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ABO blood groups and Rh factor are risk factors for Epithelial Ovarian Cancer?

Görker SEL[1], **Anıl T Çakır**[2], **Müge Harma**[3], **Mehmet I Harma**[3]

[1]Zonguldak Bülent Ecevit University, Department of Obstetrics and Gynecology, Zonguldak, Turkey
[2]Zonguldak State Hospital of Gynecology and Pediatrics, Department of Gynecologic Oncology, Zonguldak, Turkey
[3]Zonguldak Bülent Ecevit University, Department of Gynecologic Oncology, Zonguldak, Turkey

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ABSTRACT

Objective(s): The initial aim of this study is to research the allocation of blood types ABO and Rh factor antigens in patients with epithelial ovarian cancer (EOC). *Design:* Retrospective *Setting:* University Hospital (Tertiary center) *Subjects:* From the records at Zonguldak Bulent Ecevit University Faculty of Medicine Hospital in the period January 2010- June 2018, data on 100 EOC patients were obtained concerning blood groups ABO and Rh factor in 90 women. *Intervention(s):* The control group was constituted from the Zonguldak Bulent Ecevit University Faculty of Medicine Hospital Blood Transfusion Center and included 17065 females, to make reliable comparison, same region-same gender. *Main Outcome Measure(s):* Blood types ABO and Rh factors, patients having EOC. *Result(s):* Data on 90 women with EOC and recorded blood types ABO and Rh factors were taken for retrospective analysis. Although, blood type O was seemingly related with higher risk of EOC, this difference was not statistically significant. Also, blood type B was seemingly allocated with low risk of EOC, albeit this difference was not statistically significant. *Conclusion(s):* Most

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previous studies have reported increased cancer of the ovaries associated with the A blood type compared to the O group. Contrary to our data, Zhang et al found that, blood type O is allocated with lower risk of cancer of the ovaries. Our studies results show possible allocation between the O blood type and higher risk of EOC B blood type and decreased probability EOC.

Keywords: ABO, Blood groups, Rh, EOC, ovarian cancer

1. INTRODUCTION

240,000 women are diagnosed with ovarian cancer every year and living with five-year survival below 45% (Webb et al., 2017). Cancer related deaths amongst female patients are getting higher as years passed, Epithelial ovarian cancer (EOC) is at the fourth order in this category in the developed world (Jayson et al., 2014). The higher death rate is because of the late admission with entirely metastatic disease within the abdomen or further (Jayson et al., 2014). EOC especially occurs in females that had history of gynecologic surgery, assisted reproductive drugs, smokers and higher age, adiposity, estrogen like hormone therapy; family history of ovarian, breast, or colorectal cancer, fatty diet, and therapy causing immune-suppression (Salehi et al., 2008).

Karl Landsteiner discovered the blood group system of ABO in the year of 1900 (Giangrande, 2000). His research led to identification of major blood groups, compatibility testing, and subsequent transfusion practices (Mitra et al., 2014). Aird et al., in 1953 was the first research to find probable association between major blood groups and several cancer risks, by showing blood group A antigen relationship to gastric cancer (Yuzhalin et al., 2012). After their attempt, numerous case-control trials studied on this relationship, suggesting a probable relation between major blood types and higher or lower risks of several neoplasia and diseases (Yadav et al., 2018; Franchini et al., 2012; Gates et al., 2012; Wang et al., 2012), higher risk of cancer of the ovary for blood type B, as well (Gates et al., 2011).

The initial aim of this study is to research the allocation of blood types ABO and Rh factor antigens in patients with EOC.

2. SUBJECTS - METHODS

This research was approved by the ethics committee for clinical studies with the approval number of 2018-213-24/10-6 of Zonguldak Bulent Ecevit University (ZBEU), Zonguldak, Turkey.

Before the research began, whole participants gave informed consent. From the medical records at ZBEU Research and Health Center Hospital in the period January 2010- June 2018, data on 100 EOC patients were obtained concerning blood groups ABO and Rh factor in 90 women. Ten patients' blood groups could not be reached. The total number treated for EOC during this period was 100.All of the patientsthat researched in this trial were pathologically confirmed EOC.

The FIGO 2014 criteria were used in EOC staging. The standard surgical procedure included a median laparotomy incision, examination of intraperitoneal organs, ascites or peritoneal lavage aspiration for cytology, biopsy from suspicious sites from peritoneal examination, total hysterectomy and salpingo-oophorectomy, omentectomy, appendectomy and pelvic para-aortic lymphadenectomy.

