Association of ABO blood groups with diabetes mellitus

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Objective: So far no studies have been performed in Malaysia to look at association of diabetes mellitus (DM) with blood groups. We studied the association of ABO blood groups with DM type 2.

Patients and methodology: It was a case control study conducted at Kepala Batas Hospital Batas, Penang, Malaysia in the year 2009, involving 70 patients with DM type 2 and 140 healthy controls. Ethical approval was obtained from Universiti Sains Malaysia. Blood samples were collected from the patients after consent. Samples were tested for ABO blood groups using ID-Card gel method.

Results: Chi-square test results showed that there was an association between the ABO blood groups and DM type 2. It was found that A and O blood groups were negatively associated with DM type 2 ($P < 0.05$) with higher percentage of A and O groups individuals were non-diabetic. No significant association was noted between DM type 2 and blood groups B ($P = 0.423$) and AB ($P = 0.095$). It was also noted that B blood group was distributed with highest percentage among patients with DM type 2 (53.71%) compared to controls (22.52%), but no statistical significance achieved.

Conclusion: The results obtained suggest that there was a negative association between ABO blood groups A and O with DM type 2, with A and O group having less chances of diabetes. Large studies in other ethnic groups are needed to confirm these results.

Keywords: *blood group A*; *blood group O*; *diabetes mellitus*

Diabetes mellitus (DM) is a syndrome characterized by hyperglycemia resulting from defects of insulin secretion and/or increased cellular resistance to insulin (1).

DM is generally divided as insulin-dependent diabetes mellitus (IDDM or type I), characterized by an absolute deficiency of circulating insulin and non-insulin-dependent diabetes mellitus (NIDDM or type 2), characterized by elevated insulin levels that are ineffective in normalizing blood sugar levels or by impaired insulin secretion (1). It was reported that DM type 2 is the most common type, accounting for 90–95% of all diabetic cases (2).

In 1998 it was estimated that there were almost 140 million people with diabetes and the predictions by Hilary King indicate that this figure would rise up to 300 million by the year 2025 (3). The prevalence of diabetes in Malaysia has increased steadily from 6.3% in 1986 to 8.3% in 1996 (4).

The major human blood group system is ABO. The blood group of a person depends upon the presence or absence of two genes, A and B. The majority of ABO determinants are expressed on the ends of long polylactosamine chains (5).

No diseases are known to result from the lack of expression of ABO blood group antigens, but the susceptibility to a number of diseases has been interrelated to a person's ABO phenotype. Such correlations remain conflicting and include the observation that gastric cancer is more common in group A individuals, whereas gastric and duodenal ulcers occur more commonly among blood group O individuals (6).

In Malaysia, data was lacking on association between blood groups and DM and our study was conducted to look at such association.

Materials and methods

Description of the cases and calculation of statistical power of study

The present study was a case control study. The study was approved by the Research and Ethics Committee, Universiti Sains Malaysia. Patients with DM type 2 at Kepala

Batas Hospital (KBH), Penang, Malaysia, were included in this study. The control samples were collected by the staff from the donors in mobile blood bank of the hospital (mobile donation) and selected randomly. Exclusion criteria were patients with psychiatric illness, acute illness, age less than 18 years old, and history of diabetic ketoacidosis.

Sample size was calculated using Power and Sample Size Calculations software Version 2.1.31 (PS) program for independent case control study. ($\alpha = 0.05$, power = 80%, $P0 = 0.5$, $P1 = 0.7$, $M = 2$).

α: The type 1 error probability for a two-sided test.

$P0$: The probability of exposure in control (the events among control).

$P1$: The probability of exposure in cases (the events among cases).

M: The ratio of control to cases.

Power: is probability of correctly rejecting the null hypothesis assuming that relative risk (odds ratio) equals 1 in given n cases.

The study was adequately powered (80%) to detect a difference (20%) between cases and controls in terms of their association with ABO blood groups. Although sample size was small for such a study, it was intended due to time constrains and a 20% difference was presumed between cases and controls to keep sample size small.

