Original Article

HEALTH SCIENCES
MEDICINE

DOI: 10.32322/jhsm.1404257
J Health Sci Med. 2024;7(1):126-131

Distribution of ABO and Rh blood groups in gynecological cancer cases

Ramazan Adan, Veli Mihmanlı

[1]Department of Obstetrics and Gynecology, Prof. Dr. Cemil Taşçıoğlu City Hospital, İstanbul, Turkiye

Cite this article as: Adan R, Mihmanlı V. Distribution of ABO and Rh blood groups in gynecological cancer cases. *J Health Sci Med.* 2024;7(1):126-131.

Received: 14.12.2023 • **Accepted**: 10.01.2024 • **Published**: 15.01.2024

ABSTRACT

Aims: To investigate the relationship between blood type and gynecological cancers (ovarian, endometrial, and cervical).

Methods: In the study, between 2017 and 2022, 457 patient files who underwent surgery for gynecological cancer at İstanbul Prof. Dr. Cemil Taşçıoğlu City Hospital were reviewed. Seventy-eight of these files were excluded from the study due to missing data. Out of the remaining files, 379 were considered suitable for the study. Twenty-five of these were further excluded due to being cases of other gynecological cancers. A total of 354 patients were included in the study (n=354). Participants' sociodemographic data such as age and gender, cancer type, and blood groups (ABO-Rh) were retrospectively collected from patient records and the hospital automation system. Cases with missing data or inaccessible sociodemographic records were excluded from the study. The study was planned retrospectively and observationally. Gynecological cancers were examined in the three most common groups: ovarian cancer, endometrial cancer, and cervical cancer. The patients' blood group, Rh status, and pathology reports were analyzed. Based on the pathological diagnosis, three groups were initially formed, and below them, Rh and blood group status were noted. The blood group and Rh status in cancer groups were first presented in numbers and then calculated as percentages.

Results: The AB+ ratio in cervical cancers was statistically significantly higher compared to the reference article and endometrial cancers (p=0.021, p=0.049).

Conclusion: There are studies indicating a significant relationship between blood groups and various diseases. The expression of blood group antigens on blood cells and other epithelial surfaces acting as receptors or signal transducers contributes to these findings. The possibility of ABO antigens serving as receptors in tumor structures caused by infections, such as cervical cancer, should not be overlooked. In this regard, the significantly higher prevalence of cervical cancer in individuals with AB Rh (+) blood type, carrying A, B, and Rh antigens, can be explained concerning the population.

Keywords: Gynecological cancers, blood group, cervical cancers

INTRODUCTION

Gynecological cancers are a collective term for cancers occurring in the cervix, ovaries, endometrium, uterus, fallopian tubes, vulva, or vagina. Endometrial cancer, ovarian cancer, and cervical cancer are the three most common gynecological cancers in women. A significant association has been found between the A Rh+ blood group and malignant melanoma, kidney, colorectal, breast, and ovarian cancers; whereas, pancreatic cancer is significantly associated with the O Rh+ blood group. It is speculated that a similar relationship may exist in gynecological cancers.

Cervix ca: The number of lymph nodes involved in patients undergoing surgical staging or lymphadenectomy also affects prognosis. In one report, five-year survival rates for patients with one, two, three to four, and five or more positive lymph nodes were 62, 36, 20, and 0 percent, respectively.[1] After radical hysterectomy and lymphadenectomy, five-year survival for patients with stage IB1 and IB2 disease is 91.6 percent and 83.3 percent, respectively, compared with 60.8 percent for those with pelvic nodal involvement.[2] Outcomes are worse in patients with para-aortic nodes (five-year survival, 37.5 percent).

