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Study of Endothelial Dysfunction in Type 2 Diabetes Mellitus

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Abstract:
Background: *Endothelial dysfunction is an early event in atherosclerosis and is known to appear long before the formation of structural atherosclerosis changes. Flow mediated dilation (FMD) is known to depend on ability of the endothelium to release NO in response to shear stress and can be used reliably as an estimate of endothelial function in various disease states.*
Methodology: *Endothelial function was assessed non-invasively by high resolution Duplex Doppler Ultrasound of Brachial Artery in 50 cases of Type 2 diabetes with or without microvascular or macrovascular complication and 20 controls who were healthy subjects. FMD was calculated as percentage increase in brachial artery diameter in response to increase in brachial artery flow.*
Results*: Endothelial dysfunction was seen in 10 (20%) diabetics, where as none of the control had endothelial dysfunction. The mean age for diabetic who had endothelial dysfunction was (61.2±13.40) in male and (±58.2±9.52) in female and the mean duration was (8.6±6.67) in male and in female was (7.90± 6.73). The mean FMD value at < 5years was 0.28± 4.0%, at 5-10 years was 2.12±1.34% and >10 years was 3.50±1.61% Mean FMD was significantly decreased in diabetics (8.38 ± 12.3) compared to healthy subjects (17.1 ± 10.5; p value <0.007).*
Conclusion*: Endothelial function as assessed by FMD is significantly impaired in diabetics compared to healthy subjects. The prevalence of endothelial dysfunction did not increase with duration of diabetes.*
Keywords*: Doppler ultrasound, Diabetes, Endothelial dysfunction; Flow mediated dilation;*

I. Introduction

Endothelial dysfunction can result from and/or contribute to several disease processes, as occurs in diabetes mellitus, hypercholesterolemia and hypertension, and also due to environmental factors, such as smoking tobacco products and exposure to air pollution [4].Specifically, endothelial dysfunction is associated with reduced nitric oxide production, anticoagulant properties, increased platelet aggregation, increased expression of adhesion molecules, increased expression of chemokines and cytokines, and increased reactive oxygen species production from the endothelium [5]. These all play important roles in the development of diabetic vascular complications including atherosclerosis and other vascular pathologies. Importantly, endothelial dysfunction has been shown to be of prognostic significance in predicting vascular events [6, 7], so endothelial function testing may potentiate the detection of cardiovascular diseases such as myocardial infarction, peripheral vascular disease, ischemic stroke, and others [8, 9].Development of non-invasive method of endothelial function assessment by brachial artery flow mediated vasodilatation (FMD), as described by Celermajer, provided an extremely useful tool for cardiovascular research and for clinical application. The test can be performed easily and has proven reproducibility. The International Task Force on brachial artery reactivity has recently laid guidelines for performance of FMD, thus standardizing the test for wider application.[1, 2, 3]

Multiple factors such as insulin resistance, metabolic abnormalities (e.g. hyperglycemia dyslipidemia, elevated free fatty acid level etc.), and formation of advanced glycosylation end products, hypertension, obesity, inflammation, all individually as well as interdependently contribute to early onset and accelerated progression of atherosclerosis in diabetes. Many of the factors mentioned above can directly or indirectly result in endothelial dysfunction.

Insulin itself has a direct vasodilator effect mediated through nitric oxide, an effect that has been shown to be impaired in patients with diabetes.[1, 5.10,] The endothelium is a very sensitive sensor for elevation in blood glucose. Abnormalities in endothelial function in healthy human beings in vivo develop rapidly (as early as 6 hours) in response o hyperglycemia muscle cells decrease glucose transport to maintain a normal intracellular glucose concentration.[13, 14]

II. Aims And Objectives Of The Study

To correlate duration of Diabetes Mellitus with prevalence of endothelial dysfunction.

III. Methodology

This study was done at Maharajah Institute of Medical Sciences between august 2014 to august 2015. The patients with type 2 Diabetes Mellitus were included in the study. This is a case control study, which has sample size of 50 Subjects and 20 Controls who are healthy individuals & subjected to detailed history, clinical examination and routine laboratory investigations including FBS and PPBS, Urine routine & microscopy, microalbumineria, Blood urea and Serum creatinine,. Lipid profile, ECG,. Fundoscopy, Colour Doppler ultrasonography of the brachial artery, by HELWETT- PACKARD Image point machine with colour Doppler using 7.5 and 10 MHz linear probe. Inclusion criteria 1.Age 30-75 years 2.Newly detected Type2 Diabetes Mellitus or Type2 Diabetes Mellitus on treatment with oral hypoglycemic or insulin or both. 3 Patients with or without micro vascular or macro vascular complications. Exclusion criteria Age <30 years and >75 years. Type 1 Diabetes Mellitus.

IV. Observations And Results

Distribution of subjects basrd on , endothelial dysfunction

Endothelial Dysfunction FMD%*	Cases	Controls	Total
Absent (<4.5)	40 (80)	20 (100)	60 (85.7)
Present (<4.5)	10 (20)	-	10 (14.3)
Total	50 (100)	20 (100)	70 (100)

*Endothelial Dysfunction defined As FMD% <4.5

In this study group it is observed that endothelial dysfunction (FMD<4.5%) was present among 10 (20) cases where as none of controls had , endothelial dysfunction

V. Discussion

The mean baseline diameter is (3.800±0.51) in cases and (3.610±0.54) in controls was comparable to study done by Bhargava K et al mean baseline diameter was (3.733±0.729) & Good fellow J, Ramsay MW et al, mean base line diameter case 4.82(0.6) in controls 4.47(1.05).[1,15] The mean baseline flow is (676.58±196.46) in cases and (631.62±224.40) in controls compared to studies conducted by Good fellow J et al and Bhargava K et al. (131±71.5) [1, 15]

Percentage hyperemic flow in diabetic (81.64±74.94, p value <0.014) was found to be significantly lower compared to non diabetic (122.97±55.39). However, Bhargava K et al in their study noticed that the mean and SD was (294.7±165.1) in cases, which high compared to present sudy[1, 15]

The mean FMD% in diabetics was (8.38±12.32) and among the controls was (17.12±10.53; p value 0.007). FMD% was significantly reduced in diabetics compared to controls which is comparable to Bhargava K et al the mean FMD% (5.506±2.12).[1] Dipti Chand et al in their study showed FMD was significantly reduced in diabetic compared to control group (3.6±3.3% vs. 6.8±4.4%, p<0.01).[16] Ramkumar et al in their study it was noticed that FMD% in diabetic was (1.72±2.8) non-diabetic (6.64±4.38).[17] Similarly, Yu Hi et al also found FMD to be significantly impaired in diabetes as compared to controls.[1] In both present study and previous studies FMD % is significantly reduced in diabetics compared to controls.

VI. Summary

Assessment of endothelial function can provide valuable insight into pre-intrusive phase of atherosclerosis and can be used as an early marker of future atherosclerotic diseases. Modification of risk factors can prevent further progression of disease and vascular complication. As the patients with type 2 diabetes mellitus suffer unduly from premature and severe atherosclerosis and since atherosclerosis is a generalized phenomenon and is more or less present equally in coronary, cerebral and carotid arteries, hence ultrasonographic assessment of easily accessible arteries such as brachial artery prompt early intervention in diabetic populations.[1]This study focuses on the importance of flow mediated dilation as a simple, non-invasive, safe and cheap screening test for assessing the endothelial function in type 2 D.M patients .

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