A total of 70 consecutive DM type 2 patients were sampled at medical clinics KBH and 140 consecutive adult healthy controls (donors in blood bank of the hospital) were collected. None of the consecutive controls or cases met the exclusion criteria. Patient recruitment lasted for six months from January to June 2009.

Blood sampling
One to two ml of blood sample for grouping was collected from patients and controls by a staff nurse in KBH. ABO blood group was determined using ABO gel card test.

ABO blood group determination by using ID-Card gel method (ID-Micro Typing System)
The gel test was first released in Europe and then in USA (7). The technology was developed by Lapierre et al. (8).

We used ID-Card gel forward grouping and ID-Card gel reverse grouping, which were supplied by DiaMed.

Results
In our study, Chi-square test results showed a negative or inverse association between ABO blood groups and DM type 2. A and O blood groups showed negative association with DM ($P < 0.05$), which implied that A and O blood group patients have less chances of DM type 2. However, no significant association was found between DM type 2 and blood groups B ($P = 0.423$) and AB ($P = 0.095$) (Table 1).

The frequency of B blood group (25; 35.71%) followed by O blood group (24; 34.28%) was high among patients with DM type 2, as shown in Table 2.

Among 140 samples from healthy controls, blood group A was the most prevalent (55; 39.28%), followed by group A (35; 25%) (Table 3).

Table 4 shows the racial distribution among patients with DM. A total of 57 patients were Malay of which 20 (35.09%) had blood group B. Among the Chinese there was nearly equal distribution among the eight patients. Indians represented only five patients with A and AB representing 40% of cases followed by O group (20%).

As shown in Table 5, blood group O was most dominant in the control group among males (43.94%) and females (35.14%). However, in the patients group, blood group B was dominant among females (40.54%) and blood group O was most dominant among males (39.4%). There was no significant difference in gender distribution among the control group ($P = 0.764$) and the patients group ($P = 0.069$).

Discussion
Most of the populations where evidence of association between genetic markers and type 2 DM has been found

Table 1. Association of blood groups with diabetes mellitus type 2

Blood groups	Patients	Control	Chi-square test patients vs. controls	P-value
A	11 (15.17%)	35 (25%)	12.522	<0.001
B	25 (35.71%)	31 (22.14%)	0.643	0.423
AB	10 (14.29%)	19 (13.57%)	2.793	0.095
O	24 (34.29%)	55 (39.29%)	12.165	<0.001

Note. The frequency of blood groups is shown in parentheses.

Table 2. ABO blood groups percentage distribution in patients with diabetes mellitus

Blood groups	Number of patients	Percentage (%)
A	11	15.71
B	25	35.71
AB	10	14.28
O	24	34.28

Table 4. ABO blood groups distribution among races for patients with diabetes mellitus

| Blood groups | Race | | | Total |
	Malay	Chinese	Indian	
A	10 (17.5%)	1 (12.5%)	0	11
B	20 (35.1%)	3 (37.5%)	2 (40%)	25
AB	7 (17.5%)	1 (12.5%)	2 (40%)	10
O	20 (35.1%)	3 (37.5%)	1 (20%)	24
Total	57 (100%)	8 (100%)	5 (100%)	70

are hybrid populations formed by recent mixing of parental populations (9).

The data on association between the distribution of the ABO blood types and diseases is conflicting, some studies reporting no association and others showed positive association. Despite the fact that the association of blood groups with certain diseases is clearly demonstrated, and the evidence that blood groups may play an important role in certain diseases, for example, peptic ulcer and gastric cancer (10), some studies report no association between ABO blood group with those diseases, including DM. It is not surprising that the data on association of diabetes with ABO blood groups is scanty and mostly shows no association. However, there is evidence of positive association as well.

Rahman (11) reported in a study from Bangladesh with a sample size of 2,312 patients and 8,936 controls that there was no association between ABO blood groups and DM.

