

Incidence of ABO and Rh blood groups in human cancers and the concomitant expression level differences of the A, B and Rh antigens

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Several studies have established an association between the ABO blood group and different cancer types. It is suspected that these relationships between blood group antigens (BGAs) and cancers extend beyond their demographic distributions and may involve mutations in genes encoding these BGAs. In the present study, blood samples from cancer patients were typed for ABO and Rh blood groups to examine the associations of specific BGAs with different types of cancer. Further, the concomitant differences in BGAs' expression levels were determined using the hemagglutination assay (HA). The cancer types studied included mostly carcinomas (CAs), sarcomas, lymphomas, and leukemias, as well as certain other types such as gliomas and hepatomas. The results indicated that blood group O was the most prevalent among the various cancer types studied, and that most samples were Rhesus (Rh)-positive. The BGA expression levels varied significantly among cancer types. The HA titre for the BGA A and B was highest in CAs, whereas the lowest titre values for these BGAs were found in non-CAs, such as acute leukemia. Interestingly, the HA titre values for almost all BGAs differed between samples obtained from the same patients over a 24 h interval. Although the exact mechanism of these differences is not yet ascertained, the very fact that they occur provides a new angle on the implications of BGAs in human cancers.

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MANY studies have been carried out to establish an association between blood groups and different cancer types. One of the earliest, statistically significant associations between cancers and the ABO blood group was reported by Aird *et al.*¹ in 1953, who found a higher prevalence of stomach cancer among individuals with blood

type A. The present study paved the way for several such associative studies across different cancer types. One such finding was that a higher frequency of blood type A was observed in individuals with pernicious anemia². It is also known that the ABO blood group antigens act as receptors for some pathogens, such as *Helicobacter pylori*³ and individuals with the infection are more susceptible to gastric ulcers and associated cases of gastric cancers⁴. Using these premises, Wang *et al.*⁵ proposed that individuals with antigen A may be more susceptible to *H. Pylori* infections. However, this assumption was contradicted by several studies which established that *H. Pylori* infections were found to be more prevalent in individuals with blood type O than in the non-O blood types^{6,7}. Many such studies establishing an association between the ABO and Rhesus (Rh) blood groups and cancer have been carried out, most of which are epidemiological⁸⁻¹⁰ and whose findings can serve as an epidemiological marker or a primary screening tool for identifying at-risk individuals in the population.

It is known that somatic mutations in the human Glycophorin-A (GPA) locus, which encodes the MN blood group antigens (BGAs), can be induced by ionising radiation, and similar events also support the somatic-cell-mutational theory of carcinogenesis. Hence, the GPA mutation assay is used as one of the biodosimetric assays to detect and quantify radiation exposures¹¹. Thus, in addition to studying the association between blood groups and different cancer types, we hypothesized that specific somatic mutations at the human ABO and Rh blood group loci may be associated with distinct cancer types. To determine whether such an effect exists, we examined differences in the expression levels of the A, B, and Rh antigens across various human cancer samples. The associations between blood groups and different cancers were studied by analysing blood group frequencies in the samples. The BGA expression levels were examined using the hemagglutination assay (HA), in which the HA titre value is a quantitative measure of erythrocyte surface antigens, as can be obtained using antigen-specific antibodies, such as blood group typing sera.

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