PROGNOSIS, RESPONSE TO TREATMENT OF HIGH RISK GTN DISEASE DUE TO POSSIBLE RISK FACTOR: IS BLOOD TYPE EFFECTIVE ON RESPONSE TO THE TREATMENT?

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ABSTRACT

Introduction: Gestational trophoblastic disease or GTD includes a diverse group of neoplastic disorders that arise from epithelial trophoblastic of placenta and is characterized by high levels of blood βHCG. Researchers are trying to find more information about the markers associated with this disease to find better prognosis and a greater understanding of the disease. One of the markers focused by researchers in various fields of medical science is the blood type. In this research we studied high risk GTN patients (gestational trophoblastic neoplasia) with the aim of surveying prevalence of the disease based on blood type. Method: In a cross-sectional study of descriptive analysis with the aim of determining the effect of blood type on prevalence of high risk GTN disease and also its effect on the response to treatment, 160 patients and case files were examined, 37 cases of which were excluded due to factors such as lack of cooperation and missing documents. Then a questionnaire consisting of patient's demographic data, blood type, type of GTD and the patient's response to treatment was prepared, and the information were recorded in questionnaires and analyzed for selected patients. Results: Blood types of patients were often O and A. 69 people had blood group A who constitute 56.1%. The number of people with O blood group was 33 who constituted 26.8%. 21 people with blood type B/AB constituted 17.1%. The chance of treatment response showed no significant difference in any of the various blood groups (P> 0.05). Conclusion: Gestational trophoblastic disease is more common in patients with blood types A and O but the chance of treatment response in these
patients was not significantly associated with blood type, of course, to cite more accurate results, more research is needed in different societies.

KEYWORDS: gestational trophoblastic disease (GTD), blood groups (types) ABO, βHCG.

INTRODUCTION

Gestational trophoblastic disease or GTD includes a diverse group of Neoblastic disorders that arise from epithelial trophoblastic placenta and is characterized by high levels of blood βHCG.\textsuperscript{[1-3]} the incidence of this disease in North America and Europe is 0.57 to 1.2 per 1000 pregnancies, and its prevalence is 7 to 10 times more in South East Asian Nations.\textsuperscript{[4-6]} In fact, gestational trophoblastic disease or GTD constitute a wide range of placenta diseases including relative or complete hydatidiform mole, invasive mole, pregnancy choriocarcinoma and placental site trophoblastic tumor, but Gestational trophoblastic neoplasms (GTN) includes invasive mole, choriocarcinoma and placental site tumor and it is divided into two metastatic and nonmetastatic categories. In general, the higher levels of βHCG in GTT patients is the reason of higher risk of disease and HCG is used as a marker of high risk in GTN process.\textsuperscript{[7]} High risk GTN may be seen after a molar pregnancy (50%), term pregnancy (25%), abortion (25%) and even ectopic pregnancies (76/0-4%). After molar discharge, in 15% of cases, stable mole may remain in the uterus and in 4% it may turn into choriocarcinoma and metastasis may occur.\textsuperscript{[8]} Various factors are involved in causing this disease including genetics, race, age, hormonal and immunological factors.\textsuperscript{[9]} Basically all kinds of nonmetastatic GTN are treated by chemotherapy. Nowadays GTN is known as the Women's most treatable Cancer.\textsuperscript{[10]} Researchers are looking to find more information about markers associated with this disease so that they can find better prognosis and understanding of this disease. One of the markers focused by the researchers in various fields of medical science is the blood group. ABO antigens are the main blood groups and in addition to blood cell surface, they are also present on the surface of other cells. Since these antigens are made of polysaccharide similar to some bacterial polysaccharides, they may affect function of immune system either directly or indirectly and weaken or strengthen the immune response.\textsuperscript{[11]} Genetic factor plays an important role in the immune system of different people and accordingly the immune response of people towards stimulating agents (pathogens) are different and histocompatibility molecules are of utmost importance in this regard. Some studies have pointed to differences in prevalence of diseases in ABO blood groups. For example, it was found in one study that the incidence of Dermatophytosis in O and A blood
groups is higher than other blood groups.\textsuperscript{[12]} Also another study showed that the concentration of anti-hepatitis C immunoglobulins in patients with hepatitis C has the highest amount in patients with blood group O and the lowest amount in patients with blood type AB.\textsuperscript{[13]} In another study it was found that a large percentage of patients with coronary artery disease belong to blood group O.\textsuperscript{[14]} Also, people with blood groups O and AB have the highest frequency in patients with malaria.\textsuperscript{[15]} On the other hand, many studies have not mentioned a meaningful and significant difference between ABO blood groups and increase or decrease in the incidence of disease. For example, in separate studies, no significant correlation was found between blood groups ABO and the incidence of breast cancer,\textsuperscript{[16]} infection with the virus,\textsuperscript{[17]} Chilcunganya, or anti-virus immunoglobulin concentration.\textsuperscript{[18]} Therefore, consideration of blood types among GTN patients may lead to the discovery of a new paradigm of diagnostic markers. Of course little research has been done in this field one case of which states that the risk of choriocarcinoma in patients with blood type A is more than blood group O.\textsuperscript{[19]} However, in this paper we have studied patients with high risk GTN with the aim of investigating the prevalence of this disease based on blood groups.

