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Original Research Article

Association of microvascular complications of type 2 diabetes mellitus with ABO blood group

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ABSTRACT

Background: Micro vascular complications are the major outcome of Type 2 Diabetes Mellitus progression, which reduces the quality of life and increases diabetic morbidity & mortality. As the incidence of type 2 diabetes is growing day by day; our search for its aetiology and pathogenesis is also ever growing to predict its risk factors and early screening for better care and prevention of its complications. Many studies have tried to link susceptibility of type 2 diabetes with ABO blood group though results have been inconsistent. The present study aims to analyse association of micro vascular complication with different blood groups if any.
Methods: A cross sectional study was conducted among patients of type 2 diabetes Mellitus in a tertiary care hospital. Determination of ABO and Rh status was done by standard slide method of agglutination. Detailed information about age, gender, BMI, duration of diabetes, age of onset of diabetes was noted with the help of a proforma. The records (clinical examination and investigations done by physician) were screened for type of micro vascular complications.
Results: Out of a total of 319 patients suffering from type 2 diabetes, 209 subjects (65.15%) had one or the other complications. A statistically significant (p=0.00) difference was observed between the presence or absence of complications in different blood groups. In patients with Blood group B, 76.14% presented with complications. Though Nephropathy was the most common complication observed among different blood groups, none of the type of micro vascular complication was found to be significantly associated with different blood groups.
Conclusions: The findings in our study suggest that although there was a significant association between presence or absence of complications and different blood groups, but this association was not significant for different types of complications.

Keywords: ABO blood group, Diabetes mellitus, Micro vascular complications, Type 2 diabetes

INTRODUCTION

Diabetes mellitus (DM) is recognized as a global major public health problem. Diabetes affects more than 240 million population worldwide and is expected to reach roughly 370 million by 2030.[1] The major driver of the epidemic is type 2 diabetes, which accounts for more than 90 percent of all diabetic cases.[2] Patients with type 2 diabetes have an increased risk of developing both micro vascular and macro vascular complications3. 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 chain.[4]

The gene for ABO group is present on chromosome 9 and on chromosome1 for Rh system. No diseases are known to result from the lack of expression of ABO blood group antigens, but susceptibility to number of diseases has been interrelated to a person's phenotype.[5] Since the discovery of ABO system by Karl Landsteiner in 1901, many researchers have made attempts to determine the significance of particular ABO phenotype for susceptibility to disease.[6,7] Association of ABO blood group with type 2 diabetes and its complications is still not defined, but 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 increased serum marker of inflammation, soluble intercellular adhesion molecule-1.[8] 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.[9] The pathological hallmark of DM involves the vasculature leading to both micro vasculature and macro vascular complications. Diabetes induces changes in the micro vasculature, causing extracellular matrix protein synthesis and capillary basement membrane thickening which are the pathognomic features of diabetic microangiopathy. These changes with advanced glycation end products, low grade inflammation and neovascularization can lead to macrovascular complications.[10] As diabetes mellitus is emerging as a modern epidemic, prevalence of type 2 diabetes has been steadily increasing, study in this field is also ever growing to predict its risk factors and causative factors to improve the prognosis and treatment outcomes. The data on association between complications risk in different blood groups and type of micro vascular complication in type 2 diabetes is scanty, so the present study attempts an insight into this delicate relationship between ABO blood group, type 2 diabetes and its complications.

Aims and objectives

- To study the association of different blood groups with presence or absence of any complications in type 2 diabetes.
- To find any association of different blood groups with type of micro vascular complications of type 2 diabetes.

METHODS

Study design

A cross sectional study was conducted in hospital settings of a tertiary care hospital. All the cases with known diagnosis of type 2 diabetes attending medical OPD or admitted in hospital for some complaint, during the 10 months study period were included in the study.

Inclusion criteria

Age more than 30 years, had given written consent, already diagnosed case of type 2 diabetes (according to the American Diabetes Association[11] venous blood glucose values higher than or equal to 7 mmol/l ≥126 mg/dL), undergoing treatment and coming for follow up to hospital or admitted in hospital for some ailment.

Exclusion criteria

Subject with Type 1 DM or diabetes due to metabolic disease, gestational diabetes, drug induced, past history of pancreas surgery was excluded from the study.

After selecting the subjects, the purpose of the study was explained to each subject and written consent was taken. The study subjects were interviewed so as to ensure privacy and all the information collected was incorporated on a pretested, predesigned semi structured questionnaire prepared for the study purpose. The study has received approval from Institutional Ethical Committee of the college.

After the detailed history taking which included age of onset of disease, duration of disease, blood glucose record of past 6 months, presence or absence of complications. Age, height and weight were noted for all the participants. BMI was calculated.

Body Mass Index

Weight in kg and height in cms were measured using standard methodology as per WHO guidelines. Body mass index (Quetelet index) was calculated using formula BMI = Wt (kg)/ Ht (m^2).[12]

Screening for complication was done by reviewing the clinical records (clinical examination done, and other appropriate tests advocated by physician according to different guidelines by ADA).[13] The main micro vascular complications that were frequently observed were Diabetic nephropathy, peripheral neuropathy, and retinopathy. Some cases also reported presence of two or more complications and some triopathy.

