

RESEARCH COMMUNICATION

ABO Blood Group and Risk of Pancreatic Cancer in a Turkish Population in Western Blacksea Region

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Abstract

Background: We aimed to investigate the relationship between blood groups and pancreatic cancer in a Turkish population in Western Blacksea region. **Methods:** This is a retrospective study. Zonguldak Karaelmas University outpatient oncology clinic records were screened for the period between 2004 and 2011. **Results:** The median age of patients were 56 (± 16) and 132 of 633 study population had pancreatic cancer. Pancreatic cancer patients had significantly higher rates of blood group A compared to controls (OR 1.8, 95% CI, p 0.005). Rates of blood group AB was significantly lower than the control group (OR 0.37, 95% CI, p 0.04). The median survival (IR) time in subjects having the blood groups A, B, AB and O were 7.0 (1-28), 7.0 (2-38), 10 (2-36) and 9.0 (2-48) months respectively; the blood group O had significantly higher overall survival (OS) compared to the non-O groups (p 0.04). **Conclusions:** Pancreatic cancer patients had more common blood group A in our population. Moreover, blood group AB appeared to be a protective factor against pancreatic cancer in our population. Blood group O had a significantly longer survival compared to non-O, regardless of prognostic factors.

Keywords: Blood group - pancreatic cancer - survival - Turkey

Asian Pacific J Cancer Prev, 13, 131-133

Introduction

Pancreatic cancer is one of the most commonly seen type of cancer in the world and it is the 4th leading cause of cancer-related deaths in Western populations. High mortality may be caused by late diagnosis and poor chemotherapeutic response in advanced stages of disease (Jemal et al., 2009). While curative surgery is the only option for longterm survival, only 10% of the patients can experience longterm survival (Sener et al., 1999). As minimal contribution to survival from cancer has been observed during the last 30 years, individual predisposing risk factors has become the point of interest in the last decade (Sant et al., 2009). For pancreatic cancer, many genetic and environmental risk factors were defined. The main ones include smoking, obesity, diabetes mellitus, chronic pancreatitis and familial history of pancreatic cancer (Lowenfels et al., 2006). Relationship between ABO blood groups and pancreatic cancer has regained its popularity lately. In a Spanish study (Vioque et al., 1991), a statistically nonsignificant elevation was detected for the blood group A among 108 patients with pancreatic cancer and 374 healthy controls. In an Italian study (Annese et al., 1990), an increased risk for blood group B and a decreased risk for blood group O were observed. In a prospective cohort study (Wolpin et al., 2009), approximately 107,500 American healthcare staff members showed an increased overall risk for blood groups A, B and AB. In a

recent genomic study (Amundadottir et al., 2009), single nucleotide polymorphism (SNP) in intron 1 of ABO (rs505922) gene was found to be a genetic risk factor for pancreatic cancer (OR 1.20; 95% CI 1.12-1.28). In a large study performed in China, blood groups A and AB were significantly more common in 1431 patients with pancreatic cancer and 1449 controls (OR 1.36 and 1.39 95%CI) (Ben et al, 2011). In the light of these studies, our study aimed to investigate the relationship between blood groups and pancreatic cancer in a Turkish population in Western Blacksea region as there is an interpopulation variation for this condition.

Materials and Methods

This is a retrospective study and the ethical approval was obtained from the ethical committee of Zonguldak Karaelmas University, Turkey. To estimate the ABO frequencies in our region, Zonguldak Karaelmas University Outpatient oncology clinic's records were screened for the period between 2004 and 2011. Of 184 pancreatic cancer patients in the registry, 132 had a full historical or current ABO blood group data and survival records were also available. 350 healthy controls and 145 cancer patients without pancreatic cancer were also included into the study. For all patients the stage of pancreatic cancer was determined based on the 2002 UICC cancer staging system. Only patients with adenocarcinoma of pancreas

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are included, whereas patients having neuroendocrine tumors, cysts, or patients who were unable or unwilling to give informed consent were excluded. We sampled controls stratified by age and sex to match the distribution of the case series. ABO blood type and Rh factor data were obtained using routine clinical tests. Patient follow-up was obtained through review of hospital records.

