RESEARCH ARTICLE

ABO and Rh Blood Groups in Relation to Ovarian, Endometrial and Cervical Cancer Risk Among The Population of South-East Siberia

Arseniy E Yuzhalin[1,2], Anton G Kutikhin[2,3]*

Abstract

Background: There is a large amount of evidence that the ABO blood group system may play a role in disease etiology. A relationship between ABO and Rhesus blood groups and cancer risk has been demonstrated in a number of studies. However, in relation to gynecological malignancies, these findings are inconsistent and contradictory. Aim: To perform a case-control study for analysis of the distribution of ABO and Rh blood antigens among women from South-East Siberia who suffered from ovarian, endometrial and cervical cancer, and to assess the potential role of these antigens in carcinogenesis. Design, Subjects and Methods: A total of 1,163 cases with ovarian cancer (n=551), endometrial cancer (n=440) and cervical cancer (n=172) were involved in the study. The control group was formed from 22,581 female blood donors. Blood groups were determined through patients medical records and blood donor records. Odds ratios (OR) with 95% confidence intervals (CI) were calculated. The blood group O was defined as the referent group, as it has the greatest frequency in the populations of Southern Siberia. P values less than 0.05 were regarded as statistically significant. Results: We found that carriage of non-O blood types increased the risk of ovarian cancer by 40-60%, and the magnitude of this relationship was strongest in women with the AB (IV) blood group. Carriage of the A (II) blood group strongly correlated with an increased risk of ovarian cancer in premenopausal, but not in postmenopausal women. No statistically significant correlations were obtained for endometrial cancer and cervical cancer. Additionally, we did not observe a relationship between Rhesus factor and cancer risk. Conclusion: We suggest that carriage of non-O blood groups may elevate risk of ovarian cancer and can play a role in its development.

Keywords: ABO - Rh - ovarian cancer - endometrial cancer - cervical cancer - South-East Siberia

Asian Pacific J Cancer Prev, **13 (10)**, 5091-5096

Introduction

Gynecologic cancer is a wide group of malignancies that affect female reproductive organs, including ovaries, fallopian tubes, uterus, cervix, vagina, and vulva. According to the latest reports, gynecologic cancer is the fourth most common malignancy in women (Jemal et al., 2011). Early defined, most of the gynecological cancers have a good cure rate; however, more than 270,000 deaths from cervical cancer and 140,000 death from ovarian cancer were registered worldwide in 2008 (Jemal et al., 2011). As for today, etiological factors for gynecological cancer are well known. For cervical cancer, common risk factors are HPV infection, administration of oral contraceptives, smoking, Chlamydia infection, and HIV/AIDS infection. Regarding the endometrial cancer, etiological factors are administration of tamoxifen, endometrial hyperplasia, and diabetes. Ovarian cancer frequently occurs in individuals that had gynecologic surgery, received fertility drugs, smoked and had excessive alcohol consumption (Salehi et al., 2008). Moreover, common risk factors for all of these cancer types are age, obesity, estrogen or other hormone therapy, family history of ovarian, breast, or colorectal cancer, diet, and immunosuppression (Salehi et al., 2008). In addition, such factors as polycystic ovarian syndrome, intrauterine device use, pelvic radiation therapy, hypertension, and lack of children are also believed to increase risk of gynecological cancers (Salehi et al., 2008). Nevertheless, many aspects in the etiology and pathogenesis of gynecologic malignancies remain to be elusive. As for today, prevention and early diagnosis are the key points for successful treatment of the gynecological cancer.

The *ABO* gene is located on chromosome 9 (9q34), and contains 7 exons that span more than 18 kb of genomic DNA. The *ABO* gene encodes glycotransferases that catalyze the transfer of nucleotide donor sugars to the H antigen to form the ABO blood group antigens. It has long been established that different ABO blood types may affect occurrence and development of various pathogenic processes within the body. First, there is a large amount of evidence that ABO blood group system have a great

