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# Association between ABO Blood Group and Various Types of Cancer: A Case–Control Study in Greek Adults

**Nikolaos Andreas Chrysanthakopoulos**

*Oncologist (MSc Oncol), PhD in Oncol (cand), Department of Pathological Anatomy, Medical School, University of Athens, 401 General Military Hospital of Athens, Athens, Greece*

## ABSTRACT

**Introduction:** The association between ABO blood group and cancer has been identified in many epidemiological researches. The aim of the current research was to investigate the association between ABO blood group and the risk of several types of cancer in a Greek adult population. **Materials and Methods:** A total of 459 individuals who suffered from various types of cancer and 918 non-cancer individuals were enrolled. Blood group data obtained from registration on identity patient's card. The associations between ABO blood group and cancer estimated using a multivariate logistic regression analysis model, whereas a multinomial model was carried out to estimate adjusted odds ratios for each type of cancer separately. **Results:** The risk of overall cancer in blood groups A and B individuals was significantly higher than that in O and AB groups, ($P = 0.001$, OR = 1.96, 95%CI = 1.33–2.87, and $P \leq 0.0001$, OR = 2.04 95% CI=1.43–2.90, respectively). Compared to blood type O, blood type A was significantly associated with an increased risk of gastric ($P = 0.002$, OR = 2.55, 95% CI = 0.55–4.30), colorectal ($P = 0.046$, OR = 2.06, 95%CI = 0.82–2.58), pancreatic ($P = 0.034$, OR = 2.23, 95% CI = 1.02–2.83), and lung cancer (LC) ($P = 0.022$, OR = 2.78, 95% CI = 1.63–5.49), whereas blood type B was significantly associated with an increased risk of esophagus cancer ($P = 0.051$, OR = 1.26, 95% CI = 0.83–1.50), after adjusting for age, gender, educational and socio-economic status, smoking, and family history of cancer. **Conclusion:** The overall cancer risk in blood groups A and B individuals was significantly higher compared to blood type O and AB, whereas blood type A was significantly associated with an increased risk of gastric, colorectal, pancreatic, and LC.

**Key words:** ABO blood group, Adults, Cancer, Risk factors

## INTRODUCTION

Cancer is the second leading cause of death worldwide and responsible for 9.6 million deaths in 2018. In Europe, cancer causes the second highest number of deaths after cardiovascular disease. Its development is a result of interactions between genetics and environmental factors.

Genetic factors include advanced age, male gender, cancer family history, and genetic susceptibility. Especially, genetic mutations are responsible for 5–10% of all cancer cases.[1] Environmental etiological and risk factors include cigarette smoking, and obesity, previous diseases such as infections with hepatitis B or C (HBV/HCV), chronic obstructive pulmonary disease, and radiation.

However, the mentioned etiological or risk factor scan explain only a part of cancer incidence as its clear etiology still remains unknown.[2,3] Hereditary types of cancer show, in general, a low prevalence, however, inherited biomarkers such as ABO blood group have been associated with the risk of various diseases and types of cancer according to the previous and current researches.[3]

**Address for correspondence:**
Dr. Nikolaos Andreas Chrysanthakopoulos, 35, Zaimi Street, PC 26 223, Patra, Greece.

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The ABO blood groups system discovered decades ago,[4] is the most immunogenic of all the blood group antigens, its antigens are biomarkers expressed in various types of cells including erythrocytes, mucosa, lung epithelial, and gastrointestinal cells.[5,6] The ABO gene is an autosomal gene that is located on chromosome 9 at q34.1–q34.2 region and encodes for a specific glycosyltransferase enzyme that adds a glucose residue to a carbohydrate structure, the H antigen, that is present in the membrane of erythrocytes and other types of endothelial and epithelial cells as already mentioned.[7] Distribution of the four different blood groups varies among countries in different geographical, ethnic, and socioeconomic groups.[8] In general, blood group shows the highest prevalence, while blood Group AB shows the lowest. Although the elaborate physiologic function of the ABO blood group antigens remains unknown, no disease results from the lack of ABO blood group antigens expression.[7]

An association between ABO blood group and various diseases was proposed 50 years ago.[9] In recent years, several reports haves shown that ABO blood group was associated with many diseases and pathological conditions and various types of cancer,[10,11] although the explanation for that relationship is still not understood. Most recent reports based on the finding that such an association was initially suggested through the observation that gastric cancer (GC) patients were more likely to have blood type A than control individuals,[12] documented a relative link between susceptibility to cancer and ABO blood group or found a relationship between ABO blood group and risk of certain malignancies.

In herited human ABO blood group, antigens were associated with various types of malignancies including pancreatic,[10,13-20] renal cell,[21] skin,[11] ovarian,[22,23] esophageal,[16,24-26] hepatocellular,[27,28] colorectal,[16,29] oral cavity,[30-33] larynx,[34] bladder,[35] breast,[36] gastric,[12,16,17,37-40] prostate,[41] and lung cancer (LC),[16,42-45] but the associations, in general, were inconsistent. For instance, an association between ABO blood group and nasopharyngeal cancer (NPC) remains controversial as a research by Seow *et al.*[46] demonstrated the absence of such an association, whereas Turkoz *et al.*[47] found that ABO blood group was associated with NPC susceptibility. Similarly, previous reports investigated the possible association between ABO blood group antigens and risk of LC and proposed a possible association; however, the data on the role of ABO blood group factor in LC are limited and inconsistent.[42,44,45]

Most previous studies were based on self-reporting of blood type which is prone to recall and information biases. In addition, the relative small sample sizes of most previous studies have limited the opportunity to comprehensively estimate the link between ABO blood group and cancer risks, particularly for rare types of cancers.

