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ASSESSMENT OF ANKLE BRACHIAL INDEX AND AUTONOMIC REACTIVITY AMONG ABO BLOOD GROUPS IN TYPE 2 DIABETIC PATIENTS

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ABSTRACT **Background:** Diabetes mellitus is a potential risk factor for many cardiovascular complications. Similar toneuropathy, peripheral arterial disease (PAD) is one of the reasons for repeated foot ulcers, chronic infections and poor wound healing in diabetes. ABO blood group antigen expression is also considered as an independent risk factor for cardiovascular complications due to the association with the lipid metabolism and coagulation status. There is paucity of reports in assessing the cardiovascular risk by autonomic functions among the ABO blood groups in diabetes mellitus. **Aim:**To assess the ankle brachial index and autonomic reactivity amongABOblood groups in type2 diabetes mellitus **Methodology:** In this cross-sectional study, 67 type2 diabetic mellites patients without any complication participated. Autonomic reactivity tests and ankle brachial index were estimated and compared between non-O and O blood group participants. Mann-Whitney test and t-test were used to compare the mean between the groupsbased on the type of data distribution. **Results&Conclusion:** Thoughheart rate response in the postural challenge (lying to standingtest) was within the normal range in both non-O and O blood groups, there was relatively lower vascular response in the isometric handgrip test observedin the non-O blood group. Reduction in the ankle brachial index was also observed in the non-O blood group and it was statistically significant compared to O blood group, in the type 2 diabetic patients without any complications.

KEYWORDS : ABO blood group, ankle brachial indexAutonomic reactivity test, Type 2 diabetes mellitus

INTRODUCTION:

Diabetes mellitus (DM) is a group of common metabolic disorders characterized by hyperglycemia. With the increasing prevalence worldwide, DM is the leading cause of many complications including non-traumatic lower extremity amputations even in the developed countries. ' Though uncontrolled, prolonged hyperglycemia is related with the complications, the exact mechanisms of diverse cellular and organ dysfunctions are still unclear. ' Peripheral arterial disease (PAD) is one of the reasons for repeated foot ulcers and chronic infections other than neuropathy, abnormal foot-biomechanics and poor wound healing in diabetes.' Autonomic dysfunctions resulting in anhidrosis, altered superficial blood flow, promote dry skin, fissures eventually resulting in infections of the lower extremities. Framingham Offspring Study has established the association of blood groups, as a risk factor, with the manifestation of PAD It has been observed that subjects with non-O blood groups have a higher risk of PAD occurrence when compared to O-blood group. '–

Ankle Brachial Index (ABI) is a non-invasive test with a reasonable reproducibility and is one of the accurate markers of PAD. — It is defined as the ratio of the systolic blood pressure in the ankle divided by the systolic blood pressure in the arm. – Autonomic reactivity tests are useful in predicting cardiovascular risk in diabetic patients. 30:15 ratio and diastolic blood pressure change, during sustained isometric handgrip, are two useful tests available to assess autonomic index.

Though association of diabetes and blood group with the development of PAD have been studied individually as risk factors, they have not been explored together, to the best of our knowledge. Therefore, in this study, we investigated the ABI and autonomic reactivity in O and non-O blood group patients with diabetes to further explore the association of diabetes and blood group with the manifestation of PAD in these patients.

Material and Methods:

The study was conducted in the Department of Physiology, in collaboration with Department of Endocrinology, JIPMER, Puducherry, with the approval of Postgraduate Research Monitoring Committee (PGRMC) and the Institute Ethical Committee (IEC). Patients with type 2 diabetes attending endocrinology OPD who were willing to participate in the study were recruited. A total of 67 patients with type 2 diabetes met the inclusion and exclusion criteria participated in this study. The fasting lipid profile values were also taken and used for analysis.

Inclusion Criteria:

Participants with Diabetes for less than five years duration, from both genders in the age group of 18 to 60 years, especially female participants having regular menstrual cycle were included.