Endometrium ca: The prognosis of endometrial carcinoma is determined primarily by the stage, grade and histology of the disease.[3] The prognosis for most patients with endometrial carcinoma is favorable, as the majority of patients have endometrioid histology and present with early-stage disease. Survival rates according to stages Localized 94.9% regional 69.8% distant 18.4% unknown 57.6%

Corresponding Author: Ramazan ADAN, r.adan187.ra@gmail.com

Ovarian ca: Approximately 80 percent of patients with early-stage disease do not experience recurrence within five years. However, most patients with advanced ovarian cancer experience recurrence. Mortality is high among those with recurrent disease. Five-year survival rates for epithelial ovarian and fallopian tube carcinomas by stage are shown in the table. Five-year survival is 89% in stage 1, 71% in stage 2, 41% in stage 3, and 20% in stage 4.[4]

Cancer is among the leading causes of death in developed countries. The role of ABO and Rhesus (Rh) blood groups in cancer biology has been studied by various researchers. ABO blood group antigens are expressed on the erythrocyte membrane and many other cell surfaces. When examining the pathophysiology between ABO blood groups and cancer, it is understood that irregularities in the enzymatic activities of Glycosyltransferase A and Glycosyltransferase B, responsible for the formation of membrane-derived signals in the immune response, lead to angiogenesis and tumor formation by modulating plasma levels of the Von Willebrand factor. The relationship between ABO antigens and intercellular adhesion molecules has been reported to be effective in tumor initiation and progression. Since the discovery of blood groups by Karl Landsteiner in 1901 and Aird's declaration in 1953 that the A blood group is associated with gastric cancer, blood groups have been the subject of research in many cancer types. ABO blood group genes are mapped to the 9q34.2 region, where genetic changes are common in many cancers. Therefore, blood group antigen expression can be influenced by genetic changes in the tumor. The glycoconjugate structures in RBCs have various functions, including receptors, carriers, channels, structural proteins, adhesion molecules, and enzymes for exogenous ligands, viruses, bacteria, and parasites.[5] However, the exact mechanisms explaining the relationships between blood group antigens and diseases in adhesion molecules are still unknown. Since infectious agents often use cell surface glycoconjugates as receptors for binding, glycosylation polymorphisms in ABO blood type can affect host-pathogen interactions and lead to sensitivity differences among individuals with different glycosylation profiles.[6] Previous studies suggest a possible relationship between the ABO blood group and some epithelial cancers, including pancreatic and gastric cancers. Various mechanisms, including inflammatory changes, intercellular adhesion, and membrane signal alterations, have been proposed to explain the observed relationship between ABO blood groups and cancer risk. However, it has been reported that the relationship between ABO blood group types and cancer risk is not definitive.

In this study, we aimed to evaluate the distribution of ABO-Rh blood groups according to gynecological cancer disease and its subtypes, which are accessible in the clinic.

In a study conducted in İstanbul, based on the results of blood type analysis of 123,900 individuals, the distribution is as follows: 47,496 (38.3%) individuals are A Rh (+), 6,793 (5.5%) individuals are A Rh (-), 36,427 (29.4%) individuals are O Rh (+), 5,451 (4.4%) individuals are O Rh (-), 16,294 (13.2%) individuals are B Rh (+), 2,560 (2.1%) individuals are B Rh (-), 7,971 (6.4%) individuals are AB Rh (+), and 908 (0.7%) individuals are AB Rh (-). Looking at the Rh blood group, 108,188 (87.31%) individuals are Rh (+), and 15,712 (12.69%) individuals are Rh (-). Conclusion: The demographics of İstanbul reflect a summary of Turkiye. The distribution of blood types in our region is similar to the overall rates in Turkiye and the İstanbul region.[7]

METHODS

The study was initiated with the approval of the İstanbul Prof. Dr. Cemil Taşçıoğlu City Hospital Clinical Researches Ethics Committee (Date:26.12.2022, Decision No:366). Additionally, written authorization was secured from the establishments where the research was carried out, and informed agreement was acquired from the patients. The study was conducted by the Principles of the Declaration of Helsinki.

