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Association of ABO and Rh blood groups with type 2 diabetes mellitus

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Abstract. – OBJECTIVE: The phenotypic "ABO" blood groups are inherited antigenic substances which are found on the surface of red blood cells in addition to other tissues. Certain hypothesis advocates that genetic predisposition like "ABO" blood group would be associated with occurrence of diseases including type 2 diabetes. This study aimed to investigate the potential association between "ABO" and "Rhesus" blood groups with type 2 diabetes.

MATERIALS AND METHODS: We identified 47 research documents in a data based search including ISI-Web of Science, EMBASE and PubMed. Literature was explored using the key terms including "ABO blood groups" "type 2 diabetes". Studies in which "ABO" blood types and diabetes mellitus were discussed included without restrictions of research documents, types, status and language of the publications. Finally, 15 publications which matched our criteria were included, and remaining studies were excluded.

RESULTS: Blood group "B" was associated with high incidence of type 2 diabetes and blood group "O" has a minimum association with type 2 diabetes. Blood group "A" and "AB" were almost equally distributed in both diabetic and non-diabetic population. However, we were unable to find an association between "Rh+ve" and "Rh-ve" blood groups with type 2 diabetes.

CONCLUSIONS: Subjects with blood group "B" are at high risk while individuals with blood group "O" are at low peril of evolving type 2 diabetes. It is suggested that subjects with blood group "B" should be closely monitored by physicians as these subjects have an increased risk of type 2 diabetes.

Key Words:
Blood groups, ABO blood groups, Type 2 diabetes.

Introduction

The phenotypic ABO blood groups are polymorphic, inherited, antigenic substances found on the surface of red blood cells in addition to other tissues. The "ABO" blood group was first discovered by Karl Landsteiner in 1900. "ABO" and "Rhesus" blood group antigens are major human blood group system antigens with prime importance in transfusion medicine[1]. The blood type of an individual defined by small carbohydrate epitopes depends on the presence or absence of genes "A" and "B". The gene is positioned on chromosome 9q34 and consists of 7 exons spread over 18 kb called "ABO" blood groups[2]. The "ABO" system contains four major "ABO" phenotypes "A", "B", "O", and "AB". The "ABO" blood group system is associated with some diseases including gastric and duodenal ulcer[3], hepatitis-B[1], vascular diseases[4], abdominal aortic aneurism[5] and cancers[6,7]. Some epidemiological studies demonstrated the linkage among the "ABO" blood group and the risk of type 2 diabetes mellitus (DM), although, the findings were not consistent and not yet clearly clarified.

The incidence of diabetes mellitus has broken all the previous incidence records. The current global numbers of diabetic patients are 382 million, and the number is likely to rise to 592 million by the year 2035. Moreover, about 183 million people are unaware that they have diabetes[8]. The incidence of diabetes mellitus has been linked with many factors such as genetic, environment, diet, obesity, lack of exercise. But, still limited studies are added in the current science literature regarding the correlation of "ABO"

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and "Rhesus" blood groups with type 2 DM. Therefore, this study aimed to find out the possible linkage between "ABO" and "Rhesus" blood groups with type 2 diabetes mellitus.

Materials and Methods

Selection of Studies

This study was designed and conducted in the Department of Physiology, College of Medicine, King Saud University, Riyadh, Saudi Arabia. We found 47 research documents in a database including Institute of Scientific Information, ISI-Web of Science, PubMed and EMBASE. We gathered the literature, using key terms including "ABO blood groups", "Blood group A", "Blood group B", "Blood group AB", "Blood group O" "Rhesus+ve" "Rhesus-ve" and diabetes mellitus. In addition, we entered the key-words in Google Scholar, after finding any related research document, we re-submitted the title of the article in the ISI-Web of Science and PubMed to verify for any missing article. The summary of the paper was appraised to determine the suitability for the documents. All articles in which "ABO", "Rh+ve" and "Rh-ve" blood groups and diabetes mellitus was debated were eligible for inclusion without restrictions of research documents, standings and language of the publications. We comprehensively analyzed 47 papers, finally 15 publications which matched our criteria were included and remaining studies were excluded.

Inclusion and Exclusion Criteria

The inclusion criteria were cohort studies, cross-sectional studies which reported relative risks for diabetes mellitus in relevance of "ABO" and Rhesus blood groups were included. The studies published in non-ISI indexed journals without usable data or of low quality were excluded.

Data Extraction and Quality Assessment

Findings were extracted independently by two investigators; the results were determined by using a standardized form including a full description of the document characteristics.

Ethics Statement

We analyzed the data based research documents on "ABO" blood groups, "Rhesus+ve" and "Rhesus-ve" blood groups and type 2 diabetes; hence, ethical approval was not needed.

Results

The Table I demonstrates an association of "ABO", "Rhesus+ve" and "Rhesus-ve" blood groups and type 2 diabetes. Blood group "B" is associated with high incidence of type 2 diabetes and blood group "O" has least association with type 2 diabetes mellitus. Blood group "A" and "AB" were equally distributed (Figure 1). However, we did not find any association between "Rh+ve" and "Rh-ve" blood groups with type 2 diabetes mellitus.