*[1]Research Institute for Complex Issues of Cardiovascular Diseases under the Siberian Branch of the Russian Academy of Medical Sciences, [2]Central Research Laboratory, [3]Department of Epidemiology, Kemerovo State Medical Academy, Kemerovo, Russian Federation *For correspondence: antonkutikhin@gmail.com*

impact on individual susceptibility to infectious diseases. It has been reported that carriers of A and B antigens are more resistant to cholera in comparison with blood group O, while AB confers the most resistance (Barua and Paguio, 1977; Clemens et al., 1989). Furthermore, it has been recently demonstrated that blood group O protects against severe *Plasmodium falciparum* malaria through the mechanism of reduced resetting, since sugars located on the non-O blood cells are involved in the creation of the large clumps of cells (Rowe et al., 2007). Additionally, it has been indicated that patients presenting with blood group A are more susceptible to infections caused by *Pseudomonas aeruginosa*, due to specific adhesion of *P.aeruginosa lectins* with N-acetyl-galactosamine, the terminal carbohydrate forming the antigen A (Steuer et al., 1995). However, in contrast to the above-mentioned studies, several authors obtained contradictory correlations regarding the ABO distributions in patients with smallpox (Harris et al., 1963; Downie et al., 1966). It should also be noted that carriers of A or AB blood types were found almost 3 times more susceptible in acquiring chikungunya disease, which is caused by CHIKV virus (Kumar et al., 2010).

There is also some evidence that ABO blood group system may play role in the development of noninfectious diseases. First, the higher prevalence of non-O blood type among patients with venous thromboembolism (VTE) has been shown not long ago (Ohira et al., 2007). The authors suggested that this observation may be due to the fact that subjects with non-O blood type have higher levels of the clot-inducing proteins factor VIII and von Willebrand factor in their blood (Ohira et al., 2007). Second, it has been revealed that ABO blood group system affects the ability of *Helicobacter pylori* to attach to the lining of the stomach, since individuals of blood group A and B phenotypes were found to have fewer *H.pylori* receptors compared to those with blood group O (Boren et al., 1993). Therefore, it could be hypothesized that carriage of blood group O may indirectly contribute to the development of *H.pylori* infection, which consequently may result in gastritis, gastric ulcer, and gastric adenocarcinoma. Interestingly, this finding is in contrast with the results of one British research group (Aird et al., 1953) who more than fifty years ago demonstrated that the frequency of blood group A is greater and the frequency of blood group O is less in patients with gastric cancer. Notably, this study (Aird et al., 1953) was the first attempt to find possible relationship between ABO blood types and cancer risk. Since then, numerous case-control studies have been performed to shed the light on this issue; however, these reports are often inconsistent and unconvincing, and require further in-depth research. Thus, the primary aims of our study are to analyze the distribution of ABO and Rh blood antigens in subjects with gynecological malignancies and evaluate their potential impacts on carcinogenesis.

Materials and Methods

Our study was conducted on the basis of Kemerovo Regional Clinical Oncological Dispensary. We collected data of medical records from 1,163 cancer patients aged 30-75 living in Kemerovo and neighboring settlements for five-year period of time (2006-2011). Data are presented on 551 cases of ovarian cancer, 440 cases of endometrial cancer and 173 cases of cervical cancer. All the cases included in the study were individuals with histopathologically confirmed ovarian, cervical or endometrial neoplasia. Notably, due to technical difficulties we were not able to obtain information about such confounders as parity, duration of oral contraceptive use, duration of breastfeeding, smoking status, and lactose intake. The subjects who had a hysterectomy, oophorectomy, menopause due to pelvic irradiation, or cancer other than non-melanoma skin cancer, were excluded from the study.

The control group was formed from the database of blood donor records from Kemerovo Regional Blood Transfusion Station and included 22,581 female individuals. The distribution of ABO and Rh blood groups in the control group is supposed to reflect the general population of Kemerovo Oblast and Southern Siberia. Determination of blood groups in both cases and controls was performed by conventional serological methods. Monoclonal anti-A, anti-B, and anti-AB antibodies were used to determine ABO blood groups, while Rhesus factor was identified by anti-D (IgM) monoclonal antibodies ("Gematolog", Moscow).

Statistical analysis was performed by utilizing the MedCalc software (MedCalc, inc). Odds ratios with 95% of confidence intervals were generated. The blood group O was defined as referent group, since it has the most frequency in the population of Southern Siberia. In addition, stratification by menopausal status has been performed. P values that were less than 0.05 have been regarded as statistically significant. The study is in compliance with the Helsinki declaration, and it has been approved by the Medical Ethical Committee of Kemerovo State Medical Academy.