In the study, between 2017 and 2022, 457 patient files who underwent surgery for gynecological cancer at İstanbul Prof. Dr. Cemil Taşçıoğlu City Hospital were reviewed. Seventy-eight of these files were excluded from the study due to missing data. Out of the remaining files, 379 were considered suitable for the study. Twenty-five of these were further excluded due to being cases of other gynecological cancers. A total of 354 patients were included in the study (n=354). Participants' sociodemographic data such as age and gender, cancer type, and blood groups (ABO-Rh) were retrospectively collected from patient records and the hospital automation system. Cases with missing data or inaccessible sociodemographic records were excluded from the study. The study was planned retrospectively and observationally. Gynecological cancers were examined in the three most common groups: ovarian cancer, endometrial cancer, and cervical cancer. The patients' blood group, Rh status, and pathology reports were analyzed. Based on the pathological diagnosis, three groups were initially formed, and below them, Rh and blood group status were noted. The blood group and Rh status in cancer groups were first presented in numbers and then calculated as percentages.

Statistical Analysis

The results were compared with the distribution of blood groups and Rh in the general population. SPSS 15.0 for Windows program was used for statistical analysis. Descriptive statistics were provided for categorical variables in terms of number and percentage. Ratios in independent groups were compared using Chi-Square Analysis. A statistical alpha significance level of $p<0.05$ was determined.

RESULTS

Demographic findings are summarized in Table 1.

Table 1. Age Distribution by endometrium, ovarian, cervical cancer and blood types

Blood Type	Age					p
	N	Avg.	SD	Min	Max	
Total						0.490*
A	156	59.0	11.4	32	93	
AB	30	60.1	10.0	34	76	
B	60	60.3	11.2	32	82	
O	108	57.7	11.4	31	84	
Endometrium						0.579*
A	72	58.3	11.6	32	93	
AB	10	59.8	6.8	52	72	
B	33	61.3	10.4	43	82	
O	47	60.5	11.9	32	84	
Ovarian						0.122*
A	65	59.5	12.2	33	84	
AB	12	63.8	9.4	40	76	
B	22	59.3	13.1	32	77	
O	49	55.6	11.3	31	77	
Cervical						0.462**
A	19	59.7	7.6	41	71	
AB	8	54.8	12.6	34	72	
B	5	57.8	8.1	52	72	
O	12	55.3	7.8	41	65	

*One Way ANOVA **Kruskal Wallis Test

In our study (n=354), the blood type distribution is as follows: A Rh (+) 137 (38.70%), A Rh (-) 19 (5.36%), O Rh (+) 94 (26.55%), O Rh (-) 14 (3.95%), B Rh (+) 55 (15.53%), B Rh (-) 5 (1.41%), AB Rh (+) 26 (7.34%), AB Rh (–) 4 (1.12%). In terms of Rh factor, 309 individuals (87.28%) are Rh (+), and 42 individuals (11.86%) are Rh (-).

In the endometrial cancer distribution of our study (n=162), the blood type breakdown is as follows: A Rh (+) 64 (39.50%), A Rh (-) 8 (4.93%), O Rh (+) 39 (24.07%), O Rh (-) 8 (4.93%), B Rh (+) 29 (17.90%), B Rh (-) 4 (2.46%), AB Rh (+) 9 (5.55%), and AB Rh (-) 1 (0.61%).

In the ovary cancer distribution of our study (n=148), the blood type distribution is as follows: A Rh (+) 56 (37.83%), A Rh (-) 9 (6.08%), O Rh (+) 43 (29.05%), O Rh (-) 6 (4.05%), B Rh(+) 21 (14.18%), B Rh(-) 1 (0.67%), AB Rh(+) 10 (6.75%), and AB Rh(-) 2 (1.35%).

In the cervix cancer distribution of our study (n=44), the blood type distribution is as follows: A Rh (+) 17 (38.63%), A Rh (-) 2 (4.54%), O Rh (+) 12 (27.27%), O Rh (-) 0 (0%), B Rh (+) 5 (11.36%), B Rh (-) 0 (0%), AB Rh (+) 7 (15.90%), and AB Rh (-) 1 (2.27%).

The AB+ blood type ratio in cervical cancers was found to be statistically significantly higher compared to the reference article and statistically significantly higher than endometrial cancers (p=0.021, p=0.049, respectively). Findings are summarized in Table 2 .