The control group was constituted from the ZBEU Faculty of Medicine Hospital Blood Transfusion Center and included 17065 females, to make reliable comparison; same region-same gender. Ninety patients were subtracted from 17065 patients while making comparison between EOC and EOC free (control) patients. The percentage of blood types ABO and Rh factors in the control group reflects the general female population of Western Black sea region of Turkey. The percentages of the blood groups of the control group were similar to the country's general profile, as well.

Statistical analysis was studied with SPSS for Windows 19.0, using the Pearson chi-square test. Only p value below 0.05 was considered significant. Calculated values were expressed as numbers and proportions.

3. RESULTS

Data on 90 women with EOC and recorded blood types ABO and Rh factors were taken for retrospective analysis. The data regarding blood types ABO and Rh factors between EOC and control patients are presented in Tables 1 and 2, respectively. The data regarding allocation of blood types ABO and Rh factors in EOC versus control patients are presented in Tables 3 and 4, respectively.

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Table 1 Blood groups allocation between EOC patients and general population

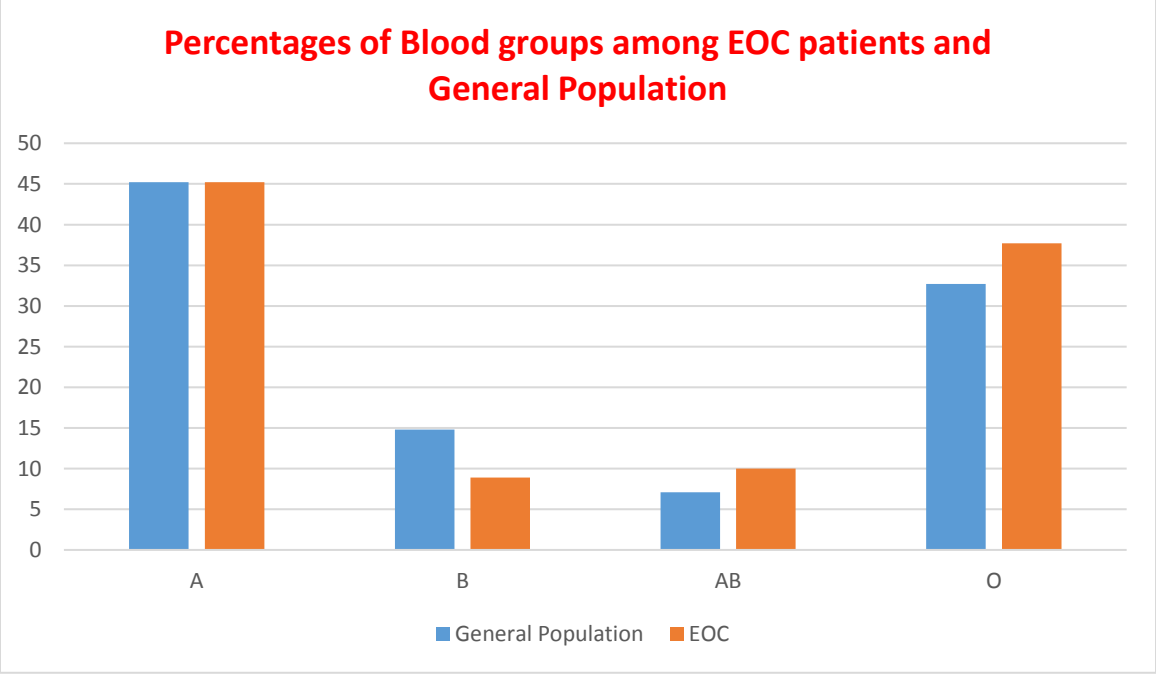
Blood groups	EOC		General Population		Total
	Number	Percent in row	Number	Percent in row	
A	39	0.5%	7674	99.5%	7713
B	8	0.3%	2533	99.7%	2541
AB	9	0.7%	1208	99.3%	1217
O	34	0.6%	5560	99.4%	5594
Total	90		16975		17065

Table 2 Rh factor allocation between EOC patients and General Population

Rh	EOC		General Population		Total
	Number	Percent in row	Number	Percent in row	
Rh +	80	0.5%	15045	99.5%	15125
Rh -	10	0.5%	1930	99.5%	1940

Table 3 Blood groups allocation among EOC patients and General Population

Blood groups	General Population		EOC	
	Number	Percent in column	Number	Percent in column
A	7713	45.2%	39	45.2%
B	2541	14.8%	8	8.9%
AB	1216	7.1%	9	10.0%
O	5594	32.7%	34	37.7%



Bar Chart 1

As it is shown on Table 3 and on bar chart 1, EOC patients were distributed regarding to their blood types, the ratio of blood group A was similar between EOC versus general population (45.2% vs 45.2%). O blood group was seemingly related with higher risk of EOC (37.7% vs 32.7%), albeit not statistically significant ($p>0.05$) as shown on Table 3 and on bar chart 1. Also, B blood type was seemingly associated with low risk of EOC (8.9% vs 14.8%), albeit this difference was not statistically significant ($p>0.05$).