Results

The data regarding correlation between gynecological malignancies and ABO/Rh blood groups are presented in Tables 1 and 2. The results regarding stratification by menopausal status are presented in Table 3. We observed that presence of non-O blood type was associated with 40-60% increased risk of ovarian cancer (Table 1). Importantly, the strongest magnitude of this correlation was observed in subjects with simultaneous carriage of both A and B antigens (OR=1.60; 95%CI: 1.17-2.18; p=0.0026). Additionally, the correlation was little stronger for the blood type B in comparison with the type A (OR=1.48; 95%CI: 1.17-1.81; p=0.0010 and OR=1.40; 95%CI: 1.13-1.73; p=0.0019, respectively). However, we did not observe statistically significant association for endometrial cancer and cervical cancer. Antigens of Rh system also did not correlate with a risk of gynecological cancer in our study. Importantly, interesting results were obtained after stratification by menopausal status. The carriage of the blood group A strongly correlated with an increased risk of ovarian cancer in premenopausal (OR=1.59;

Table 1. Distribution of ABO Blood Groups between Cases and Controls

Blood group	Cases N (%)	Controls N (%)	OR (95%CI)	P value
Ovarian cancer (n=551)				
O	149 (27.1)	6702 (35.0)	1.0 (ref)	-
A	205 (37.2)	6570 (34.4)	1.40 (1.13-1.73)	0.0019
B	140 (25.4)	4248 (22.2)	1.48 (1.17-1.87)	0.001
AB	57 (10.3)	1599 (8.4)	1.60 (1.17-2.18)	0.0026
A+AB	262 (47.5)	8169 (42.7)	1.44 (1.17-1.76)	0.0004
B+AB	197 (35.7)	5847 (30.6)	1.51 (1.22-1.88)	0.0002
Cervical cancer (n=172)				
O	62 (36.1)	6702 (35.0)	1.0 (ref)	-
A	62 (36.0)	6570 (34.4)	1.02 (0.71-1.45)	0.9122
B	40 (23.3)	4248 (22.2)	1.01 (0.68-1.51)	0.9308
AB	8 (4.7)	1599 (8.4)	0.54 (0.25-1.13)	0.1027
A+AB	70 (40.7)	8169 (42.7)	0.92 (0.65-1.30)	0.662
B+AB	48 (27.9)	5847 (30.6)	0.88 (0.60-1.29)	0.5361
Endometrial cancer (n=440)				
O	152 (34.5)	6702 (35.0)	1.0 (ref)	-
A	162 (36.8)	6570 (34.4)	1.08 (0.86-1.36)	0.4643
B	92 (20.9)	4248 (22.2)	0.95 (0.73-1.24)	0.7297
AB	34 (7.8)	1599 (8.4)	0.90 (0.64-1.36)	0.7366
A+AB	196 (44.5)	8169 (42.7)	1.05 (0.85-1.31)	0.6066
B+AB	126 (28.6)	5847 (30.6)	0.95 (0.74-1.20)	0.6747

Table 2. Distribution of Rh Antigens between Cases and Controls

Blood group	Cases N (%)	Controls N (%)	OR (95%CI)	P value
Ovarian cancer (n=551)				
Rh^+	455 (82.6)	19032 (84.3)	1.0 (ref)	-
Rh^-	96 (17.4)	3549 (15.7)	1.13 (0.90-1.41)	0.2778
Cervical cancer (n=172)				
Rh^+	143 (83.1)	19032 (84.3)	1.0 (ref)	-
Rh^-	29 (16.9)	3549 (15.7)	1.08 (0.72-1.62)	0.6815
Endometrial cancer (n=440)				
Rh^+	373 (84.8)	19032 (84.3)	1.0 (ref)	-
Rh^-	67 (15.2)	3549 (15.7)	0.96 (0.74-1.25)	0.7799

95%CI: 1.14-2.20, p=0.0056), but not in postmenopausal women (p=0.0821). Conversely, blood types B and AB were associated with an elevated ovarian cancer risk in postmenopausal (OR=1.54 95%CI: 1.14-2.07, p=0.0041 and OR=1.66 95%CI: 1.09-2.41, p=0.0151, respectively), but not in premenopausal individuals (p=0.0847 and 0,0756, respectively). In addition, we failed to demonstrate statistically significant differences in the distribution of ABO blood groups in women with endometrial cancer and cervical cancer after stratification by menopausal status.