DISCUSSION

In our study, the blood type distribution in patients was similar to the blood type distribution in the Marmara region. Findings in endometrial and ovarian cancers were consistent with blood type distribution, and no statistically significant difference was observed. However, in cervical cancer, the AB Rh (+) ratio was found to be significantly higher compared to the blood type distribution in the Marmara region and endometrial cancer (p=0.021, p=0.049).

Table 2. Cancer areas and reference evaluations according to blood types

	Endometrial	Ovarian	Cervical	Reference Article	Ref. vs. Endometrial	Ref. vs. Ovarian	Ref. vs. Cervical
	n (%)	n (%)	n (%)	n (%)	p	p	p
O-	8 (4.93%)	6 (4.05%)	0	5451 (4.4%)	0.738	0.838	0.265
O+	39 (24.07%)	43 (29.05%)	12 (27.27%)	36427 (29.4%)	0.137	0.926	0.757
A-	8 (4.93%)	9 (6.08%)	2 (4.54%)	6793 (5.5%)	0.761	0.749	1.000
A+	64 (39.50%)	56 (37.83%)	17 (38.63%)	47496 (38.3%)	0.759	0.901	0.967
B-	4 (2.46%)	1 (0.67%)	0	2560 (2.1%)	0.719	0.380	1.000
B+	29 (17.90%)	21 (14.18%)	5 (11.36%)	16294 (13.2%)	0.074	0.709	0.726
AB-	1 (0.61%)	2 (1.35%)	1 (2.27%)	908 (0.7%)	1.000	0.296	0.277
AB+	9 (5.55%)	10 (6.75%)	7 (15.90%)	5451 (4.4%)	0.649	0.873	0.021
N	162	148	44	123900			

Cervical vs. Endometrial p=0,049 Cervical vs. Ovarian p=0,073

As observed for over 35 years, aberrant glycosylation occurs essentially in all types of experimental and human cancers, and many glycosyl epitopes constitute tumor-associated antigens. Whether abnormal glycosylation is a consequence or a cause of cancer is a long-standing debate. Many recent studies indicate that abnormal glycosylation, in some but not all cases, is a consequence of initial oncogenic transformation and is also a key event in the initiation of invasion and metastasis.[8]

ABO may also be associated with cancer risk because the A antigen can be detected in tumor cells from non-A individuals; Glycosylation, in turn, can lead to conformational changes in proteins such as the epidermal growth factor receptor or alter the immune recognition of natural killer cells. helps tumor formation.[9]

Studies on survival and cancer have revealed that patients with blood type A have a longer survival time than other blood types.[10] A retrospective analysis of 968 women affected by gynecological tumors was performed to evaluate the existence of a difference in survival between patients with different blood groups. Data on 237 cases of endometrial cancer, 92 cases of ovarian cancer, and 639 cases of invasive cervical cancer are presented, detailing their ABO blood antigenic phenotypes, stage of neoplasia, and treatment received. In terms of endometrial cancer, significantly better 5-year and 10-year survival is associated with blood type O compared to blood type A. This finding is more evident when considering 5-year survival among patients affected by ovarian cancer. Regarding cervical cancer, the analysis showed that a survival rate of slightly better than 5 years was associated with the 0 blood phenotype; On the contrary, better survival is associated with the A blood phenotype, considering survival of 10 years or more. This study confirms the evidence of the association between blood type A and gynecological tumors. Endometrial and ovarian cancer is more common in women with blood type A than in other blood groups, and blood type A is also associated with poor prognosis in the same tumors. The possible reason for these findings is currently discussed in detail, considering the possible biological importance given to the ABO group system in the complex activities of the immune system.[11]

According to a study conducted in India, blood group B and marriage age between 11 and 20 years were significantly associated with cervical carcinoma.[12] Region of residence, parity and religion reveal a varying risk for cervical carcinoma. Another study concluded that blood group B could be considered a risk factor for cervical carcinoma.[13] Another study also shows that early-stage cervical cancer patients with non-O blood type have poorer 5-year survival than those with O blood type, and this has been proven during the first 5 years.[14]

Tyagi et al.[15] found that AB blood group has a significant higher risk compared to the stable blood group O in relation of carcinoma cervix. In our study, AB blood group was found to be significantly higher in patients with cervical cancer.