For diabetic nephropathy

Diagnosis is based on measurement of urinary albumin excretion (as defined by ADA); albuminuria 30-299 mg/24h and albuminuria >/300 mg/24h.

Peripheral Neuropathy

Assessment included a careful history and either temperature or pin prick sensation and vibration sensation using a 128-Hz tuning fork (large fibre fn), light touch perception using a 10-g monofilament and ankle reflexes.

Retinopathy

Ocular examination mainly by ophthalmoscope (by using International classification of Diabetic Retinopathy as defined by ADA) and few other tests done in some cases.

ABO blood grouping and Rh typing

The ABO blood grouping and Rh typing were performed in the clinical laboratory, by the standard slide method of agglutination by using a commercial kit of Antiserums A, B, and D (Tulip Diagnostics P Ltd) for all the study subjects (cases) and controls.

Statistical analysis

The data obtained were analyzed using statistical software open epi info version 6.0. Data were expressed as frequency and percent. Statistical tests like Chi-square test (for qualitative data) and ANOVAs (for quantitative data) were applied to compare the blood groups with regards to different variables. P<0.05 was considered to be statistically significant.

RESULTS

Table 1: Presence of complication in different blood groups among cases of type 2 diabetes (chi square).

Blood group	Complication		Total (319) No (%)
	Present (209) No (%)	Absent (110) No (%)	
A	46 (56.09)	36 (43.90)	82 (100)
B	96 (76.19)	30 (28.57)	126 (100)
AB	26 (68.42)	12 (31.57)	38 (100)
O	41(56.16)	32 (43.83)	73 (100)

X^2 =12.54, p=0.00

A total of 319 cases of type 2 diabetes were studied for presence of micro vascular complications. A significant 65.51% cases had developed one or more complication.

Table 2: Distribution of various complications in different blood groups among cases of type 2 diabetes (Chi square).

Blood group	Complications					Total No (%)
	Retinopathy No (%)	Neuropathy No (%)	Nephropathy No (%)	p/o any 2 complications No (%)	Triopathy No (%)	
A	6 (13.04)	8 (17.39)	11 (23.91)	12 (26.08)	9 (19.56)	46 (100)
B	12 (12.5)	9 (9.37)	26 (27.08)	31 (32.29)	18 (18.75)	96 (100)
AB	4 (15.38)	4 (15.38)	7 (26.92)	6 (23.07)	5 (19.23)	26 (100)
O	7 (17.07)	6 (14.63)	10 (24.39)	11 (26.82)	7 (17.07)	41 (100)

X^2=3.486, df=12, p=0.99

Further analysis based on different blood groups showed that in all the blood groups A, AB and O more than half of the patients had developed complications and in Blood group B, 76.14% patients presented with complications and this difference was statistically significant (p=0.000).

Table 2 shows that in blood groups A, B and O commonest presentation of cases was with presence of combination of two complications, wherein neuropathy along with nephropathy was the most frequent. This was followed by Nephropathy alone presenting in almost one fourth of the patients with different blood groups. Distribution of different categories of complications in various blood groups failed to reach any statistical significance (p=0.99), there by implying a similar pattern.

The mean age of the study subjects (cases) was 62.13±10.22 years. In all the blood groups more than half of the subjects were in the age group of more than equal to 60 years. In all the blood groups no of males were more than females although blood group A showed that 54.34% females had complications of diabetes. The differences observed for age and sex distribution failed to achieve statistical significance (p=0.75 and 0.20 respectively). The mean duration of diabetes was 9.01±3.17 years. 41.14% patients had duration of diabetes of 5 years or less, this was followed by duration of more than 10 years in 32.53% cases with complications. Among 41 cases of blood group O duration of diabetes was more than 10 years in 41.46% cases and these findings were contrary to findings in Blood groups A, B and AB in which duration of less than 5 years was most commonly seen (41.30%, 41.66% and 46.15% respectively).This difference in findings of duration of diabetes in different blood groups failed to achieve statistical significance (p=0.8).

Table 4 shows that in patients with duration of diabetes of less than 5 years the predominant complication was nephropathy followed by combination of two complications (41.86 and 36.04% respectively). As the duration of diabetes increased to 5-10 years, maximum patients developed a combination of two complications (34.54%). In patients with duration of complications ten years or more, a combination of three types of complication was the commonest presentation (29.41%).

Table 3: Distribution of Socio demographic variables in different blood groups among cases of type 2 diabetes with complications (Anova).

