthy population (%)	28.0%	25.0%	7.0%	40.0%	

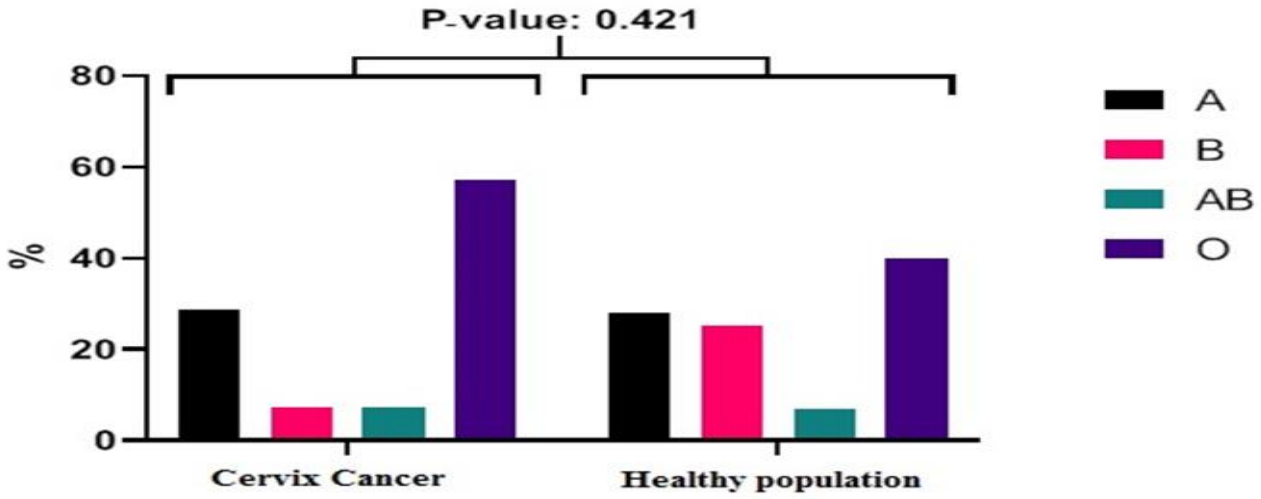

Figure 3. Blood groups ABO distribution in cervix cancer and healthy population. The highest frequency belonged to the O blood group. P-value < 0.05 indicate statistical significance.

Cervix cancer vs Healthy population

The results showed that the distribution of the Rh blood group in cervix cancer patients and the health population was similar (P-value = 1.000) (Figure 4).

Table 8: Distribution of Rh blood group in cervix cancer and healthy population

Blood type	Positive	Negative	P
Cervix cancer (%)	92.9%	7.1%	1.000
Healthy population (%)	92.38%	7.62%	

