

**Study of endothelial dysfunction in type 2 Diabetes Mellitus by brachial artery flow dilatation using linear probe 2D ultrasound**

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**Abstract**

**Introduction:** Type 2 Diabetes Mellitus is a Metabolic as well as vascular disorder and if uncontrolled results in many micro and microvascular complication. One among them is cardiovascular disease. Type 2 DM is major cause of Cardiovascular disease by affecting Endothelium. Flow mediated Dilatation (FMD) is a noninvasive mode of assessing endothelial dysfunction. **Method:** We did an observational study on 200 type 2 diabetic patients from April 2019 to June 2020 in our department. **Observation and Results:** FMD% was found to be lower in about 63% of study subjects which was found to be significant ( $p < 0.0001$ ). FMD% was found to be inversely related to lipid profile ( $r = -0.16$  and  $p < 0.02$ ), HbA1c level ( $r = -0.51$  and  $p < 0.00001$ ) and found to be significant, FMD was inversely related to BMI but not significant ( $r = -0.078$ ,  $p = 0.27$ ). FMD is also related to Endothelium independent Nitroglycerine Mediated Vasodilatation (NMD) which is statistically significant ( $r = 0.185$ ,  $p < 0.008$ ).

**Conclusion:** Type 2 DM is associated with endothelial dysfunction and ultimately to atherosclerosis. Monitoring FMD may help assessment of progression of atherosclerosis.

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**Introduction**

Type 2 DM refers to a heterogeneous group of disorders, associated with systemic insulin resistance, which promotes hyperglycemia and dyslipidemia which ultimately result in increased cardiovascular risk. Type 2 DM is not only a metabolic disease but also considered as a vascular disease because of its effect on macro and microcirculation of many vascular beds. Type 2 DM is a major cause of cardiovascular diseases.[1] Endothelium which lines the interior of blood vessels is a multifunctional organ involved in several haemostatic functions like modulating vascular tone, regulating cellular adhesion, thromboresistance smooth muscle cell proliferation, and vessel wall inflammation. Diabetic patients invariably show an impairment of endothelium-dependent vasodilation.[2]

Therefore, understanding and treating endothelial dysfunction is a major focus in the prevention of vascular complications associated with diabetes mellitus.

**Material and Method:**

It was an observational study carried out from April 2019 to June 2020 in Department of Medicine, Shyam Shah Medical College and Sanjay Gandhi Memorial Hospital, Rewa, M.P. The study included 200 patients of type 2 DM.

**Inclusion Criteria:**

1. Presence of type 2 Diabetes, as diagnosed by the American Diabetes Association (ADA) Criteria: HbA1c  $\geq 6.5\%$ , fasting plasma glucose  $>126$ mg/dl, random plasma glucose  $>200$ mg/dl with classic symptoms of hyperglycemia, or post prandial plasma glucose  $> 200$  mg/dl.
2. Dyslipidemia: LDL  $> 130$  mg/dl, Triglyceride  $>200$  mg/dl.

**Exclusion Criteria:**

1. Type 1 Diabetes mellitus

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2. Non Diabetics
3. Critically ill patient
4. Comorbidities which is likely to influence endothelial function: hypertension, Congestive cardiac failure, liver disease, chronic infections, renal disease, smoking , alcoholics.
5. Arteries with diameter <2.5 mm and >5 mm.

#### Data Collection and Method:

Investigations included were Haemoglobin level, total blood count, differential count, Lipid profile, blood urea, serum creatinine, random glucose level, glycated haemoglobin (HbA1c), liver function test and Flow mediated Dilatation.

B mode ultrasonography machine of Phillips Technology with 12 MHz linear array transducer with image point HD7-XE Ultrasound Equipment was used.

#### Image Acquisition:

The patient is positioned supine, brachial artery was scanned in longitudinal section 2 cm above the elbow in antecubital fossa and center of artery is identified. A baseline rest image of artery is estimated and its diameter is note, labelled as d1.

Thereafter arterial occlusion is created by inflating sphygomanometer cuff at least 50 mmHg above

systolic blood pressure for at least 5 minute. After 45-60 sec of cuff deflation another reading of diameter is taken which is labelled as d2.