They reported the presence of an A-like antigen (MRG-1) in cervical tissues and suggested that persons with blood group A and AB, thereby lacking antiA antibodies are more susceptible to tumours.[16]

A systematic review and meta-analysis found that the risk of developing ovarian cancer is significantly increased in individuals with blood types A and AB. However, no significant effect of ABO blood groups on the overall survival of ovarian cancer patients was found.[17]

In a subgroup of patients with high-grade serous adenocarcinoma, blood groups B and AB were associated with a better 5-year cancer-specific survival rate compared with blood groups A and 0 [(60.3±8.6% vs. 43.8±3%) ,6). p=0.04)].[18]

Another study showed that the presence of B antigen (B/AB) was an unfavorable prognostic factor in ovarian carcinoma, especially in FIGO stages I, IV and menopausal patients.[19]

While blood group A was a positive factor for endometrial cancer patients in two studies.[20,21] In another study, no relationship was found.[22]

Blood type screening, when compared to the current gold standard, is unlikely to assist in the early-stage diagnosis of endometrioid endometrial carcinomas. Furthermore, a specific blood type does not increase the risk of recurrence or undifferentiated type endometrial carcinoma.[23]

Loss of expression of normal A, B, and O (ABO) blood group antigens in tumor tissue has been associated with the clinical behavior of certain epithelial cancers. Early recurrence is observed in 78% of patients with loss of blood group antigens. The loss of blood group antigens is the most significant variable associated with early recurrence.[24]

It has been suggested that blood group-associated antigens play a role in the adhesion of trophoblasts, inflammatory cells, and metastatic tumor cells to endothelial cells in the vascular system.[25]

In general, non-O blood groups are more susceptible to diseases compared to blood group O. Increasing awareness among people about this could be beneficial because individuals with high-risk blood groups can be screened, and they can be educated to modify their lifestyles, health behaviors, and habits.[26]

Additional studies are needed to clarify whether blood types are associated with increased cancer risk and to determine how antigen expression affects tumorigenesis.

Study Limitations

The limitations of our study arise from the small patient cohort and single center. Prospective studies with large cohorts will contribute more to science.