Variables	Blood groups					X^2/t	P
	A (46)	B (96)	AB (26)	O (41)	Total (209)		
Age in years							
<60	14 (30.43)	33 (34.37)	9 (34.61)	17 (41.46)	73 (34.92)	1.19	0.75
≥60	32 (69.56)	63 (65.62)	17 (65.38)	24 (58.53)	136 (65.07)		
Sex							
M (118)	21 (45.65)	55 (57.29)	14(53.84)	28(68.29)	118 (56.45)	4.62	0.20
F (91)	25 (54.34)	41 (42.70)	12 (46.15)	13(31.70)	91 (43.54)		
Duration of DM							
≤5 years	19 (41.30)	40(41.66)	12(46.15)	15 (36.58)	86 (41.14)	2.48	0.8
5-10 years	14 (30.43)	25 (26.01)	7 (26.92)	9 (21.95)	55 (26.31)		
>10 years	13 (28.26)	31 (32.39)	7 (26.92)	17 (41.46)	68 (32.53)		
Age of onset of DM (Mean±SD)	54.62±8.74	53.53±8.89	53.26±6.90	51.72±12.12	53.34±9.53	0.57	0.63
BMI	24.86±6.20	24.82±3.46	25.15±3.80	24.61±2.84		0.06	0.98

Table 4: Association of micro vascular complications and duration of diabetes among cases.

Complications	Duration of type 2 diabetes in years		
	<5 (n=86)	5-10 (n=55)	≥10 (n=68)
Retinopathy	5(5.81)	11(20)	13(19.11)
Neuropathy	7(8.13)	9(16.36)	11(16.17)
Nephropathy	36(41.86)	4(7.27)	14(20.58)
P/o any2 complications	31(36.04)	19(34.54)	10(14.70)
Triopathy	7(8.13)	12(21.81)	20(29.41)
Total	86(100)	55(100)	68(100)

X^2=42.57, df=8,p=0.00

DISCUSSION

Type 2 diabetes makes up about 90% of cases of diabetes and is a long term metabolic disorder that is characterized by high blood sugar, insulin resistance and relative lack of insulin.[14] Type 2 diabetes is a chronic disease associated with 10yrs shorter life expectancy due to number of complications with which it is associated.[15] In the developed world and increasing elsewhere, Type 2 diabetes is the largest cause of non-traumatic blindness and kidney failure.[16]

In our study out of 319 diabetic subjects, 209 subjects (65.51% cases) had developed one or the other microvascular complications of type 2 diabetes. Mean age of cases were 62.13+10.22. Out of all cases, 56.45% were males and 43.54% were females. In all the blood groups no of male were more than no of female except for A blood group. Mean BMI was in normal range. It is interesting to note that our study did show a higher percentage of blood group B in the diabetic group but failed to show any statistical significance. The study is in agreement with Kapoor C et al.[17] The association between micro vascular complications and blood group is still unclear. Pontiroli et al did not find any association between ABO and Rh blood groups and development of complications, on the contrary Unan et al, Sushma T et al, have reported an association between the ABO blood group and micro vascular complications of type 2 diabetes.[18-20]

Among ABO blood groups significant association was observed in our study in distribution of micro vascular complications among cases (Type 2 diabetes) with B blood group (p=0.00). This observation is noted in our present study. No reference is available as per our present knowledge. Further studying about the association between different blood groups and type of complications it was revealed that nephropathy was the most common complication observed among different blood groups and combination of nephropathy along with neuropathy was the most frequent. The study is in agreement with Richelle J et al.[21] On the contrary Arora et al reported a strong association between diabetic nephropathy and retinopathy in newly diagnosed patients with diabetes.[22] However none of the micro vascular complications were found to be significantly associated with any blood group. Relation of complications in cases to duration of onset of disease (years), majority cases of blood groups A, B, AB fall in <5 year groups, on the contrary cases of blood group O (41.46%) fall in >10 yrs duration suggesting possible protective role of O blood group in type 2 diabetes though difference in findings failed to achieve statistical significance.

Distribution of type of complications on the basis of duration of diabetes, the study found maximum no of cases of diabetic nephropathy in subjects with <5 years duration, followed by more than one complication as

duration increases. Ballard et al also reported proteinuria in 8% of the patients at the time of diagnosis and 10% developed nephropathy within first 4 years of type 2 diabetes, a finding in agreement with results obtained in study of 661 patients with type 2 diabetes based on the general population by Klein R, et al.[23,24] A linear relationship between micro vascular complications and duration of disease was established by Chawla A et al in subjects with >5 years of duration.[25] The strong relation of duration of diabetes with retinopathy and neuropathy has been observed in our study. These findings are in agreement with Rema et al, Ramachandran et al and Knuiman, et al.[26-28] The association between the duration of type 2 diabetes and neuropathy was also evident in a research study by Oguejiofor, et al.[29] Presence and severity of complications are the most important determinant of treatment and monitoring regime. Diabetes is often diagnosed too late. 50% of patients have complications at the time of diagnosis or in those yet to have a diagnosis made. Effective intervention at primary level-awareness, lifestyle changes, and secondary prevention that is reducing the burden of complications by early diagnosis and proper care is the need of the hour.

CONCLUSION

As more than two–third of the patients with blood group B developed complications, it signifies the need to closely monitor these subjects for microvascular complications although need for monitoring in other blood groups cannot be undermined. However, for evaluation of relationship more prospective large sample, population based study is suggested. No significant relationship with any micro vascular complication of type 2 diabetes and any blood group is observed.

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