Table 3. Distribution of ABO Blood Groups in Cases and Controls in Relation to Menopausal Status

Blood group	Cases N (%)	Controls N (%)	OR (95%CI)	P value
Ovarian cancer;				
Premenopausal (n=225)				
O	59 (26.2)	6702 (35.0)	1.0 (ref)	-
A	92 (40.9)	6570 (34.4)	**1.59 (1.14-2.20)**	**0.0056**
B	52 (23.1)	4248 (22.2)	1.39 (0.95-2.02)	0.0847
AB	22 (9.8)	1599 (8.4)	1.56 (0.95-2.55)	0.0756
A+AB	114 (50.7)	8169 (42.7)	**1.58 (1.15-2.17)**	**0.0043**
B+AB	74 (32.9)	5847 (30.6)	**1.43 (1.01-2.02)**	**0.0385**
Postmenopausal (n=326)				
O	90 (27.6)	6702 (35.0)	1.0 (ref)	-
A	113 (34.7)	6570 (34.4)	1.28 (0.96-1.69)	0.0821
B	88 (27.0)	4248 (22.2)	**1.54 (1.14-2.07)**	**0.0041**
AB	35 (10.7)	1599 (8.4)	**1.66 (1.09-2.41)**	**0.0151**
A+AB	148 (45.4)	8169 (42.7)	**1.34 (1.03-1.75)**	**0.0262**
B+AB	123 (37.7)	5847 (30.6)	**1.56 (1.19-2.06)**	**0.0013**
Cervical cancer;				
Premenopausal (n=113)				
O	42 (37.2)	6702 (35.0)	1.0 (ref)	-
A	41 (36.3)	6570 (34.4)	0.99 (0.64-1.53)	0.9848
B	26 (23)	4248 (22.2)	0.97 (0.59-1.59)	0.9248
AB	4 (3.5)	1599 (8.4)	0.39 (0.14-1.11)	0.0797
A+AB	45 (39.8)	8169 (42.7)	0.76 (0.50-1.16)	0.2148
B+AB	30 (26.5)	5847 (30.6)	0.76 (0.48-1.21)	0.2551
Postmenopausal (n=59)				
O	20 (33.9)	6702 (35.0)	1.0 (ref)	-
A	21 (35.6)	6570 (34.4)	1.06 (0.57-1.97)	0.8301
B	14 (23.7)	4248 (22.2)	1.10 (0.55-2.18)	0.7761
AB	4 (6.8)	1599 (8.4)	0.83 (0.28-2.45)	0.7477
A+AB	25 (42.4)	8169 (42.7)	1.02 (0.56-1.84)	0.9331
B+AB	28 (47.4)	5847 (30.6)	1.60 (0.90-2.85)	0.1069
Endometrial cancer;				
Premenopausal (n=102)				
O	32 (31.4)	6702 (35.0)	1.0 (ref)	-
A	37 (36.3)	6570 (34.4)	1.17 (0.73-1.89)	0.4952
B	25 (24.5)	4248 (22.2)	1.23 (0.72-2.08)	0.4347
AB	8 (7.8)	1599 (8.4)	1.04 (0.48-2.27)	0.9061
A+AB	45 (44.1)	8169 (42.72)	1.15 (0.73-1.81)	0.5374
B+AB	32 (31.4)	5847 (30.58)	1.14 (0.70-1.87)	0.5861
Postmenopausal (n=338)				
O	120 (35.5)	6702 (35.0)	1.0 (ref)	-
A	125 (37.0)	6570 (34.4)	1.06 (0.82-1.36)	0.6378
B	67 (19.8)	4248 (22.2)	0.88 (0.65-1.19)	0.4091
AB	26 (7.7)	1599 (8.4)	0.90 (0.59-1.39)	0.6586
A+AB	149 (44.1)	8169 (42.7)	1.01 (0.79-1.29)	0.8811
B+AB	93 (27.5)	5847 (30.6)	0.88 (0.67-1.16)	0.3953