Statistical analysis

All statistical analyses were conducted by using the SPSS 18.0 statistical software program (SPSS, Chicago, IL). Proportions of ABO blood groups for pancreatic cancer cases and regional blood donors were compared using Chi-square analysis. Data with normal distribution were analyzed using unpaired t test. Mann-Whitney U test was used for analyzing not normally distributed data. Correlations were studied using Spearman’s rho test. All p values were calculated as two-tailed. P values under 0.05 were considered as statistically significant.

Results

Patient characteristics

The median age of patients were 56(±16), 328 patients were women and remaining 305 patients were men. Demographic features of 132 pancreatic cancer cases and controls are shown in Table 1. Pancreatic cancer patients had significantly higher rates of blood group A compared to controls (OR 1.8, 95%CI, p 0.005). Rates of blood group AB was significantly lower than the control group (OR 0.37, 95% CI, p 0.04). Blood group 0 and B were not significantly different from the healthy controls. When pancreatic cancer patients are compared to the cancer patients having other cancer types, there were no significant differences between the blood groups of A,

Table 1. Demographic Features of Cases, Healthy Controls and Non-pancreatic Cancer Controls

Variable	Pancreas Cancer	Control Group	Odds Ratio/P (chi-square)	Cancer Group	Odds ratio
Age ±SD	63±12	61±18	0.1	58±12	0.3
Women	49	156	0.1	82	0.001
Men	83	194	0.1	63	0.001
A rh+/rh-	68	130	1.8 (0.005)	66	
B rh+/rh-	19	70	0.68 (0.2)	26	0.77
AB rh+/rh-	6	39	0.37 (0.04)	18	0.33
O rh+/rh-	39	111	0.91 (0.7)	35	
Smoking	59(44%)	78(22%)	<0.0001	60(41%)	0.66
Diabetes	12(7.5%)	28(8%)	P 0.9	15(10%)	0.88

B, AB and O. When we analyzed the pancreatic cancer group, rate of blood group A was significantly higher than the blood groups 0, B and AB (p values were 0.004, <0.001, <0.001 respectively). Blood groups in pancreatic cancer patients are shown in Figure 1. Female sex ratio was significantly lower in the pancreatic cancer group than control cancer group because of female breast cancer population in the cancer control group. We found no significant association between the Rh type and pancreatic cancer risk (OR 1.05 95%).

Overall Survival

The median survival (IR) time in subjects having the blood groups A, B, AB and O were 7.0 (1-28), 7.0 (2-38), 10 (2-36) and 9.0 (2-48) months respectively; the blood group 0 had significantly higher overall survival (OS) compared to the non-0 group (p 0.04) and are presented in Figure 2. There were no differences in age, sex, smoking status, chemotherapy, stage of cancer between the blood group 0 and blood group non-0. There was no significant relation between the blood groups and progression free survival.

Discussion

In this study conducted on Turkish population in Western Blacksea region, blood group A was significantly more common in patients with pancreatic cancer. Blood group A seemed to be a risk factor for pancreatic cancer in our population as well. Blood group AB can be considered as a protective factor against pancreatic cancer, due to its statistically significant rarity. Another important result of our study was the longer survival time observed in patients with blood group 0, compared to all other blood groups.

Relationship between ABO blood group antigens and cancer has been investigated for decades and, today, the relationship between gastric cancer and blood group A is widely accepted (Aird et al., 1953). Similarly, pancreatic cancer is also under extensive research. Main conditions associated with familial pancreatic cancer include BRCA2 (hereditary breast and ovarian cancer syndrome), LKB1 (Peutz-Jeghers syndrome), p16/CDKN2A (FAMMM) and PRSS1 (hereditary pancreatitis) (Wolpin et al., 2009). In retrospective studies performed in 60s and 70s, a further relative risk between blood groups 0 and B and pancreatic cancer, and an increased risk between blood group A and pancreatic cancer were also mentioned (Vogel, 1970.,