Rahman described no positive association, but our results show a significantly lower percentage of O and A blood groups among diabetic patients, which means a negative association with these blood groups. A larger sample study will be needed in our population to further investigate this finding.

Another study carried out in India included 511 patients with DM type 2 at Varni Pathology Clinic, Sagar, Madhya Pradesh. The samples represented adequately the Brahmin ($n = 146$), Bania ($n = 127$), Kayasth ($n = 52$), Shudra ($n = 59$), and Muslim groups ($n = 51$). In total, 475 unrelated normal healthy individuals were sampled randomly from the same area, matching age, sex, socio-economic status, etc., but not the disease condition. For the ABO blood types, standard serological

Table 3. ABO blood groups and their percents among the healthy control

Blood groups	Number of control samples	Percentage (%)
A	35	25
B	31	22.14
AB	19	13.57
O	55	39.28

procedures was followed using the anti-A, anti-B, anti-D, and anti-sera. Statistical analysis was done using the Chi-square test and the findings suggested that there was no association between the ABO blood groups and DM type 2 (12).

An association of DM with blood group A was demonstrated by McConnell and Pyke (13) and this was confirmed by Andersen and Lauritzen (14).

There are many studies which showed a significant excess of blood group A among male diabetics, such as a combined series from Lancashire, Cheshire, and Oxford (13).

In addition, there were reports from Italy (15) and Trinidad (16) showing an increased frequency of blood group B among diabetics, but in Germany (17) and in Glasgow (18) it was concluded that there was no significant association between ABO blood groups and diabetes.

As obvious from the above discussion, certain populations do show a positive association with ABO blood groups but the evidence is mixed.

In the present study, there was a negative association between A and O blood groups and DM type 2 ($P < 0.05$), with both groups being less common in the diabetic group. However, a larger sample study will be needed in Malaysia in different racial groups to verify our findings. Our results are interesting in terms of the negative association of A and O groups with DM, which seem to have protective effect. However, it is premature to make any etiological conclusions from the study unless a large sample study is being conducted.

Qureshi and Bhatti (19) demonstrated that DM type 2 and ABO blood groups are interrelated; they found that among 70 patients with DM, blood group B was more common and represented 35.71% compared to that of control, which represented only 22.14% of the sample population, but statistical significance was not achieved ($P > 0.05$).

It is interesting to note that our study did show a higher percentage of blood group B in the diabetic group, but this failed to achieve statistical significance, and results are in agreement with Qureshi and Bhatti.

Table 5. Distribution of ABO blood groups between genders for both controls and patients

Blood groups	Control				Patients			
	Male	Percentage (%)	Female	Percentage (%)	Male	Percentage (%)	Female	Percentage (%)
A	15	22.73	20	27.03	7	21.21	4	10.81
B	15	22.73	16	21.62	10	30.30	15	40.54
AB	7	10.61	12	16.22	3	09.09	7	18.92
O	29	43.94	26	35.14	13	39.39	11	29.73
Total	66		74		33		37	

Moreover, Qureshi and Bhatti found that O and A blood groups appear to be more frequent in healthy controls (39.28 and 25%) compared to patients with DM type 2 (34.28 and 15.71%), but this as well was not statistically significant. In addition, ABO blood group distribution had statistical significance among races in the controls but was non-significant in patients, and the same was true for gender, i.e., no statistical significance.

In our study, the O blood group was the most dominant among the Chinese, representing 58.46%, which is in agreement with a report by Chan (20).

In addition, it was found that the A blood group appears, with the highest frequency among Malay healthy controls, but in Indians blood group B was the most dominant. These results are also in agreement with Chan (20).

In our study, blood group B was prevalent at a high percentage among patients with DM type 2 – 35.71% in comparison to that of controls, 22.52%, but there was no statistically significant difference ($P > 0.05$).

We conclude that there was an association between blood groups A and O and DM type 2, and the association was negative as these groups were less common in diabetics and seems to be protective from the disease. Large studies in other ethnic groups are needed to confirm these results.

Conflict of interest and funding

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