Discussion

The "ABO" and Rhesus blood group antigens are the most essential antigens in transfusion medicine[1], but their susceptibility to certain diseases or health risk has not been well discussed. In the present study, we found that blood group "B" is associated with high incidence of type 2 diabetes and blood type "O" has least association with type 2 diabetes (Figure 1). Blood group "A" and "AB" were almost equally distributed in both diabetic and non-diabetic population. However, we did not find out any linkage among "Rh+ve" and "Rh-ve" blood groups with Type 2 DM.

The relationship between blood groups and disease was first hypothesized during mid-1950s. There are some studies about the association of DM and "ABO" blood types in the literature. McConnell et al[22] found an association between diabetes mellitus and blood group "A" and this was confirmed by Andersen and Lauritzen[23]. The literature added that blood group "B" is defensive against type 2 diabetes[17].

Sindhu et al[21] conducted a study on the rapport between blood groups "ABO and Rh" and DM. They compared the blood groups of 520 of diabetic patients with 6204 normal individuals taken as control. They found an association of DM with blood group "AB" "A" and "Rh+ve" blood groups. The highest differences were noticed for "AB" groups and minimum in the group "A".

Fagherazzi et al[12] determined the link of "ABO" blood type "A", "B", "AB" and "O", "Rhesus" factor positive or negative with type 2 diabetes. Subjects with blood type "A" blood group "B" were at higher risk of type 2 diabetes mellitus compared with those with blood group "O". There was no significant difference in type 2 diabetes risk between "Rh+ve" and "Rh-ve"

Table I. Association of ABO and Rh blood groups with type 2 diabetes.

Authors name and year	Type of study	Blood groups	Association with diabetes mellitus
Kamil et al 2010[9]	Case-control study	Blood group B Blood group A and O	Blood group B was more in type 2 diabetic patients Blood group A and O have less likelihood of diabetes mellitus
Okan et al 2006[10]	Cross-sectional	Blood group O (-) and A (+) Blood group O (+)	Blood group A +ve and O-ve are more susceptible to DM Blood group O +ve was markedly lower in diabetics than controls
Karagoz et al 2015[11]	Retrospective	Blood group AB Blood group O	Higher risk of GDM Blood type O has high risk of developing DM
Fagherazzi et al 2015[12]	Prospective cohort	Blood group O Blood group A or B	Blood type O has low risk of developing type 2 DM Blood group A or B are at increased risk of type 2 diabetes
Bener and Yousafzai 2014[13]	Case-control	Blood group B Blood group O	Blood group B was common in diabetic patients Blood group O was less common in diabetics compared to non-diabetics
Qureshi and Bhatti in 2014[14]	Descriptive cross-sectional	Blood type A, B and AB Blood group O	Blood group A was 4.36%, B was 17.15% and AB 7.34% in diabetics. Blood group O was 28.94% less common in diabetics
Joseph 1964[15]		AB and B	High frequency of DM for blood group B and less frequency in AB
Zhang et al 2015[16]	Prospective population-based Cohort	A, B or O AB	Blood groups A, B or O were associated with high risk of GDM Blood type AB linked as protecting factor against GDM
Qi et al 2010[17]	Cross-sectional	Blood group B and O	Blood group B linked with low risk of DM compared to blood type O
Waseem et al 2012[18]	Cross-sectional	Blood group AB Blood group A and B	High % of blood group AB in diabetics. Positive association b/w Rh-ve blood groups and DM Blood group A and B have lower % of DM
Hadeal et al 2008[19]	Prospective randomized	Blood group B	Blood group B was associated with DM
Moinzadeh et al 2014[20]	Cross-sectional	Blood group B	Blood group B+ was common in diabetic patients (30.8%)
Sindhu et al 1988[21]	Cross-sectional	Blood group A, AB	Blood group A, AB and Rh-positive have high association

Note: Main studies and their association with type 2 DM are highlighted in the table.

blood types. They also noticed a high type 2 diabetes risk for those with the AB +ve group. The findings suggest that blood type O has a lower risk of developing type 2 diabetes.

Bener and Yousafzai[13] investigated the linkage between the "ABO" blood types and DM in Qatar. They demonstrated that, blood type "B" was significantly common and blood group "O" was significantly less common in diabetic patients compared to healthy non-diabetic population. In addition, Qureshi and Bhatti[14] determined the incidence of type 2 diabetes among "ABO" blood groups. They found that the values were 4.36% for blood group "A"; 17.15% for blood group "B" and 7.34% for blood group "AB" higher in diabetic patients. However, the value was 29.0% lower for the blood type "O". They conclude that, the incidence of blood type "B" was significantly common and blood group "O" was low in type 2 diabetics as compared to the general population.

Zhang et al[16] determined the association of blood types "ABO" and the risk of gestational diabetes. They reported that, females with blood groups "A", "B" or "O" have high association with gestational DM as compared with blood type "AB".