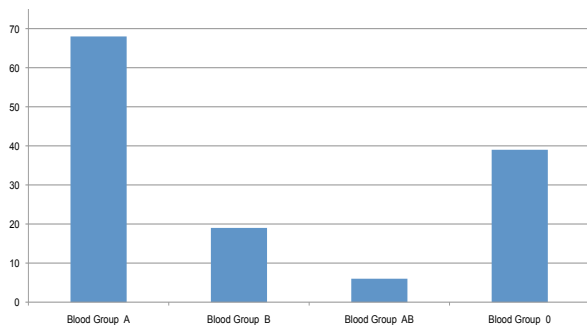


Figure 1. Blood Groups in Pancreatic Cancer Patients

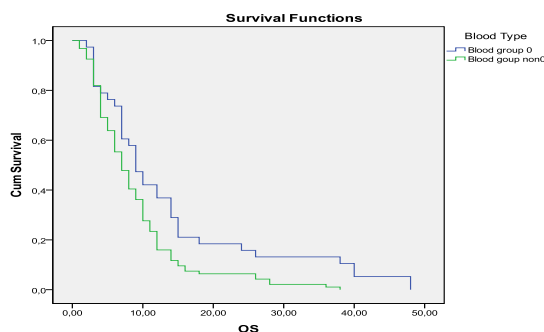


Figure 2. Overall Survival of Blood Group 0 and Blood Group Non 0 Patients

Newell et al., 1974). There are limited numbers of prospective studies for the relationship between pancreatic cancer and blood group, varying between populations. In two large prospective studies, the highest risk for pancreatic cancer was found in blood group B, but this study included the determination of blood group antigen for the declaration of the participants (Wolpin et al., 2009). In a study performed on approximately 107500 healthcare staff members, the risk for pancreatic cancer was high in all groups except the blood group O (Wolpin et al., 2009). Our study is the first study that investigated this relationship in Turkish population. While 51% of our patients diagnosed with pancreatic cancer had blood group A, this percentage was significantly higher compared to other blood groups and healthy control group.

ABO antigens are expressed in gastrointestinal, bronchopulmonary and urogenital system epithelial cells, in addition to erythrocytes (Hakomori S, 1999). In pathology studies, this expression was also demonstrated in pancreatic cells. It is thought that ABO-related glucosyltransferase-specific alterations may play a role in pancreatic tumorigenesis. Glycoconjugates play an important role in intracellular adhesion and membrane signalization as well as in the immune response of the host. The alterations of these surface molecules may promote the process of malignancy (Itzkowitz et al., 1987, Zhang et al., 1997, Hakomori, 1999, Roseman et al., 2001). In two recent genomic studies, a significant correlation was shown between single nucleotide polymorphisms (SNPs) in ABO gene locus and inflammation markers. In CHIANTI study performed on 1200 subjects, it was shown that there is a correlation between 2 SNPs in ABO locus and tumor necrosis factor, as an inflammatory marker leading to apoptosis in pancreatic ductal cells (Melzer et al., 2008). Although the correlation between the risk for pancreatic cancer and blood group is not clearly known, there are some studies that showed that inflammatory cytokines were higher in these blood groups. It was demonstrated that vWF values were higher in blood group AB (Souto et al., 2000). All these data suggest us that blood group antigens may play an important role in the pathogenesis of pancreatic cancer, by leading to an alteration in the potential systemic inflammatory response.

Similar to other studies, our study included significantly more subjects with blood group A, but significantly less subjects with blood group AB. This might be caused by our small number of subjects as well as by interpopulation variation.

Correlation between blood groups and survival in pancreatic cancer has not been adequately mentioned in the literature. In a recent study conducted in China, for the first time, the survival of the patients with blood group O was found higher compared to other blood groups in curable pancreatic cancers (Ben et al., 2011). Again, in our study, the survival was significantly longer in the patients with blood group O (13.8 vs 8.8 months, $p < 0.04$). Moreover, two groups did not show a significant difference in terms of cancer stage, chemotherapeutic status, gender or other prognostic factors.

Consequently, our study has been the first study that investigated this relationship in Turkish population.

Consistent with many other population data in the literature, blood group A was more common in our population. Moreover, blood group AB is considered as a protective factor against pancreatic cancer in our population as well. Blood group O had a significantly longer survival compared to other blood groups, regardless of prognostic factors, suggesting that a blood group other than O is a poor prognostic factor.

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