Discussion

To date, there are approximately 40 case-control studies, devoted to investigation of the impact of ABO blood groups on cancer risk. It has been reported that carriers of the blood group O had a 4% reduced risk of basal cell carcinoma and 14% reduced risk of squamous cell carcinoma within the large cohort of US individuals (Xie et al., 2010). Likewise, it has been demonstrated that subjects possessing the blood group O have a lower risk of pancreatic cancer compared to those with groups A or B (Amundadottir et al., 2009; Wolpin et al., 2010). Similarly, the carriage of A and AB groups significantly correlated with an increased risk of gallbladder cancer (Pandey et al., 1995). A recent case-control study has revealed that in comparison with healthy controls, the frequency of the blood group B was significantly higher in a large cohort of Chinese patients with cardiac cancer and esophageal carcinoma (Su et al., 2001). According to the findings by Polish researchers, carriers of A and AB blood groups had a significantly increased risk of laryngeal carcinoma (Konieczna and Turowski, 1992; Pyd et al., 1995). However, it should be noted that their further investigations did not replicate previous results (Nowinska et al., 2000). An association between the ABO blood group system and colorectal cancer risk has not been confirmed in series of studies performed in different populations and ethnicities (Halvorsen, 1986; Slater et al., 1993; Khalili et al., 2011). Similarly, a lack of statistically significant correlations was observed between the ABO

system and development of prostate cancer (Wajsman et al., 1997), benign prostate hyperplasia (Beasley, 1964), bladder cancer (Orihuela and Shahon, 1987; Raitanen and Tammela, 1993), testicular cancer (Morrison, 1976; O'Connell and Christenson, 1980) and salivary gland cancer (Pinkston and Cole, 1996). Additionally, several studies reported contradictory results. Although series of case-control studies failed to establish ABO blood groups as a major risk factor for breast cancer (Hems, 1970; Anderson and Haas, 1984; Dede et al., 2010), A group of authots (Tryggvadottir et al., 1988) reported that familial breast cancer cases had a 2-fold higher prevalence of blood group B than did the sporadic cases, and the frequency of this blood group in non-affected relatives of cases was significantly reduced. Moreover, another study has demonstrated that the absence of the Rh factor (Rh-) was positively associated with a 50% increased breast cancer risk (Ronco et al., 2009). Likewise, it has been revealed that the relative risk of metastasis in Rh- patients with breast cancer was 4.2 times higher than that in Rh+ patients (Stamatakos et al., 2009). Interestingly, the relative risk of metastasis was 1.29 times higher in subjects who simultaneously possessed Rh+ and A blood group. Although in reference No17 there was suggested that the blood group B may play a role in the development of esophageal carcinoma, several subsequent investigations failed to confirm this hypothesis (Aird et al., 1960; Beasley, 1964; Wapnick et al., 1972). Finally, two studies regarding lung cancer did not obtain any significant associations (Jakoubkova and Majsky, 1965; Roberts et al., 1988); however, another study demonstrated that the frequency of the blood group A was significantly higher in lung cancer patients in comparison with corresponding donors (Roots et al., 1988).

There are also several case-control studies investigating ABO and Rh blood groups in relation to gynecological cancer risk. Recently, one group of authors (Gates et al., 2011) performed a comprehensive study using the data from 49,153 subjects of mixed US population. The authors demonstrated that in comparison with women with blood group O, carriers of blood group AB or B had a non-significant increase in epithelial ovarian cancer incidence (RR=1.38; 95%CI: 0.88-2.16 and RR=1.38, 95%CI: 0.96-1.99, respectively). Also, Gates et al. did not observe any relationship between the blood group A or Rh factor. However, carriers of B allele genotype (AB/B) had a statistically significant 41% increase in ovarian cancer incidence (OR=1.41; 95%CI: 1.06-1.88), compared to women without B antigen (blood group O/A). Additionally, the authors revealed positive associations between the carriage of blood groups AB and B and higher body mass index (BMI) ≥30 kg/m^2 (RR=0.66; 95%CI: 0.30-1.45; RR=1.10; 95%CI: 0.65-1.85 for blood groups AB and B, respectively). Another retrospective analysis of 968 Italian women (Marinaccio et al., 1995), has revealed that endometrial and ovarian cancer occur more frequently in women with the blood type A compared to those with the blood type. According to the authors, the blood group A is associated with a poor prognosis. Moreover, they indicated that with regard to endometrial cancer, a sensibly better 5-year and 10-year survival is associated with the presence of the blood group O if compared with blood group A. Likewise, another research group (Henderson et al., 1993) showed that in comparison with the blood group O, the blood type A was significantly more common among 1261 English women with ovarian cancer. Furthermore, Henderson et al. noted that adenocarcinomas were the most common type of tumor and were associated with the presence of the blood group A. This association, moreover, was more evident in married women than in single women probably reflecting differences associated with parity. Finally, Armenian authors (Adamian, 2005) revealed that AB blood type was found to be significantly higher in 548 Armenian subjects with endometrial cancer in comparison with the blood group O.