Exclusion Criteria:

Participants with the polycystic ovarian syndrome, or other endocrine disorders, suffering from obstructive lung disease and bleeding tendencies, having major diabetic complications for more than 5 years, taking oral contraceptives were excluded from the study.

The participants were instructed to report in the Autonomic Function Testing lab after a light breakfast. They were instructed to avoid drinking coffee or tea 12 hours before the test, and avoid drugs that modify autonomic functions, after consulting their endocrinologist. Since various phases of the menstrual cycle have been shown to affect the autonomic functions differently ', we had fixed the test dates of female participants on the first week after last menstrual bleed (Proliferative phase).

After 15 minutes of supine rest in autonomic function testing lab in the department of physiology, 5 minutes continuous electrocardiogram (ECG)was taken with 8 channel polygraph, Nihon Kohden, Japan and AD Instruments, Australia.Blood pressure recordings in the isometric hand grip and ankle brachial index calculation were done using Omron Automatic BP monitor (model HEM7113), Vietnam. Blood group identification was done by hemagglutination method (ANTI-A, B&D from Agappe diagnostic Ltd, Ernakulm, India).

Height and weight measurements were taken using mounted stadiometer (BIOPLUS®) and weighing scale (Kaups®). Body Mass Index (BMI) was calculated using the Quetelet's formula viz. BMI = Weight (kg)/ (Height)2 (m2). Waist and hip measurements were recorded for waist-hip ratio calculation. World Health Organization (WHO) values for Asian Population was used as a normality indicator for anthropometric measurement analyses.

Heart rate and blood pressure (BP) response from supine to standing (30:15 ratio):

The 30:15 ratio is a simplified test to estimate parasympathetic

reactivity. A 30:15 ratio value of < 1.04 is considered abnormal. During this test, the participant was instructed to stand within 3 seconds, from the supine position, and lean against support to minimize muscular effort during standing (i.e, passive standing). In the standing position, the BP and heart rate were recorded continuously using an automated digital BP monitor and with simultaneous Lead II ECG tracings for 5 minutes. RR intervals were retrieved, and artefacts were removed manually. The 30:15 ratio, the ratio of maximum RR interval around 30th beat to minimal RR interval around the 15th beat, was calculated.
BP response to sustained handgrip:

Δ DBP in IHG is a test for quantifying sympathetic vascular response. A difference in diastolic pressure value of >15 mm Hg is considered normal, independent of age. The participant was asked to sit comfortably in a chair in an erect posture. The basal BP and heart rate were recorded. The participant was instructed to exert maximal force with dominant hand to grip the hand grip dynamometer for Maximum Voluntary Contraction (MVC) measurement. The participant was then asked to make a sustained handgrip by maintaining 30% of MVC after five minutes of rest following MVC. The difference between the baseline diastolic BP and diastolic BP measured during sustained isometric handgrip was considered as ΔDBP-IHG.

Ankle Brachial Index (ABI)
In supine position the BP was measured in both upper and lower limbs with appropriate size cuffs. Ratio of the systolic blood pressure in the ankle divided by the systolic blood pressure in the armwas taken as ABI.

Statistical Analysis:
The data obtained were analyzed using GraphPadInStat Version 3.06. Comparison of skewed parameters and normally distributed parameters were done using the Mann-Whitney test and t-test respectively, between non-O and O-blood groups. A p-value less than 0.05 was considered statistically significant.

RESULTS:
67 participants with type - II Diabetes mellitus who fulfilled the inclusion and exclusion criteria were recruited for the study. Based on their blood groups they were divided further into O and non-O group. 60% of the patients were of non-O group (40) and 40% of the patients were of O-group (27).

Table 1: General parameters between non-O and O blood groups

Variable	non-O Blood group*	O Blood group*	p-Value
Age (years)	44.84±9.44	46.04±7.95	0.589
Height (m)	1.577±0.086	1.586±0.095	0.71
BW (Kg)	65.45±12.41	63.81±11.76	0.592
BMI (Kg/m^2)	25.61±6.26	25.32±3.98	0.819
WHR	0.914±0.038	0.901±0.046	0.214
WHtR	0.552±0.11	0.57±0.064	0.403

*Values are mean±SD; Analysis was done using unpaired t-test

BW: body weight; BMI: body mass index; WHR: Waist Hip Ratio; WHtR: Weight Height Ratio.