Similar retro- or prospective studies of the association between ABO blood group and cancer risk have not been carried out in Greece.

The aim of the present retrospective case–control study was to investigate the possible association between ABO blood groups and risk of cancer overall and separately, in several organs in an adult population sample in Greece.

## MATERIALS AND METHODS

### Study design and study sample

A total of 459 individuals, 200 males and 259 females, who were suffering from various types of cancer and 918 non-cancer individuals, 473 males and 445 females, aged 45–74 years who were selected from two private medical practices enrolled in the study.

The current study was a retrospective case–control study. The case group included patients with several types of cancer and its diagnosis was confirmed according to histopathological examination of their medical files. The attempt was to choose the controls in such a way they can be the representatives of the population from which the cases were drawn. Thus, cases and controls were selected from the same city population in an effort to avoid or eliminate possible selection biases. In addition, the selection of controls was based on cases' environment, such as friends and colleagues. According to that method, eligible control individuals were selected from those, who were subjected to routine health examinations at the mentioned practices, between 2015 and 2018. Both groups, cases and controls, were matched 2–1 with cancer patients for age (± 5 year), and gender in an effort to control potential confounders.

Cancer rates were estimated according to cancer mortality rates in 2012 as no data were available which concerned cancer incidence in Greece.[48]

Participants included in the study completed a baseline questionnaire about common risk factors for cancer. Thus, they completed a self-administered questionnaire which concerned information on their medical history, smoking status, socio-economic and educational level, and cancer family history. When at least one first-degree family member was diagnosed with cancer, the family history was considered positive for cancer. The cases who had distant metastases in any-one of the organs examined or had a medical history of other malignancies were excluded and included patients with newly diagnosed cancer who were out-patients of the mentioned medical practices in an effort to eliminate potential effects by known and unknown confounders. ABO blood group was confirmed by the medical files of the participants.

### Statistical analysis

The associations between ABO blood group and risk of overall cancer were assessed using univariate and multivariate logistic regression analysis. Adjusted odds ratios (AOR's) and 95% confidence interval (CI) were recorded as well. The independent variables were included in Wald method to assess gradually the variables which showed significant associations with the dependent one.

Finally, a multinomial model was carried out to estimate AOR's between ABO blood group and the risk of each type of cancer separately, after adjusting for potential confounders, such as age, gender, smoking status, educational and socio-economic level, and family history of cancer. In this analysis, blood type O was used as a reference group.

Statistical analysis was performed using the statistical package of SPSS ver.19.0. $P < 5\%$ ($P < 0.05$) was considered to be statistically significant.

## RESULTS

The distribution of blood groups of controls was similar to the general Greek population.

Cases and controls showed a mean age of 64.5 years (± 3.7). The distribution of cancer patients and controls with ABO group and the univariate analysis are shown in Table 1. According to univariate analysis age, educational level, smoking, cancer family history, and ABO blood group were found to be significantly associated with overall cancer risk. The same table shows that the frequency of overall cancer risk was significantly higher in blood Group A individuals ($P = 0.043$), whereas blood Group AB individuals had lower overall cancer risk as compared to controls.

Table 2 presents the distribution of each cancer type according to the variables examined.

Table 3 presents the results after performing of the multivariate regression model. Step1 – Enter method showed that smoking ($P = 0.000$, OR = 1.77, 95%CI = 1.39–2.26), cancer family history ($P = 0.000$, OR = 1.84, 95% CI = 1.45–2.33), A ($P = 0.001$, OR = 1.94, 95%CI = 1.32–2.85), and B ($P = 0.000$, OR = 2.01, 95% CI = 1.41–2.86) blood groups were significantly associated with overall cancer risk. Step 4 – Wald method showed that the mentioned indices, smoking ($P = 0.000$, OR = 1.72, 95% CI = 1.36–2.17), cancer family history ($P = 0.000$, OR = 1.85, 95% CI = 1.47–2.34), A ($P = 0.001$, OR = 1.96, 95% CI = 1.33–2.87), and B ($P = 0.000$, OR = 2.04, 95% CI = 1.4–2.90), including male gender ($P = 0.046$, OR = 1.27, 95% CI = 1.01–1.60), were significantly associated with overall cancer risk. The same table also shows AOR's and 95% CI.

Table 4 shows the AOR's and 95%CI of ABO blood group categories to each type of cancer.

**Table 1:** Univariate analysis of cases and controls regarding each independent variable examined

| Variables | Cases (No) (%) | Controls (No) (%) | *P*-value | Odds ratio | 95% confidence interval |
|---|---|---|---|---|---|
| Gender: Males | 259 (56.4) | 473 (51.5) | | | |
| Females | 200 (43.6) | 445 (48.5) | 0.086 | 0.82 | 0.66-1.03 |
| Age (years): 45–49 | 104 (22.7) | 277 (30.2) | | | |
| 50–59 | 164 (35.7) | 286 (31.2) | 0.010* | ___ | ___ |
| 60–69 | 157 (34.2) | 271 (29.5) | | | |
| 70+ | 34 (7.4) | 84 (9.2) | | | |
| Socio-economic level: Low | 287 (62.5) | 539 (58.7) | | | |
| High | 172 (37.5) | 379 (41.3) | 0.173 | 1.17 | 0.93–1.48 |
| Educational level: Low | 242 (52.7) | 828 (65.2) | | | |
| High | 217 (47.3) | 442 (34.8) | 0.000* | 0.60 | 0.48–0.74 |
| Smoking: No | 148 (32.2) | 480 (52.3) | | | |
| Yes | 311 (67.8) | 438 (47.7) | 0.000* | 0.43 | 0.34–0.55 |
| Cancer family history: No | 204 (44.4) | 476 (51.9) | | | |
| Yes | 255 (55.6) | 442 (48.1) | 0.010* | 0.74 | 0.59–0.913 |
| ABO blood group: O | 108 (23.5) | 244 (26.6) | | | |
| A | 225 (49.0) | 391 (42.6) | 0.043* | ____ | _____ |
| B | 80 (17.4) | 153 (16.7) | | | |
| AB | 46 (10.0) | 130 (14.2) | | | |