Local nitroglycerine spray was used for endothelium independent Nitric oxide effect. After 4 min of spray use, another diameter is noted.

Flow mediated vasodilatation (FMD) was calculated as follows:

$$\text{FMD (\%)} = \frac{d2 - d1}{d1} \times 100$$

Where d1 - Base line brachial artery diameter

d2-Brachial artery diameter at 1 min post deflation

#### Statistical Analysis:

In the present study the data collected were analyzed statistically. Descriptive analysis was used to compute mean, Standard deviation, Standard error of mean and percentages. The difference between different parameters based on quantitative variables is compared using student's t test for independent samples and the difference is considered statically significance groups whenever p value < 0.05. We used Paired 't' test for statistical analysis.

#### Result:

In our observational Study following datas were obtained:

**Table 1: Age Wise Distribution**

Age Group	No. Of cases (n=200)
<45	12 (6%)
45-55	70 (35%)
55-65	72(36%)
>65	68 (34%)

Majority of cases in our study was above 45 yr with majority ling in age group 55-65 (36%), 45-55 yr (35%), >65 yr (34%) and least in age group <45 yr (6%) .

**Table 2: Distribution according to FMD ( $\leq 10\%$ )**

SEX	No. Of cases (n=200)
Male	78 (39%)
Female	48 (24%)
TOTAL	126 (63%)

Table no 2. show that 63% patient were having impaired FMD ( $\leq 10\%$ ) with 39% male and 24% female which is statistically significant ( $p < 0.0001$ )

**Table 3: Association of BMI and FMD ( $\leq 10\%$ )**

Lipid profile	No. Of cases	FMD( $\leq 10\%$ )
Hypertriglyceridemia	141 (70.5%)	93 (46.5%)
Elevated LDL	100 (50%)	66 (33%)

Table 3 shows that equal number of patient with impaired FMD were overweight and obese (27.5%) while patient having normal BMI were 4.5% and underweight is 3.5%.It was observed that there was inverse correlation between BMI and FMD but is not statistically significant ( $r = -0.078$ ,  $p = 0.27$ )

**Table 4: Association of Lipid Profile and FMD ( $\leq 10\%$ )**

BMI	No. Of cases with FMD ( $\leq 10\%$ )
<18.5	7 (3.5%)
18.5-24.5	9 (4.5%)
25-29.9	55 (27.5%)
30-39.9	55 (27.5%)

Table 4 show that among 70.5% patient having hypertriglyceridemia , 46.5% were found to be having impaired FMD while among 50% patient which had elevated LDL, 33% were having impaired FMD which was found to be statistically significant with  $r = -0.16, p < 0.02$ .

**Table 5: Association of HbA1c with FMD ( $\leq 10\%$ )**

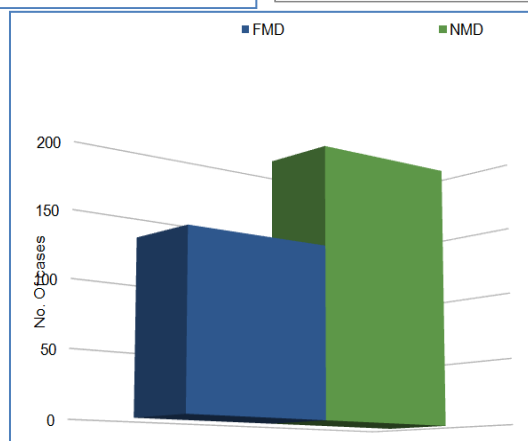
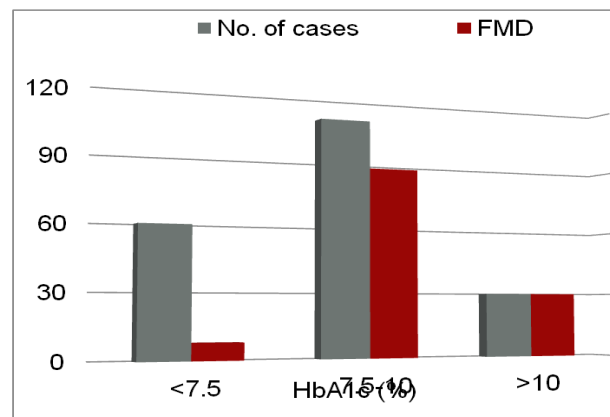
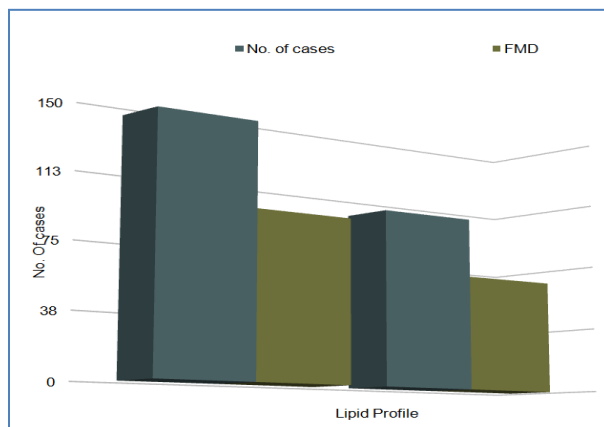
HbA1c	No. Of cases	FMD ( $< 10\%$ )
<7.5	60 (30%)	8 (4%)
7.5-10	110(55%)	88 (44%)
>10	30 (15%)	30 (15%)