The mean age, height, weight, BMI, waist-hip ratio and waist height ratio, which are determinants of autonomic function, did not vary much between the groups. This made the groups well suited for comparing autonomic reactivity.

Table 2: Comparison of lipid profile between non-O and O blood groups

Variable (mg/dL)	non-O Blood group	O Blood group	p-Value
TC	182.71±42.67	182.28±38.1	0.971
TGL	163.1±72.49	142.56±63.43	0.30
HDL	39.74±10.16	36.61±10.45	0.314
LDL	110.53±39.22	118±38.83	0.522
VLDL	32.57±14.46	28.24±12.69	0.289

TC - Total Cholesterol TGL - Triglycerides HDL - High Density Lipoprotein LDL - Low Density Lipoprotein VLDL - Very Low Density Lipoprotein

*Values are mean±SD;Analysis was done using unpaired t-test

In Table 2, it is observed that the parameters of the fasting lipid profile were slightly higher in non - O group, except LDL, which was slightly lower. These differences were not statistically significant. Lipid profile which is a very important factor in influencing the autonomic vascular response, was evenly matched between the groups.

Table 3: Comparison of autonomic reactivity & ankle brachial index between non-O and O blood groups

Variable	30: 15 Ratio*	Δ DBP in IHG*	ABI**
non-O Blood group	1.26 (0.78-2.30)	6.54 (3-21)	1.09±0.07
O blood group	1.36 (1.08-1.58)	10 (5-19)	1.19±0.145
p - value	0.743	0.293	0.002#

*30:15 Ratio, Δ DBP in IHG Values are in Median (LQR-HQR)

** ABI in mean±SD; The analysis of data was done by Mann Whitney U test... # p <0.05.

The 30:15 ratio and the Δ DBP in IHG were slightly higher in the O group but the differences were not statistically significant. While the increase in Ankle-brachial index was in non - O group was statistically significant with p < 0.002.

DISCUSSION
A total of 67 patients with type II Diabetes mellitus participated in the study. Based on the blood group they were divided into non-O and O groups. The Ankle-brachial index and autonomic reactivity (30:15 ratio, Δ DBP in IHG) were recorded in the participants of both groups and were analyzed.

30-15 ratio is considered to be the best test with high diagnostic accuracy in screening cardiac autonomic neuropathy. The average of 30:15 ratio values were >1.04 in both groups. They did not change much and the difference was statistically insignificant. It is observed that parasympathetic modulation of heart rate in lying to standing test was within normal range in the two groups, though the O group had a relatively higher value when compared to non-O group.

In the isometric hand grip test,mean Δ DBP was lower than the normal reference value in both the groups. Though the Δ DBP in non-O group was much lower, the difference in value between the groups was not statistically significant. The autonomic reactivity tests show that sympathetic vascular response is more affected than vagal modulation in the diabetic population with less than five-year duration of illness. Though Δ DBP in isometric hand grip findings are in accordance with the study made by Sucharita, et al., parasympathetic dysfunction is not observed in our study. .

In this study, the difference in mean values of ABI between both groups was statistically significant with p-value < 0.05. Numerous epidemiologic studies "————"have reported up to four-fold increased rates of cardiovascular disease and mortality with abnormal ABI. It is also reported with more mortality when ABI value is out of the referent rangebetween1.11 and 1.2 '————".It is tempting to suggest that there is an increased cardiovascular risk in the non-O blood groupin type 2 diabetic patientssince the ABI was significantly lower in them whencompared to O blood group. Though age, BMI and gender matched comparisons were made, sub-group analysis among different blood groups was not attempted as the sample size was very little for such analysis.

CONCLUSION:
Reduced sympathetic vascular response and normal vagal modulation in autonomic reactivity tests are observed in type 2 diabetic patients without any complications. Ankle brachial index is significantly lower in non-O blood group compared to O blood group diabetic patients.

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