**P*-value: Statistically significant

**Table 2:** Distribution of each type of cancer according to independent variables

| Variables | OC and NPC | OEC | GC | CRC | HCC | PC | LC |
|---|---|---|---|---|---|---|---|
| | *n* (%) | *n* (%) | *n* (%) | *n* (%) | *n* (%) | *n* (%) | *n* (%) |
| Gender | | | | | | | |
| Males | 7 (70.0) | 5 (71.4) | 29 (60.4) | 38 (45.2) | 28 (53.8) | 28 (58.3) | 124 (59.0) |
| Females | 3 (30.0) | 2 (28.6) | 19 (39.6) | 46 (54.8) | 24 (46.2) | 20 (41.7) | 86 (41.0) |
| Age (years) | | | | | | | |
| 45–49 | 2 (20.0) | 1 (14.3) | 8 (16.7) | 28 (33.3) | 12 (23.1) | 8 (16.7) | 45 (21.4) |
| 50–59 | 3 (30.0) | 1 (14.3) | 25 (52.1) | 38 (45.2) | 15 (28.8) | 25 (52.1) | 57 (27.1) |
| 60–69 | 3 (30.0) | 3 (42.9) | 11 (22.9) | 15 (17.9) | 17 (32.7) | 10 (20.8) | 98 (46.7) |
| 70+ | 2 (20.0) | 2 (28.5) | 4 (8.3) | 3 (3.56) | 8 (15.4) | 5 (10.4) | 10 (4.8) |
| Socio-economic level | | | | | | | |
| Low | 6 (60.0) | 5 (71.4) | 32 (66.7) | 37 (44.0) | 27 (51.9) | 12 (25.0) | 168 (80.0) |
| High | 4 (40.0) | 2 (28.6) | 16 (33.3) | 47 (56.0) | 25 (48.1) | 36 (75.0) | 42 (20.0) |
| Educational level | | | | | | | |
| Low | 7 (70.0) | 4 (57.2) | 30 (62.5) | 32 (38.1) | 31 (59.6) | 17 (35.4) | 121 (57.6) |
| High | 3 (30.0) | 3 (42.8) | 18 (37.5) | 52 (61.9) | 21 (40.4) | 31 (64.6) | 89 (42.4) |
| Smoking | | | | | | | |
| No | 2 (20.0) | 1 (14.2) | 14 (29.2) | 18 (21.4) | 17 (32.7) | 13 (27.1) | 83 (39.5) |
| Yes | 8 (80.0) | 6 (85.7) | 34 (70.8) | 66 (78.6) | 35 (67.3) | 35 (72.9) | 127 (60.5) |
| Cancer family history | | | | | | | |
| No | 3 (30.0) | 2 (28.6) | 18 (37.5) | 35 (41.7) | 23 (44.2) | 20 (41.7) | 103 (49.0) |
| Yes | 7 (70.0) | 5 (71.4) | 30 (62.5) | 49 (58.3) | 29 (55.8) | 28 (58.3) | 107 (51.0) |
| ABO blood group | | | | | | | |
| O | 1 (10.0) | 1 (14.2) | 9 (18.8) | 21 (25.0) | 10 (19.2) | 13 (27.1) | 53 (25.2) |
| A | 3 (30.0) | 2 (28.6) | 21 (43.8) | 38 (45.2) | 24 (46.1) | 18 (37.5) | 119 (56.7) |
| B | 4 (40.0) | 2 (28.6) | 10 (20.8) | 13 (15.4) | 12 (23.1) | 12 (35.0) | 27 (12.8) |
| AB | 2 (20.0) | 2 (28.6) | 8 (16.6) | 12 (14.4) | 6 (11.6) | 5 (10.4) | 11 (5.3) |
| Total | 10 | 7 | 48 | 84 | 52 | 48 | 210 |

OC and NPC: Oral and nasopharyngeal cancer, OEC: Esophageal cancer, GC: Gastric cancer, CRC: Colorectal cancer, HCC: Hepatocellular cancer, PC: Pancreatic cancer, LC: Lung cancer

Gastric, colorectal, pancreatic, and LC were significantly associated with blood Group A, whereas esophageal cancer was significantly associated with blood Group B after performance of multinomial regression model and after adjusting for age, gender, educational level and socio economic status, smoking, and family history of cancer.

## DISCUSSION

The association between ABO blood type and many diseases has been investigated for more than 50 years; however, findings to date have little practical value as prevention indices.

The results showed that GC risk was higher among individuals with blood type A than those with blood type O. Many similar studies have found such an association, however, no clear evidence has been suggested,[16,17,38,39] whereas it has also been recorded that individuals with blood Group O demonstrated a decreased risk of GC,[12,37-39] and in a previous overview was observed an inverse association for blood Group O compared to non-O groups.[16] The heterogeneity among studies reviewed could be a possible explanation for those findings.[16] Only one study[10] failed to confirm the relationship between ABO blood groups and GC.