Importantly, our findings are consistent with those obtained by other authors investigating the same issue. An overwhelming majority of studies indicate a correlation between non-O blood groups and an increased cancer risk. In our study we found that the presence of both A and B antigens may contribute to an increased risk of ovarian cancer incidence. Interestingly, we observed that the association was stronger for A antigen compared to B. Since hormonal factor is believed to play a role in gynecological cancer etiology, we performed stratification by menopausal status. However, our results are somewhat inconclusive and cannot be interpreted clearly. We observed that blood group A correlated with an increased risk of ovarian cancer in premenopausal subjects, while blood types B and AB, conversely, were associated with an elevated ovarian cancer risk in postmenopausal subjects. Possibly, this could indicate different mechanisms of interaction between A and B antigens with hormonal background.

Direct mechanisms of the impact of ABO blood group system on cancer development are elusive. However, there are several hypotheses which may explain the associations observed. It could be that A and B antigens might somehow help cancers grow more aggressively. It has been shown that the presence of A and B antigens may increase cellular motility and facilitate the interactions between tumor cells (Le Pendu et al., 2001). Moreover, it has been observed that ABO antigens may contribute to the resistance to apoptosis and immune escape (Melzer et al., 2008). Alternatively, some research has shown that structure of certain tumor antigens is similar to the structure of antigens of ABO system. For example, Forssmann antigen is synthesized predominantly in stomach and colon tumors, and structurally it is almost identical to the A antigen determinant (Smith and Prieto, 1992). Therefore, carriers of blood group A may have diminished tumor immune response due to reduced ability to recognize and attack tumor cells that express Forssmann antigen. Finally, it should be noted that several studies have demonstrated an association between *ABO* genotype and altered levels of soluble E-selectin, ICAM-1, and tumor necrosis factor-alpha (Pare et al., 2008; Paterson et al., 2009a, Paterson et al., 2009b) which also may suggest potential role of ABO in cancer development.

Importantly, our study has several limitations. First, the sample size of our study was relatively small. In particular, the low sample size may be a reason for the

lack of statistically significant associations observed in patients with endometrial cancer (n=440) and cervical cancer (n=172). Moreover, due to the insufficient sample size we were unable to test for three-way interactions (ABO*Rh*menopausal status). Second, since we analyzed medical records, we were unable to assess the role of various potential confounders, such as smoking status, oral contraceptive use, duration of breastfeeding, etc. Third, due to technical difficulties, the data on tumor histopathological subtypes were also not obtained; therefore, we were not able to stratify according to cancer histological type.

To summarize, our findings suggest possible association between the non-O blood groups and an increased risk of ovarian cancer. Further revealing of risk markers in antigens of erythrocytes can be applied in programs of cancer prevention and screening. We hope that our study will stimulate further investigations devoted to this issue.

Acknowledgements

The authors would like to express their gratitude to Brusina EB, Kolesnikov YaM, Magarill YuA, Kuptsov DE, Lukashova MD, Zharova KN, and Agienko AS, who helped perform this study. Additionally, the authors would like to express their special appreciation to Baba Lida.

References

Aird I, Bentall HH, Roberts JA (1953). A relationship between cancer of stomach and the ABO blood groups. *Br Med J*, **1**, 799-801.

Aird I, Lee DR, Roberts JA (1960). ABO blood groups and cancer of oesophagus, cancerof pancreas, and pituitary adenoma. *Br Med J*, **1**, 1163-6.

Adamian RT (2005). Blood-type and rhesus distribution in Armenian women with endometrial carcinoma. *Vopr Onkol*, **51**, 575-6.

Amundadottir L, Kraft P, Stolzenberg-Solomon RZ, et al (2009). Genome-wide association study identifies variants in the ABO locus associated with susceptibility to pancreatic cancer. *Nat Genet*, **41**, 986-90.

Anderson DE, Haas C (1984). Blood type A and familial breast cancer. *Cancer*, **54**, 1845-9.

Barua D, Paguio AS (1977). ABO blood groups and cholerax. *Ann Hum Biol*, **4**, 489-92.

Clemens JD, Sack DA, Harris JR, et al (1989). ABO blood groups and cholera: new observations on specificity of risk and modification of vaccine efficacy. *J Infect Dis*, **159**, 770-3.