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Table 4 Rh factor allocation among EOC patients and General Population

Rh	General Population		EOC	
	Number	Percent in column	Number	Percent in column
Rh +	15124	88.6%	80	88.9%
Rh -	1940	11.3%	10	11.1%

As shown on Table 2 and Table 4, Rh factor allocation between groups were almost the same, not statistically significance was observed ($p>0.05$). Zonguldak Bulent Ecevit University Faculty of Medicine Hospital's blood groups and Rh factor distribution were similar to the country's general data (Salduz et al., 2015).

4. DISCUSSION

The blood typesABO have been allocated with several diseases. For instance, they have found to have a profound influence on hemostasis (Zhang et al., 2012). Higher allocation of myocardial infarction, ischemic stroke and venous thromboembolism was observed with blood types A and AB, probably with functional ABO glycol transferases modulation of thrombosis (Mitra et al., 2014; Wiggins et al., 2009). An increased risk of cerebral venous thrombosis has been suggested in blood types other than O blood type (Tufano et al., 2013).

Most previous studies have reported increased cancer of ovary risk associated with blood type A compared to the O group (ORs ranged from 1.17 to 1.28) (Björkholm, 1984; Henderson et al., 1993; Osborne et al., 1963; Poole et al., 2012; Zhang et al., 2014). Meantime a recent study of Veronika Seebacher et al., concludes that neither AB0 blood groups nor Rhesus factor expression were associated with clinico-pathological parameters, recurrence-free, cancer-specific, or overall survival (Seebacher et al., 2018). On the other hand Gates et al found that presence of the B antigen was positively allocated with cancer of the ovaries, whereas blood type A was not associated with this high risk (Gates et al., 2011). Yuzhalin et al., researched that blood types other than O having high the risk of ovarian cancer by 40-60%, and this allocation was strongest in women with the AB blood type (Yuzhalin et al., 2012). Blood type A was strongly associated with high risk of ovarian cancer in premenopausal, but that relationship was not observed in post menopausal group (Yuzhalin et al., 2012). Contrary to our data, Zhang et al., found that, blood type O is related with lower risk of ovarian cancer (Zhang et al., 2014). In this study we found that blood type O is related with higher percentage of EOC (38.2% vs 32.7%), although statistically not significant ($p>0.05$).

Direct mechanism of the effect of ABO blood types and Rh factor on cancer development is not known. Nonetheless, there are several hypotheses about this relation. For instance; A and B blood type antigens could increase mobility of the cells and increase the relations between tumor cells (Le Pendu et al., 2001). Also, it has been shown that ABO antigens contribute to the resistance to apoptosis (Melzer et al., 2008). Forssmann antigen is almost identical to the A antigen, that is synthesized primarily on stomach and colon tumors (Smith et al., 1992). Therefore, carriers of blood group A may have lower tumor immune response due to reduced ability to recognize and attack tumor cells that present Forssmann antigen (Yuzhalin et al., 2012).

Recent studies have reported associations between ABO blood types and levels of soluble ICAM-1 (Pare et al., 2008), TNF-α and soluble E-selectin (Melzer et al., 2008; Paterson et al., 2009; Qi et al., 2010). The strengths of this study include the availability of electronic data about blood groups and pathology reports. None of the blood groups were self-reported, all of them were noted down from the data of our hospital, to avoid misclassification. We made comparison between the same population's blood groups, including same hospital and same gender. The limiting factors of our study were small sample size of EOC patients and we did not include and exclude contributing factors for the EOC because of the retrospective design of the study.

5. CONCLUSION

Our results are suggesting a probable relationship between the O blood type and higher risk of EOC, B blood type and lower percentage of EOC. Nevertheless, with this conflicting results of previous trials, prospective large sample sized studies are needed to further conclude this relationship.

Acknowledgement

In our research we strictly obeyed to "Compliance with Ethical Standards". Informed consent was taken from patients.

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Conflict of interest statement

The authors declare none of conflict of interest. All authors participate equally for the contribution of the manuscript.

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