An increased risk of ESOC for individuals with blood Group B was also found, whereas the significance level was marginal ($P = 0.051$), and the sample of ESOC individuals was extremely low. Similar findings were observed in the previous studies.[16,24-26] In another report was recorded that ESOC risk for blood Group O was significantly lower than non-O groups.[16]

**Table 3:** Presentation of correlation between independent variables and overall cancer according to Enter (1a step) and Wald (4a step) method of multivariate logistic regression analysis model

| Variables in the equation | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **Variables** | | | | | | 95% C.I. for EXP (B) | | |
| | **B** | **S.E.** | **Wald** | **df** | **Sig** | **Exp(B)** | **Lower** | **Upper** |
| Step 1[a] | | | | | | | | |
| Gender | 0.226 | 0.119 | 3.563 | 1 | 0.059 | 1.253 | 0.991 | 1.584 |
| Age | 0.010 | 0.062 | 0.025 | 1 | 0.875 | 1.010 | 0.894 | 1.141 |
| Smok.stat | 0.570 | 0.124 | 20.974 | 1 | 0.000* | 1.768 | 1.386 | 2.257 |
| Educ.level | 0.225 | 0.132 | 2.918 | 1 | 0.088 | 1.252 | 0.967 | 1.621 |
| Socioec.lev | -0.138 | 0.133 | 1.083 | 1 | 0.298 | 0.871 | 0.671 | 1.130 |
| Family hist | 0.608 | 0.122 | 24.934 | 1 | 0.000* | 1.837 | 1.447 | 2.332 |
| O group | | | 23.651 | 1 | 0.000 | | | |
| A group | 0.660 | 0.196 | 11.302 | 3 | 0.001* | 1.936 | 1.317 | 2.845 |
| B group | 0.696 | 0.181 | 14.782 | 1 | 0.000* | 2.007 | 1.407 | 2.862 |
| AB group | 0.150 | 0.203 | 0.544 | 1 | 0.461 | 1.162 | 0.780 | 1.729 |
| Constant | 1.921 | 0.214 | 80.960 | 1 | 0.000 | 0.146 | | |
| Step 4[a] | | | | | | | | |
| Gender | 0.238 | 0.119 | 3.999 | 1 | 0.046* | 1.269 | 1.005 | 1.602 |
| Smok.stat | 0.540 | 0.119 | 20.626 | 1 | 0.000* | 1.716 | 1.359 | 2.166 |
| Family hist | 0.617 | 0.120 | 26.605 | 1 | 0.000* | 1.853 | 1.466 | 2.343 |
| O group | | | 23.956 | 3 | 0.000 | | | |
| A group | 0.672 | 0.196 | 11.772 | 1 | 0.001* | 1.957 | 1.334 | 2.873 |
| B group | 0.711 | 0.181 | 15.491 | 1 | 0.000* | 2.035 | 1.429 | 2.900 |
| AB group | 0.173 | 0.201 | 0.739 | 1 | 0.390 | 1.189 | 0.801 | 1.764 |
| Constant | 1.869 | 0.191 | 95.730 | 1 | 0.000 | 0.154 | | |

The reference category is: O blood group/ Smok.status: Smoking status, educ.level: Educational level, socioec.lev: Socioeconomic level, Family hist: Family history. **P*-value: statistically significant

The current study showed that individuals with blood Group A had as significantly increased risk of colorectal cancer (CRC) compared to those with non-A blood group, findings that were in agreement with those from a previous report.[29] A decreased risk of CRC for individuals with blood Group O was recorded in a systematic review; however, a high heterogeneity was found among the studies examined.[16] On the contrary, similar previous reports found no association.[49]

Individuals with blood group a had an increased risk of LC in the current report. In a similar multicenter retrospective study recorded that non-O blood type was associated with an increased risk of LC, and blood Group O was associated with a 14% risk reduction of LC,[42] whereas a significant excess risk was found among individuals with blood Group A in another study.[43] In contrary to previous, similar reports recorded no association between ABO blood groups and risk of LC.[44,45] A protective effect of LC for blood Group B compared to non-B groups was shown in a review, but was not statistically significant, whereas statistically significant heterogeneity was observed among the studies reviewed.[16]

The possible association between ABO blood group and pancreatic cancer (PC) risk has been investigating for decades, however, that association has not been consistently recorded. A significant association was observed in the current study between blood type A and the risk of PC, finding that was confirmed by previous and recent studies.[10,14,18,19] A meta-analysis showed that only one study recorded an inverse association for blood Group A compared to non-A groups, but was not statistically significant, where as a median heterogeneity was present.[16] In contrary to those findings, similar studies recorded increased rates of blood Group B among PC patients.[15,17]

In addition, the previous reports suggested that compared with blood Group O individuals, those with non-O blood types (A, AB, or B) were more likely to develop PC, or were associated with an elevated risk of PC.[17] It has also been demonstrated that blood Group O individuals had a lower risk of PC,[13] compared with blood Groups A and AB.[13] Only one study revealed that blood Group AB was protective against PC risk.[20]

**Table 4:** Presentation of correlation between ABO blood group and each type cancer according to multinomial logistic regression analysis model