Karagoz et al[11] investigated the association of various blood groups with the incidence of DM.

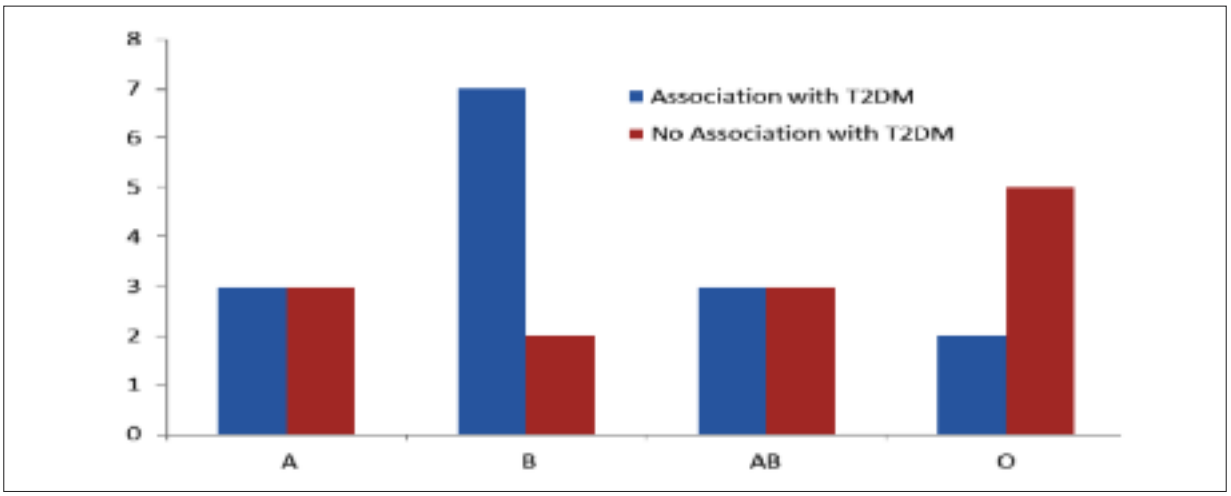

Figure 1. Positive or negative association of blood group A, B, AB and O with type 2 diabetes. *Note:* Existing literature based observation on "ABO" blood groups and their positive or negative relevance with type 2 DM.

They found a substantial difference between the distribution of "ABO" blood groups and gestational DM. They noticed higher risk of gestational DM in patients with blood group "AB" and "O". Moreover, "Rh+ve" factor was also considered a risk factor.

Waseem et al[18] assessed the link "ABO" and "Rh blood types" with DM. The author reported a higher fraction of blood group "AB" among diabetics (15.0%) as compared to controls (10.0%). Blood groups "A" and "B" were less communal in diabetic group as compared to normal subjects. Blood group "O" was equally distributed among both groups. However, "Rh-ve" blood type was more common in the diabetic group.

Moinzadeh et al[20] evaluated 8126 participants, 5143 were male and 2983 were female. They observed that blood group "B+ve" was more frequent in diabetic patients (30.8%) compared to control group 24.9%. However, Sharma et al[24] did not find an association with "ABO" blood groups with T2DM.

The possible mechanism in the development of an association among "ABO", Rhesus blood types and incidence of type 2 diabetes is still not well defined. The recent genome-wide association studies suggest that the "ABO" blood group antigen enhances the general body inflammatory state. Single nucleotide polymorphisms at the "ABO" locus are linked with two serum markers of inflammation, TNF-α and soluble intercellular adhesion molecule-1[25,26]. Increased expression of TNF-α has been associated with inflammation[27]. It is well known that the systemic inflammation is the main cause of insulin resistance and ultimately plays a role in the development of type 2 diabetes[28,29]. The experimental and epidemiologic studies suggest that "ABO" blood groups and type 2 diabetes may be interrelated because of broad genetic and immunologic basis. Moreover, the genetic makeup, which may lead to a link between the high association of blood group "B" with the incidence of type 2 diabetes and blood group "O" has less association with diabetes mellitus.

Study Lmitations

This study has few limitations. There was a lack of individual "ABO" and "Rh+ve" and "Rh-ve" blood group data and its association with T2DM. There was no uniformity in the literature type and sample size, and lack of literature from the various corners of the globe. Further large sample sized data from both experimental and epidemiologic studies are desired to provide better analysis and conclusions with more insights into the exact mechanism of association between "ABO" and "Rh" blood groups with type 2 diabetes risk.

Conclusions

Blood group "B" is associated with high incidence of type 2 diabetes and blood group "O" has minimum association with type 2 diabetes. Blood group "A" and "AB" were almost equally

distributed among diabetic and non-diabetic population. However, we were unable to find out an association between "Rh+ve" and "Rh-ve" blood groups with type 2 diabetes. The current findings suggest that, physicians should be more careful and closely monitor the individuals with blood group "B" as these subjects are more prone to develop type 2 diabetes.

Acknowledgements

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Conflict of Interest

The Authors declare no conflicts of interest.

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