Beasley WH (1964). The ABO blood groups of carcinoma of the oseophagus and of benign prostatic hyperplasia. *J Clin Pathol*, **17**, 42-4.

Boren T, Falk P, Roth KA, Larson G, Normark S (1993). Attachment of *Helicobacter pylori* to human gastric epithelium mediated by blood group antigens. *Sci*, **262**, 1892-5.

Dede DS, Aksoy S, Dizdar O, et al (2010). Blood ABO groups and risk of breast cancer. *Med Oncol*, **27**, 1433.

Downie HW, Meiklejohn G, Vincent LS, et al (1966). Smallpox frequency and severity in relation to A, B and 0 blood groups. *Bull WHO*, **33**, 623.

Gates MA, Wolpin BM, Cramer DW, Hankinson SE, Tworoger SS (2011). ABO blood group and incidence of epithelial ovarian cancer. *Int J Cancer*, **128**, 482-6.

Ichikawa D, Handa K, Hakomori S (1998). Histo-blood group A/B antigen deletion/reduction vs. continous expression in human tumor cells as correlated with their malignancy. *Int J Cancer*, **76**, 284-9.

Jakoubkova J, Majsky A (1965). Blood groups and neoplastic disease. *Neoplasma*, **12**, 611-6.

Jemal A, Bray F, Center MM, et al (2011). Global cancer statistics. *CA Cancer J Clin*, **61**, 69-90.

Halvorsen TB (1986). ABO blood groups, rhesus types, and colorectal adenocarcinoma. A retrospective study of 747 cases. *Scand J Gastroenterol*, **21**, 979-83.

Harris R, Harrison GA, Rondle CJ (1963). Vaccinia virus and human blood-group-A substance. *Acta Genet Stat Med,* **13**, 44-57.

Hems G (1970). Epidemiological characteristics of breast cancer in middle and late age. *Br J Cancer*, **24**, 226-34.

Henderson J, Seagroatt V, Goldacre M (1993). Ovarian cancer and ABO blood groups. *J Epidemiol Community Hlth*, **47**, 287-9.

Khalili H, Wolpin BM, Huang ES, et al (2011). ABO Blood Group and Risk of Colorectal Cancer. *Cancer Epidemiol Biomarkers Prev*, **20**, 1017-20.

Konieczna A, Turowski G (1992). ABO blood groups system in laryngeal cancer patients and after survival of 3 and 5 years. *Mater Med Pol*, **24**, 266-7.

Kumar NC, Nadimpalli M, Vardhan VR, Gopal SD (2010). Association of ABO blood groups with Chikungunya virus. *Virol J*, **7**, 140.

Le Pendu J, Marionneau S, Cailleau-Thomas A, et al (2001). ABH and Lewis histo-blood group antigens in cancer. *APMI*, **109**, 9-31.

Marinaccio M, Traversa A, Carioggia E, et al (1995). Blood groups of the ABO system and survival rate in gynecologic tumors. *Minerva Ginecol*, **47**, 69-76.

Melzer D, Perry JR, Hernandez D, et al (2008). A genome-wide association study identifies protein quantitative trait loci (pQTLs). *PLoS Genet*, **4**, e1000072.

Morrison AS (1976). Some social and medical characteristics of Army men with testicular cancer. *Am J Epidemiol*, **104**, 511-6.

Nowińska E, Namysłowski G, Scierski W, Kocierz S (2000). ABO blood groups in the patients with laryngeal cancer. *Otolaryngol Pol*, **54**, 209-11.

O'Connell KJ, Christenson PJ (1980). Relationship of blood type to nonseminomatous testes tumor. *Clue to genetic link*. *Urology*, 15, 409-10.

Ohira T, Cushman M, Tsai MY, et al (2007). ABO blood group, other risk factors and incidence of venous thromboembolism: the Longitudinal Investigation of Thromboembolism Etiology (LITE). *J Thromb Haemost*, **5**, 1455-61.

Orihuela E, Shahon RS (1987). Influence of blood group type on the natural history of superficial bladder cancer. *J Urol*, **138**, 758-9.

Pandey M, Gautam A, Shukla VK (1995). ABO and Rh blood groups in patients with cholelithiasis and carcinoma of the gall bladder. *BMJ*, **310**, 1639.