| Cancer general | | 95% C.I. for EXP(B) | | |
|---|---|---|---|---|
| | | Interval for Exp(B) | | |
| | Sig. | Exp(B) | Lower bound | Upper bound |
| Oral and nasopharyngeal Ca | | | | |
| A group | 0.098 | 0.936 | 0.516 | 1.387 |
| B group | 0.118 | 0.673 | 0.347 | 1.148 |
| AB group | 0.214 | 0.549 | 0.313 | 1.133 |
| Esophageal cancer | | | | |
| A group | 0.068 | 1.297 | 0.485 | 1.194 |
| B group | 0.051 | 1.225 | 0.825 | 1.502 |
| AB group | 0.302 | 0.872 | 0.443 | 1.108 |
| Gastric cancer | | | | |
| A group | 0.002 | 2.552 | 0.546 | 4.297 |
| B group | 0.061 | 1.907 | 0.774 | 2.698 |
| AB group | 0.536 | 0.857 | 0.239 | 1.284 |
| Colorectal cancer | | | | |
| A group | 0.046 | 2.059 | 0.815 | 2.579 |
| B group | 0.078 | 1.308 | 0.623 | 1.748 |
| AB group | 0.119 | 1.113 | 0.445 | 1.274 |
| Hepatocellular cancer | | | | |
| A group | 0.103 | 0.613 | 0.212 | 1.176 |
| B group | 0.066 | 1.112 | 0.483 | 1.62 |
| AB group | 0.087 | 0.949 | 0.490 | 1.203 |
| Pancreatic cancer | | | | |
| A group | 0.034 | 2.297 | 1.023 | 2.826 |
| B group | 0.077 | 1.049 | 0.575 | 1.424 |
| AB group | 0.337 | 0.541 | 0.285 | 1.177 |
| Lung cancer | | | | |
| A group | 0.022 | 2.783 | 1.627 | 5.486 |
| B group | 0.178 | 1.147 | 0.694 | 1.298 |
| AB group | 0.251 | 0.912 | 0.542 | 1.031 |

No association was observed between ABO blood group and the risk of hepatocellular cancer HCC. However, previous studies observed associations between the ABO blood group and liver diseases including HCC.[28] Recent reports found higher risk for HCC in the presence of A antigen,[27,43,50] while it also found that males with blood type A or B had a significantly higher HCC risk compared with males with blood Type O which was independent of the known HCC risk factors.[27]

On the basis of the current study, no association was recorded between the ABO blood group and the risk of ONPC, findings that were in agreement with those of recent genome wide association studies on NPC.[51] In the contrary, previous studies have shown that blood Group B individuals were at a greater risk to develop OC.[31,32] Similarly, cancer of the buccal mucosa blood Group B showed the highest frequency; however, it was not statistically significant.[52] Blood Group A individuals showed a higher risk of developing OC[33] or were more susceptible to the development of OC,[47] whereas blood Group O had a protective effect.[47] In a systematic review and meta-analysis was found that NPC risk for blood Group A was significantly higher than non-A groups and for blood group

O the risk was significantly lower than non-O groups, without evidence of heterogeneity across studies.[16]

Another similar research recorded that blood Types A or AB was associated with an increased risk of NPC.[53] Those differences could be attributed to diversity in sample size, study design, and races of participants, whereas the association between ABO blood groups and the cancer risk may vary among different geographic locations and races or ethnicities.[11]

The biological mechanism by which genetic variants in ABO gene locus influence the risk of GC still remains unknown. The antigens ABO/ABH are crucial intercellular adhesion and membrane signaling mediators, are involved in the malignant cells progression and dissemination[54] and, are also recognized by the host immune system and may affect immunosurveillance for malignant cells.[54] Another explanation is the differences found among ABO alleles in atrophic gastritis prevalence and *Helicobacter pylori* infection, as both conditions are risk factors for GC development.[40] A potential explanation for the increased incidence of GC in blood Group A individuals could be the fact that those individuals were more susceptible to pernicious anemia, compared with non-A blood group ones,[55] as individuals who suffer from pernicious anemia are more prone to GC.[56] A possible explanation for the association between ABO blood types and risk of CRC could be the alterations on the ABH blood group antigens which can change the cell-cell and cell-extracellular matrix interactions, abnormalities that can lead to tumor development, and the alteration of ABO/Lewis antigen that have been found to be related to malignant transformation in some tumors.[57] One hypothesis proposes that the difference in ABO antigens in gastric mucins affects the properties of *H. Pylori* binding, and explains the difference in PC risk among ABO blood types,[20] whereas was found that only the A1 allele was associated with significantly higher risk for pancreatic ductal adenocarcinoma after comparison ABO allele frequencies in PC patients and blood donors.[58] Chronic pancreatitis is a predisposing factor for pancreatic tumorigenesis,[59] and the ABO blood antigens may affect the systemic inflammatory reaction.

Tumor necrosis factor-α (TNF-α) is a pro-inflammatory cytokine which regulates pancreatic ductal cell apoptosis,[59] whereas plasma levels of soluble inter-cellular adhesion molecule (sICAM-1) are associated with the risk of diabetes mellitus development,[60] which increases the susceptibility for PC. It is possible that ABO antigens may alter the systemic inflammatory conditions and influence the risk of PC development. It has also been shown the deletion and the novel expression of A, B, and Hantigens on the PC cells surface compared with surrounding normal ductal cells,[6] suggesting that alterations in glycosyltransferase specificity may occur during pancreatic tumorigenesis. Alterations in the host inflammatory state due to ABO blood antigens may provide a further mechanism to explain such an association.[61] ABO blood group is associated with various serum biomarkers such as the inflammatory associated cytokines TNF-α, epidermal growth factor (EGF), sICAM-1, P-selectin, E-selectin,[62,63] and EGF receptor which are involved in HCC development,[64] whereas its gene polymorphisms have been suggested to be associated with HCC risk.[65] ABO antigens act as receptors or ligands for bacteria and immunologically enzymes that are involved in malignant progression and dissemination.[54] Thus, the abnormal ABO blood antigens expression in liver cells tissue might be associated with HC carcinogenesis. In healthy liver cells, the ABO blood antigens A, B, and H, are not expressed on their surfaces, however, increased ABH expression or neo expression has been found in HCC cells.[66] The non-O blood group is an independent risk factor for the progression of liver fibrosis in HCV infection,[67] whereas individuals with blood Group A show more liver dysfunction and earlier appearance of liver cirrhosis compared to those with blood Group A.[27] Those observations suggest an association between ABO blood groups and liver inflammation and fibrosis progression inpatients with HCV which can lead to HC carcinogenesis. Previous investigations indicated that ABO antigens mediate microbial infections, including *H. pylori*[14] and Norwalkvirus.[68] Thus, it is possible that ABO status may also interact with EBV and influence NP carcinogenesis. However, the lack of information on EBV infections sets limits the current study, which may display a bias in the analysis.