CONCLUSION

There are studies indicating a significant relationship between blood groups and various diseases. The expression of blood group antigens on blood cells and other epithelial surfaces acting as receptors or signal transducers contributes to these findings. The possibility of ABO antigens serving as receptors in tumor structures caused by infections, such as cervical cancer, should not be overlooked. In this regard, the significantly higher prevalence of cervical cancer in individuals with AB Rh (+) blood type, carrying A, B, and Rh antigens, can be explained concerning the population.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of İstanbul Prof. Dr. Cemil Taşçıoğlu City Hospital Clinical Researches Ethics Committee (Date:26.12.2022, Decision No:366).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Weissinger M, Kommoss S, Jacoby J, et al. Multiparametric dual-time-point [18F] FDG PET/MRI for lymph node staging in patients with untreated FIGO I/II cervical carcinoma. *J Clin Med.* 2022;11(17):4943.
2. Wright JD, Matsuo K, Huang Y, et al. Prognostic performance of the 2018 International Federation of Gynecology and Obstetrics Cervical Cancer Staging Guidelines. *Obstet Gynecol.* 2019;134(1):49.
3. Berek JS, Matias-Guiu X, Creutzberg C, et al. FIGO staging of endometrial cancer: 2023. *Int J Gynaecol Obstet.* 2023;162:383.
4. Torre LA, Trabert B, DeSantis CE, et al. Ovarian cancer statistics, 2018. *CA Cancer J Clin.* 2018;68(4):284.
5. Şahin F, Aydın E, Öcal EU, et al. Evaluation of colposcopy and LEEP results performed in gynecology and gynecological oncology surgery services. *Eur J Gynaecol Oncol.* 2024. doi:10.22514/ejgo.2023.071
6. Yamamoto F, Cid E, Yamamoto M, et al. ABO research in the modern genomics era. *Transfusion Med Rev.* 2012;26(2):103-118.
7. Canan E. İstanbul ilinde ABO ve Rh kan grupları dağılımının analizi. *Dicle Tıp Derg.* 2019;46(2):241-246.
8. Lin S, Cao Y, Zhu K, et al. Identification of a novel prognostic signature based on N-linked glycosylation and its correlation with immunotherapy response in hepatocellular carcinoma. *J Hepatocell Carcinoma.* 2023;10:1749-1765.
9. Thakur SK, Sompal S, Dinesh Kumar N, et al. Link between human ABO blood groups with diseases influencing blood donors and recipients frequency at RBTC, Delhi, India. *Bioinformation.* 2023;19(5):576-581.
10. Cozzi GD, Levinson RT, Toole H, et al. Blood type, ABO genetic variants, and ovarian cancer survival. *PLoS One.* 2017;12(4):e0175119.
11. Marinaccio M, Traversa A, Carioggia E, et al. Blood groups of the ABO system and survival in gynecological tumors. *Minerva Ginecol.* 1995;47(3):69-76.
12. Kai LJ, Raju K, Lingaiah HKM, et al. Importance of blood type and social factors in carcinoma cervix in a semi-urban population in India. *Asian Pac J Cancer Prev.* 2013;14(8):4811-4814.
13. Fotra R, Upma U, Gupta S, et al. Association of ABO and Rh blood groups with the carcinoma of the cervix with special reference to Jammu region. *Biosci Biotech Res Asia.* 2011;8(1):313-316.
14. Hanprasertpong J, Jiamset I. Atjimakul T. Prognostic value of ABO blood group in patients with early stage cervical cancer treated with radical hysterectomy with pelvic node dissection. *Tumor Biol.* 2016;37(6):7421-7430
15. Tyagi SP, Tiagi GK, Pradhan S. ABO blood grops in relation to cancer cervix. *Indian J Med Sci.* 1967;21:611-615.
16. Vaillant AJ, Bazuaye P, McFarlane-Anderson N, et al. Association between ABO blood type and cervical dysplasia/carcinoma in Jamaican women. *Brit J Med Med Res.* 2013;28;3(4):2017-2021.
17. Razzaghi N, Seraj H, Heydari K, et al. ABO blood groups associations with ovarian cancer: a systematic review and meta-analysis. *Indian J Gynecol Oncolog.* 2020;18(4):112.
18. Seebacher V, Polterauer S, Reinthaller A, et al. AB0 blood groups and rhesus factor expression as prognostic parameters in patients with epithelial ovarian cancer - a retrospective multicenter study. *BMC Cancer.* 2018;18(1):447.
19. Song Q, Wu JZ, Wang S, Chen ZB. ABO blood type is an independent prognostic factor in ovarian cancer patients. *J Cancer.* 2019;10(26):6754-6760.
20. Xu WH, Zheng W, Xiang YB, et al. ABO blood type is associated with endometrial cancer risk in Chinese women. *Chin J Cancer.* 2011;30(11):766-771.
21. Mandato VD, Torricelli F, Mastrofilippo V, et al. Prognostic impact of ABO blood group on type I endometrial cancer patients- results from our own and other studies. *J Cancer.* 2017;8(14):2828-2835.
22. Gitas G, Proppe L, Alkatout I, et al. Is ABO blood group a risk or prognostic factor for patients with endometrioid endometrial cancer? a retrospective analysis in Germany. *Blood Transfus.* 2020;18(6):465-470.

23. Şahin F, Odacılar AŞ, Günkaya OS, et al. Is neutrophil lymphocyte ratio magic or not? *J Health Sci Med.* 2023;6(3):618-622.
24. Raev SA, Raque M, Kick MK, Saif LJ, Vlasova AN. Differential transcriptome response following infection of porcine ileal enteroids with species A and C rotaviruses. *Virol J.* 2023;20(1):238.
25. Teuwen LA, Geldhof V, Pasut A, et al. COVID-19: vascular system released. *Nature Rev Immunol.* 2020;20(7):389-391.
26. Abegaz SB. Human ABO blood groups and their associations with different diseases. *Biomed Res Int.* 2021;2021:6629060.