**METHOD**

After collecting the permission from the Ethics Committee of the Ahwaz University of Medical Sciences, in a cross-sectional descriptive analysis study aimed to determine the effect of blood type on the prevalence of GTN disease and also its effect on the response to the treatment the first stage began. Out of 160 patients and case files, 37 were excluded due to factors such as lack of cooperation and missing documents. Then a questionnaire was prepared consisting of patient's demographic data, blood type, type of GTD and the patient's response to treatment, and this information was recorded in questionnaires for selected patients. The obtained information was coded and then analyzed by SPSS\textsubscript{20} software. Chi-square tests were used for statistical analysis to examine the association between blood group and response to treatment. To evaluate the correlation intensity, Spearman phi correlation coefficient was used. To evaluate the influence of each of the blood groups, Logistic regression was used.

**RESULTS**

The age range of patients was 19-40. The blood types of most patients were A and O. 69 people had blood type A who constituted 56.1%. People with blood type O were about 33 who constituted 26.8%, and 21 people with blood type B/AB constituted 17.1%. (Figure A).
Although the prevalence of high-risk GTN disease is higher in blood groups A and O than the other ones, but no significant relation was evident between treatment response and blood groups and findings suggested that the number of people with blood group A who responded to the treatment formed 48.8% and the people with blood type A who didn't response to treatment constituted 7.3%. The people with blood group O who responded to treatment were 24.4%. People who didn't respond to treatment and had blood group O constituted 2.4%. People who responded to treatment with the blood type B/AB constituted 13%. People who didn't response to treatment with the blood type B/AB constituted 4.1%. In order to determine the relationship between blood group and response to treatment Chi-square test was used in which the obtained P-VALUE value was equal to 0.299 and phi and Spearman correlation coefficient were used to determine correlation where the Pearson correlation coefficient was -0.062 and obtained p-value was equal to 0.493 where there was no significant correlation between blood groups and response to treatment. To evaluate the influence of blood groups on treatment response logistic regression was used that the chance of response to treatment of blood group A versus blood group B / AB was equal to 2.038 but because of the amount of P-VALUE= 0.24, the chance of treatment of blood group A versus blood group B / AB was not statistically significant. Also the chance to response to treatment of blood group O versus blood group B / AB was equal to 3.125 but because of the amount of P-VALUE=0.151 the chance of treatment of blood group O versus blood group B / AB was not statistically significant (Figure Two).
DISCUSSION AND CONCLUSION

Review of the related studies conducted on patients with high-risk GTN has shown that the effect of blood groups in this area has been focused by few researchers and few studies have investigated this marker. As we can see GTD is divided into two types of benign and malignant that benign type includes hydatidiform moles (complete and partial), while malignant lesions of the group include invasive mole, placental site trophoblastic tumor (PSTT) and choriocarcinoma. This subtype of malignant lesions with variable characteristics in terms of invasion and metastasis, are called gestational trophoblastic neoplasia (GTN).\textsuperscript{[20-22]} Therefore, it can be observed that the conducted studies to evaluate the effects of blood types are performed on only one of the mentioned GTN types. The studies conducted in the the second half of the twentieth century indicate the high prevalence of the disease in people with blood group $\text{A}^{[23-25]}$ and most similar studies conducted in ovarian cancer indicate the high prevalence of the disease in people with blood group A for example these reports can be found in the oldest studies conducted in twentieth century. In one of these studies Swedish researchers through the analysis of blood group ABO and Rh between 1958 and 1973 on 1930 patients with ovarian cancer showed that the rate of spread of the disease in a blood group A was higher than blood group O. The stated that blood type can increase the risk of ovarian carcinomas.\textsuperscript{[26]} In England a study was conducted on 1261 women with ovarian cancer during 1968 to 1986 which indicated that ovarian cancer in women with blood group A was higher than other people.\textsuperscript{[27]} However, apart from similar studies in other cancers,
studies conducted in recent years on high-risk GTN patients were not performed to analyze the primary objective of the effect blood group risk factor on the patients but the researchers following other clinical symptoms and the treatment outcomes for these patients presented reports of the spread of blood groups in these patients as well or they have discussed etiologies leading to GTN such as malignant or benign lesions based on blood groups. However, studies have been associated with contradictory results and no dramatic coherence is observed in different studies. For example, in the study of Haidar Khan et al the highest frequency was among Molar patients (36%), related to people with blood group B.\[28\] But in another study by Nahar blood group A has the highest frequency rate of 32% in similar patients.\[29\] However, in another study by Reddy et al 52% of the patients had blood group O.\[30\] Kitong et al in their study conducted on Hydatidiform patients did not show a significant difference between the blood group groups of patients.\[31\] The analysis of other studies suggests that not only the possible effect of blood group has not been considered, but the studies have only provided as brief report of frequency of blood groups among these patients and have not examined the relationship between the outcome and recovery and blood groups. But one of the strengths of this study is to investigate the relationship between blood groups and patients' response to treatment; however, as expressed in the results, this relationship was not statistically significant. It should be noted that the present study is conducted on a small population yet it has been able to present a 20 year report on these patients but it is suggested to perform future analysis of the effect of blood group on prevalence of the disease, mortality and morbidity in these patients with a greater population and longer period so obtain more documented results of effects of blood group on high risk GTN patients.

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