The current case–control study has certain limitations as does not have the reliability of the prospective ones, whereas selection, recall, random, referral biases, and the effect of known and unknown con-founders are likely higher and could lead to biased secondary associations. Possible confounding factors which are related with increased risk of various types cancer were not included. The results for overall cancer may be conducted by the cancer sites with more studies included, as the number of studies on different cancer sites included in the current study varied largely. Another limitation relates to the selection of controls, which may attitude a challenge for ABO phenotype and other features with an ABO distribution which varies by geography and ethnicity. Although the current study had a relatively large sample size in general, the number of individuals in some subgroups was small. In addition, the data analyses based on cancer mortality as data which concerned the cancer incidence in Greece were not available. Some strengths of the current study were that it was a matched case–control study, and used randomly selected population-based controls. Potential limitations which concern each type of cancer are also important. HCC could be attributed to chronic hepatitis B/C; however, the data are insufficient for our statistical analysis. The number of ONP and ESO cancer patients in the current study was insufficient for analysis. A potential source of bias was the medical status of

the controls. Lack of consideration of chronic pancreatitis as a potential cause of PC in the analysis could also be a limitation in the present study. In addition, the current study did not examine the possible susceptibility to PC in diabetic cases. Finally, some of the known risk factors of cancer were examined and not specific as drinking consumption, previous infection by EBV, exposure to atmosphere pollutants, nutrition habits, etc.

## CONCLUSION

The current study showed that the overall cancer risk in blood Group A and B individuals was significantly higher compared to blood type O and AB, whereas blood type A was significantly associated with an increased risk of gastric, colorectal, pancreatic, and LC, and blood type B was significantly associated with an increased risk of esophagus cancer.

## REFERENCES


1. Garber JE, Offit K. Hereditary cancer predisposition syndromes. J Clin Oncol 2005;23:276-92.
2. Anand P, Kunnumakkara AB, Sundaram C, Harikumar KB, Tharakan ST, Lai OS, *et al*. Cancer is a preventable disease that requires major lifestyle changes. Pharm Res 2008;25:2097-116.
3. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, *et al*. Cancer incidence and mortality worldwide: Sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer 2015;136:E359-86.
4. Landsteiner K. Zur Kenntnis der antifermentativen, lytischen und agglutinierenden Wirkungen des Blutserums und der Lymphe. A knowledge for antifermentative, lytic and agglutinating effects of blood serum and lymph 1900;27:357-62.
5. Strauchen JA, Bergman SM, Hanson TA. Expression of A and B tissue isoantigens in benign and malignant lesions of the breast. Cancer 1980;45:2149-55.
6. Schuessler MH, Pintado S, Welt S, Real FX, Xu M, Melamed MR, *et al*. Blood group and blood-group-related antigens in normal pancreas and pancreas cancer: Enhanced expression of precursor Type 1, Tn and sialyl-Tn in pancreas cancer. Int J Cancer 1991;47:180-7.
7. Yamamoto F, Clausen H, White T, Marken J, Hakomori S. Molecular genetic basis of the histo-blood group ABO system. Nature 1990;345:229-33.
8. Beardmore JA, Karimi-Booshehri F. ABO genes are differentially distributed in socio-economic groups in England. Nature 1983;303:522-4.
9. Moniwa H. Statistical studies on the correlation between the ABO-blood groups and some diseases. Tohoku J Exp Med 1960;72:275-89.
10. Iodice S, Maisonneuve P, Botteri E, Sandri MT, Lowenfels AB. ABO blood group and cancer. Eur J Cancer 2010;46:3345-50.
11. Xie J, Qureshi AA, Li Y, Han J. ABO blood group and incidence of skin cancer. PLoS One 2010;5:e11972.
12. Aird I, Bentall HH, Roberts JA. A relationship between cancer of stomach and the ABO blood groups. Br Med J 1953;1:799-801.
13. Wang DS, Chen DL, Ren C, Wang ZQ, Qiu MZ, Luo HY, *et al*. ABO blood group, hepatitis B viral infection and risk of pancreatic cancer. Int J Cancer 2012;131:461-8.
14. Risch HA, Yu H, Lu L, Kidd MS. ABO blood group, Helicobacter pylori seropositivity, and risk of pancreatic cancer: A case-control study. J Natl Cancer Inst 2010;102:502-5.
15. Nakao M, Matsuo K, Hosono S, Ogata S, Ito H, Watanabe M, *et al*. ABO blood group alleles and the risk of pancreatic cancer in a Japanese population. Cancer Sci 2011;102:1076-80.
16. Zhang BL, He N, Huang YB, Song FJ, Chen KX. ABO blood groups and risk of cancer: A systematic review and meta-analysis. Asian Pac J Cancer Prev 2014;15:4643-50.
17. Sun W, Wen CP, Lin J, Wen C, Pu X, Huang M, *et al*. ABO blood types and cancer risk-a cohort study of 339,432 subjects in Taiwan. Cancer Epidemiol 2015;39:150-6.
18. Rizzato C, Campa D, Pezzilli R, Soucek P, Greenhalf W, Capurso G, *et al*. ABO blood groups and pancreatic cancer risk and survival: Results from the PANcreatic Disease research (PANDoRA) consortium. Oncol Rep 2013;29:1637-44.
19. Pelzer U, Klein F, Bahra M, Sinn M, Dörken B, Neuhaus P, *et al*. Blood group determinates incidence for pancreatic cancer in Germany. Front Physiol 2013;4:118.
20. Engin H, Bilir C, Ustun H, Gökmen A. ABO blood group and risk of pancreatic cancer in a Turkish population in Western Blacksea region. Asian Pac J Cancer Prev 2012;13:131-3.
21. Joh HK, Cho E, Choueiri TK. ABO blood group and risk of renal cell cancer. Cancer Epidemiol 2012;36:528-32.
22. Poole EM, Gates MA, High BA, Chanock SJ, Cramer DW, Cunningham JM, *et al*. ABO blood group and risk of epithelial ovarian cancer within the ovarian cancer association consortium. Cancer Causes Control 2012;23:1805-10.
23. Gates MA, Wolpin BM, Cramer DW, Hankinson SE, Tworoger SS. ABO blood group and incidence of epithelial ovarian cancer. Int J Cancer 2011;128:482-6.
24. Caygill CP, Royston C, Charlett A, Wall CM, Gatenby PA, Ramus JR, *et al*. Barrett's, blood groups and progression to oesophageal cancer: Is nitric oxide the link? Eur J Gastroenterol Hepatol 2011;23:801-6.
25. Aminian A, Mirsharif R, Alibakhshi A, Khorgami Z, Dashti H, Hasani SM. Relationship between esophageal cancer and blood groups. World Appl Sci J 2010;8:503-8.
26. Kumar N, Kapoor A, Kalwar A, Narayan S, Singhal MK, Kumar A, *et al*. Allele frequency of ABO blood group antigen and the risk of esophageal cancer. Biomed Res Int 2014;2014:286810.
27. Li Q, Yu CH, Yu JH, Liu L, Xie SS, Li WW, *et al*. ABO blood group and the risk of hepatocellular carcinoma: A case-control study in patients with chronic hepatitis B. PLoS One 2012;7:e29928.
28. Okada Y, Arima T, Togawa K, Nagashima H, Jinno K, Moriwaki S, *et al*. Neoexpression of ABH and Lewis blood group antigens in human hepatocellular carcinomas. J Natl Cancer Inst 1987;78:19-28.
29. Urun Y, Ozdemir NY, Utkan G, Akbulut H, Savas B, Oksuzoglu B, *et al*. ABO and Rh blood groups and risk of colorectal adenocarcinoma. Asian Pac J Cancer Prev 2012;13:6097-100.
30. Cerovic R, Juretić M, Balen S, Belusić L, Rogić M. Examining the presence of ABO (H) antigens of blood types in the saliva of patients with oral cancer. Coll Antropol 2008;32:509-12.