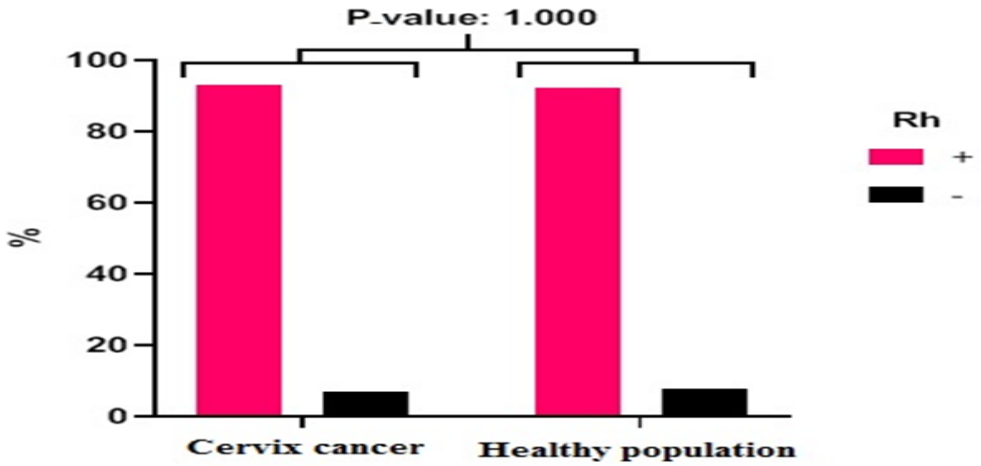

Figure 4. Rh blood group distribution in cervix cancer and healthy population

DISCUSSION

Our study aimed to investigate the relationship between the ABO Blood-Group System and Rh-Hr Blood-Group System and the risk of breast cancer and cervix cancer. It is not yet clear what the underlying mechanisms are that cause ABO blood groups or ABO locus genetic variants to cause cancer[19]. An admissible hypothesis to explain these mechanisms is the dysregulation of ABO glycosyltransferases, which are involved in the process of cell adhesion, cell signaling, and host immune responses[20,21]. The distribution of ABO blood groups in the present study among breast cancer patients was O, B, A, and AB respectively. Recently Hassan Farhan et al. reported a similar result to our study [22]. However, in a study conducted by R. Dixit et al., the distribution of ABO blood groups was B, O, A, and AB respectively [23]. In some studies, distribution was A, O, B, and AB Also, the Neelima Kumari et al reported A, B, O, and AB respectively [8, 24-29]. However, a study reported A, B, O, and AB as ABO blood group distribution in breast cancer respectively and in another study, the distribution was O, A, B, and AB respectively [6, 7, 17].

Our results have shown that none of the ABO blood groups has a significant association with breast cancer and their distribution was similar to the healthy population. In agreement with the present study three studies conducted by R. Dixit et al. Serkan Akin et al. and Margaret A. Gates et al. reported that ABO blood groups have no relationship with breast cancer[17, 23, 24]. Nevertheless, recent studies have shown that blood group A is associated with breast cancer [6-8, 10, 26, 27, 29]. Also, a study in Turkey on 3944 breast cancer patients indicated that there was no significant difference between ABO blood group and grade, type, stage, and hormonal status of breast cancer[24.]

A meta-analytical study of breast cancer patients reported that Caucasians with blood type A were more susceptible to developing this type of cancer than other Caucasians with other blood types[30]. In this regard, patients with blood groups B and AB had a substantial increase in the incidence of breast cancer and had poorer general survival compared to those with blood groups O and A [31]. Hao Yu et al. reported that patients with the A blood group have a higher risk of developing gastric cancer, while patients with the AB blood group have a lower risk of developing gastric cancer. They also declared that the ABO blood group system has no considerable impact on the clinicopathological factors of gastric cancer [32]. Furthermore, a recent study reported that non-O blood groups can be associated with a favorable prognosis in breast cancer patients [28].

Moreover, a cross-sectional study of 197 females with breast cancer indicated that there was no association between RH blood type and breast cancer[29]. However, a study suggested that Rh-positive is associated with the risk of breast cancer[27]. According to the obtained results, all ABO blood groups were not associated with Clinico-pathological characteristics including the site of the tumor, tumor type, and grade. Recent studies carried out by R. Dixit et al. and Margaret A. Gates et al. supported our findings [17, 23]. Furthermore, this is consistent with the results of Sungmin Park et al. [28]. Another study demonstrated that ABO blood groups do have not a relationship with blood groups and Clinico-pathological breast cancer except for the O blood group that has shown a significant association with lower stage and the subject of Rh-positive is relevant to lobular histological type of breast cancer [24]. Similar to our results, there was no significant relationship between the ABO blood group and the incidence or mortality of laryngeal carcinoma [33] or malignant mesothelioma [34.]

We acknowledge that there is no significant relevance between ABO blood groups and HER2/neu, estrogen receptor, progesterone receptor, and Ki67 status as a breast cancer biomarker. In this regard, R. Dixit et al. have released a similar report recently[23]. Moreover, two studies demonstrated that ABO blood groups have no association with breast cancer [17, 28]. Another study has shown ABO blood group have not any relationship with hormonal status but Rh-positive is associated with overexpression of estrogen receptors [24]. However, a recent study demonstrated a relationship between B blood type and HER2 overexpression in breast cancer [15]. Moreover, another investigation disclosed no relationship between the ABO blood group and survival rate in 468 patients with triple-negative breast cancer [35].

In the subject of cervix cancer, our evaluation has shown that the distribution of the ABO blood group was O, A, B, and AB respectively and it was consistent with a study conducted by Angel Justiz Vaillant et al.[11]. In a study performed by Roopali Fotra et al., ABO blood group distribution was O, B, AB, and A, respectively [2]. In another study, the distribution of the ABO blood group was B, O, A, and AB, respectively [11].

Furthermore, our investigation showed there is no significant between ABO and Rh blood groups and cervix cancer. However, some studies suggested that the B blood group may as a risk factor for cervix carcinoma [2, 3.] Although another study reported O blood group was slightly associated with Cervical Carcinoma [11].

LIMITATIONS

Constraints of this study contain the absence of access to patients, inability to follow patients to assess survival rates, non-availability of other tumor-risk factors (such as smoking or alcohol consumption), and absence of pathological information, and family history of patients.

CONCLUSION

In conclusion, our study shows no relevance between ABO and Rh blood groups and breast and cervix cancer. However, other studies have a controversial report that some of them support our results and others do not. Hence it should be more and larger studies are necessary to find out blood types and how and much affect breast and cervix cancer.

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