Pare G, Chasman DI, Kellogg M, et al (2008). Novel association of ABO histo-blood group antigen with soluble ICAM-1: results of a genome-wide association study of 6,578 women. *PLoS Genet*, **4**, e1000118.

Paterson AD, Lopes-Virella MF, Waggott D, et al (2009). Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Research Group: Genome-wide association identifies the ABO blood group as a major locus associated with serum levels of soluble E-selectin. *Arterioscler Thromb Vasc Biol*, **29**, 1958-67.

Paterson AD, Lopes-Virella MF, Waggott D, et al (2009). Genome-wide association identifies the ABO blood group as a major locus associated with serum levels of soluble E-selectin. *Arterioscler Thromb Vasc Biol*, **29**, 1958-67.

Pinkston JA, Cole P (1996). ABO blood groups and salivary gland tumors (Alabama, United States). *Cancer Causes Control*, **7**, 572-4.

Pyd M, Rzewnicki I, Suwayach U (1995). ABO blood groups in patients with laryngeal and hypopharyngeal cancer. *Otolaryngol Pol*, **49**, 396-8.

Raitanen MP, Tammela TL (1993). Relationship between blood groups and tumour grade, number, size, stage, recurrence and survival in patients with transitional cell carcinoma of the bladder. *Scand J Urol Nephrol*, **27**, 343-7.

Roberts TE, Hasleton P, Swindell R, Lawson R (1988). Blood groups and lung cancer. *Br J Cancer*, **58**, 278.

Ronco AL, Stoll M, De Stefani E, et al (2009). Rh factor, family history and risk of breast cancer: a case-control study in Uruguay. *Cancer Detect Prev*, **32**, 277-85.

Roots I, Drakoulis N, Ploch M, et al (1988). Debrisoquine hydroxylation phenotype, acetylation phenotype, and ABO blood groups as genetic host factors of lung cancer risk. *Klin Wochenschr*, **66**, 87-97.

Rowe JA, Handel IG, Thera MA, et al (2007). Blood group O protects against severe *Plasmodium falciparum* malaria through the mechanism of reduced rosetting. *Proc Natl Acad Sci U S A*, **104**, 17471-6.

Salehi F, Dunfield L, Phillips KP, Krewski D, Vanderhyden BC (2008). Risk factors for ovarian cancer: an overview with emphasis on hormonal factors. *J Toxicol Environ Health B Crit Rev*, **11**, 301-21.

Slater G, Itzkowitz S, Azar S, Aufses AH Jr (1993). Clinicopathologic correlations of ABO and Rhesus blood type in colorectal cancer. *Dis Colon Rectum*, **36**, 5-7.

Stamatakos M, Kontzoglou K, Safioleas P, et al (2009). Breast cancer incidence in Greek women in relation to ABO blood groups and Rh factor. *Int Semin Surg Oncol*, **6**, 14.

Smith DF, Prieto PA (1992). Forssmann antigen. In: « Encyclopedia of immunology», Eds Roitt IM and Delves PH. Academic Press, London pp 591-2.

Steuer MK, Hofstadter F, Prцbster L, Beuth J, Strutz J (1995). Are ABH antigenic determinants on human outer ear canal epithelium responsible for *Pseudomonas aeruginosa* infections?. *ORL J Otorhinolaryngol Relat Spec*, **57**, 148-52.

Su M, Lu SM, Tian DP, et al (2001). Relationship between ABO blood groups and carcinoma of esophagus and cardia in Chaoshan inhabitants of China. *World J Gastroenterol*, **7**, 657-61.

Tryggvadottir L, Tulinius H, Robertson JM (1988). Familial and sporadic breast cancer cases in Iceland: a comparison related to ABO blood groups and risk of bilateral breast cancer. *Int J Cancer*, **42**, 499-501.

Wajsman Z, Saroff J, Murphy GP (1977). Blood group distribution in prostatic cancer patients. *J Surg Oncol*, **9**, 289-91.

Wapnick S, Zanamwe LN, Chitiyo M, Mynors JM (1972). Cancer of the esophagus in Central Africa. *Chest*, **61**, 649-54.

Wolpin BM, Kraft P, Gross M, et al (2010). Pancreatic cancer risk and ABO blood group alleles: results from the pancreatic cancer cohort consortium. *Cancer Res*, **70**, 1015-23.

Xie J, Qureshi AA, Li Y, Han J (2010). ABO blood group and incidence of skin cancer. *PLoS One*, **5**, e11972.