Table 5 shows that among 30% patient of HbA1c <7.5%, only 4% had impaired FMD. When compared among 55% patient having HbA1c 7.5-10% , 44% showed impaired dilatation. While patient with HbA1c >10 % all patient (15%) showed Impaired FMD which is found to be statistically significant with  $p < 0.00001$ .

**Table 6: Association of FMD with NMD**

FMD ( $\leq 10\%$ )	NMD
126	200

Table 6 show all patient of diabetes were having Nitroglycerine mediated dilation which was found to be significant (  $r = 0.185, p < 0.008$ )



**Discussion:**

Endothelial dysfunction occurs early in atherosclerosis, predating clinical disease. Endothelial dysfunction in diabetes occurs very early. Flow mediated dilatation of brachial artery is a non invasive method useful for early diagnosis of atherosclerosis. The FMD was found to be significantly lower in our study population. Thus it shows that FMD% is significantly lower in type 2 diabetes patient suggesting endothelial dysfunction.

The study conducted by Menon R Sarath et al showed that Flow mediated dilatation was impaired with increase in age, BMI, lipid profile. FMD was seen inversely related to all glycemic parameter like RBS, FBS, PPBS, HbA1c ( $p < 0.001$ ). It demonstrated that endothelial function declined with increase in severity of glycemic parameters and common cardiovascular risk factors.[3]

Similar Study conducted by Tsuchiya K et al showed that FMD was significantly lower in diabetic patients. It demonstrated that accumulation of cardiovascular risk factor impaired FMD in diabetic patients, and insulin resistance showed the most significant association with FMD.[4]

Study conducted by Eliana F et al concluded that there was a correlation between FMD value with 2 hour post prandial blood glucose level ( $p < 0.01$ ) and HbA1c ( $p < 0.001$ ).[5]

Study conducted by Nuthalapati RK et al concluded that poor glycemic control and insulin resistance have predictive value for the occurrence of Morning Blood Pressure Surge in T2DM patients, which is significantly associated with endothelial dysfunction.[6]

Study conducted by Kotb NA et al examined that circulating endothelial cells (CEC) was found to be significantly elevated in patients with T2DM than healthy control ( $p < 0.001$ ) and in HbA1c  $> 7$  than in patient with HbA1c  $< 7$  ( $p < 0.001$ ). Nitric oxide and FMD% both were found lower in diabetic patients ( $p < 0.001$ ). FMD% and NO were found lower in patient with HbA1c  $> 7$  than compared to HbA1c  $< 7$ . [7]

**Conclusion:**

Endothelial dysfunction occurs early in patient of type 2 diabetes mellitus. Thus by initially identifying endothelial dysfunction and by good glycemic control, atherosclerosis can be prevented and the risk of cardiovascular morbidity and mortality can be reduced. Flow Mediated Dilatation was proved to be a

good and noninvasive method of early identifying endothelial function.

**Limitation:**

Long term follow up study is needed to find out treatment modalities aimed at improving endothelial function.

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**Conflict of Interest:** Nil

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