31. Akhtar K, Mehdi G, Sherwani R, Sofi L. Relationship between various cancers and ABO blood groups-a Northern India experience. Int J Pathol 2010;13:1.
32. Mortazavi H, Hajian S, Fadavi E, Sabour S, Baharvand M, Bakhtiari S. ABO blood groups in oral cancer: A first case-control study in a defined group of Iranian patients. Asian Pac J Cancer Prev 2014;15:1415-8.
33. Jaleel BF, Nagarajappa R. Relationship between ABO blood groups and oral cancer. Indian J Dent Res 2012;23:7-10.
34. Nowińska E, Namysłowski G, Scierski W, Kocierz S. ABO blood groups in the patients with laryngeal cancer. Otolaryngol Pol 2000;54 Suppl 31:209-11.
35. Chihara Y, Sugano K, Kobayashi A, Kanai Y, Yamamoto H, Nakazono M, *et al*. Loss of blood group A antigen expression in bladder cancer caused by allelic loss and/or methylation of the ABO gene. Lab Invest 2005;85:895-907.
36. Tyagi SP, Pradhan S, Agarwal P. Blood groups in malignant diseases. J Indian Med Assoc 1965;45:645-50.
37. Wang Z, Liu L, Ji J, Zhang J, Yan M, Zhang J, *et al*. ABO blood group system and gastric cancer: A case-control study and meta-analysis. Int J Mol Sci 2012;13:13308-21.
38. Edgren G, Hjalgrim H, Rostgaard K, Norda R, Wikman A, Melbye M, *et al*. Risk of gastric cancer and peptic ulcers in relation to ABO blood type: A cohort study. Am J Epidemiol 2010;172:1280-5.
39. El H, Hashash JG, Baz EM, Abdul-Baki H, Sharara AI. ABO blood group and gastric cancer: Rekindling an old fire? South Med J 2007;100:726-7.
40. Nakao M, Matsuo K, Ito H, Shitara K, Hosono S, Watanabe M, *et al*. ABO genotype and the risk of gastric cancer, atrophic gastritis, and helicobacter pylori infection. Cancer Epidemiol Biomarkers Prev 2011;20:1665-72.
41. Kvist E, Krogh J, Hjortberg P. Prognostic variables in patients with prostate cancer: Influence of blood group ABO (H), the Rhesus system, age, differentiation, tumour stage and metastases. Int Urol Nephrol 1992;24:417-23.
42. Urun Y, Utkan G, Cangir AK, Oksuzoglu OB, Ozdemir N, Oztuna DG, *et al*. Association of ABO blood group and risk of lung cancer in a multicenter study in Turkey. Asian Pac J Cancer Prev 2013;14:2801-3.
43. Hsiao LT, Liu NJ, You SL, Hwang LC. ABO blood group and the risk of cancer among middle-aged people in Taiwan. Asia Pac J Clin Oncol 2015;11:e31-6.
44. Oguz A, Ünal D, Taşdemir A, Karahan S, Aykas F, Mutlu H, *et al*. Lack of any association between blood groups and lung cancer, independent of histology. Asian Pac J Cancer Prev 2013;14:453-6.
45. Chrysanthakopoulos NA, Dareioti NS. ABO blood group and the risk of lung cancer in Greek adults: A case-control study. Exp Oncol 2018;40:249-50.
46. Seow LJ, Kwa SB, Teoh CK. A preliminary survey of abo blood group frequency in nasopharyngeal carcinoma in Chinese patients. Singapore Med J 1964;4:93-5.
47. Turkoz FP, Celenkoglu G, Dogu GG, Kalender ME, Coskun U, Alkis N, *et al*. Risk factors of nasopharyngeal carcinoma in Turkey-an epidemiological survey of the Anatolian society of medical oncology. Asian Pac J Cancer Prev 2011;12:3017-21.
48. Ferlay J, Soerjomataram I, Ervik M, Dikshit R, Eser S, Mathers C, *et al*. Cancer incidence and mortality worldwide: Sources, methods and major patterns in GLOBOCAN 2012. Int J Cancer 2015;136:E359-86.
49. Khalili H, Wolpin BM, Huang ES, Giovannucci EL, Kraft P, Fuchs CS, *et al*. ABO blood group and risk of colorectal cancer. Cancer Epidemiol Biomarkers Prev 2011;20:1017-20.
50. Shim HJ, Lee R, Shin MH, Kim HN, Cho D, Ahn HR, *et al*. Association between ABO genotype and risk of hepatocellular carcinoma in Koreans. Asian Pac J Cancer Prev 2015;16:2771-5.
51. Keng L, Feng Q, Shulin C, Xia H, Songguo P, Hao C. Lack of association between the distribution of ABO blood groups and nasopharyngeal carcinoma in a population of Southern China. J Cancer Res Ther 2018;14:785-8.
52. Sharma G, Choudhary R, Bharti D. Studies showing the relationship between ABO blood-groups and major types of cancers. Asian J Exp Sci 2007;21:129-32.
53. Sheng L, Sun X, Zhang L, Su D. ABO blood group and nasopharyngeal carcinoma risk in A population of Southeast China. Int J Cancer 2013;133:893-7.
54. Hakomori S. Antigen structure and genetic basis of histo-blood groups A, B and O: Their changes associated with human cancer. Biochim Biophys Acta 1999;1473:247-66.
55. Roberts JA. Blood groups and susceptibility to disease: A review. Br J Prev Soc Med 1957;11:107-25.
56. Hoskins LC, Loux HA, Britten A, Zamcheck N. Distribution of ABO blood groups in patients with pernicious anemia, gastric carcinoma and gastric carcinoma associated with pernicious anemia. N Engl J Med 1965;273:633-7.
57. Dall'olio F. Protein glycosylation in cancer biology: An overview. Clin Mol Pathol 1996;49:126-35.
58. El Jellas K, Hoem D, Hagen KG, Kalvenes MB, Aziz S, Steine SJ, *et al*. Associations between ABO blood groups and pancreatic ductal adenocarcinoma: Influence on resection status and survival. Cancer Med 2017;6:1531-40.
59. Garcea G, Dennison AR, Steward WP, Berry DP. Role of inflammation in pancreatic carcinogenesis and the implications for future therapy. Pancreatology 2005;5:514-29.
60. Meigs JB, Hu FB, Rifai N, Manson JE. Biomarkers of endothelial dysfunction and risk of Type 2 diabetes mellitus. JAMA 2004;291:1978-86.
61. Zhang S, Zhang HS, Cordon-Cardo C, Reuter VE, Singhal AK, Lioyd KO, *et al*. Selection of tumor antigens as targets for immune attack using immunohistochemistry: II. Blood group-related antigens. Int J Cancer 1997;73:50-6.
62. Barbalic M, Dupuis J, Dehghan A, Bis JC, Hoogeveen RC, Schnabel RB, *et al*. Large-scale genomic studies reveal central role of ABO in sP-selectin and sICAM-1 levels. Hum Mol Genet 2010;19:1863-72.
63. Paterson AD, Lopes-Virella MF, Waggott D, Boright AP, Hosseini SM, Carter RE, *et al*. Genome-wide association identifies the ABO blood group as a major locus associated with serum levels of soluble E-selectin. Arterioscler Thromb Vasc Biol 2009;29:1958-67.
64. Berasain C, Perugorria MJ, Latasa MU, Castillo J, Goñi S, Santamaria M, *et al*. The epidermal growth factor receptor: A link between inflammation and liver cancer. Exp Biol Med (Maywood) 2009;234:713-25.
65. Abu Dayyeh BK, Yang M, Fuchs BC, Karl DL, Yamada S, Sninsky JJ, *et al*. A functional polymorphism in the epidermal growth factor gene is associated with risk for hepatocellular carcinoma. Gastroenterology 2011;141:141-9.
66. Terada T, Nakanuma Y. Expression of ABH blood group

antigens, receptors of Ulex europaeus agglutinin I, and factor VIII-related antigen on sinusoidal endothelial cells in adenomatous hyperplasia in human cirrhotic livers. Hum Pathol 1991;22:486-93.
67. Poujol-Robert A, Boelle PY, Wendum D, Poupon R, Robert A. Association between ABO blood group and fibrosis severity in chronic hepatitis C infection. Dig Dis Sci 2006;51:1633-6.
68. Nilsson J, Rydell GE, Le Pendu J, Larson G. Norwalk virus-like particles bind specifically to A, H and difucosylated Lewis but not to B histo-blood group active glycosphingolipids. Glycoconj J 2009;26:1171-80.

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