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Study of association between Left Ventricular Dysfunction and Retinopathy in patients with Diabetes Mellitus.

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Abstract: *Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycemia. The metabolic dysregulation associated with DM causes secondary pathophysiologic changes in multiple organ systems that impose a tremendous burden on the individual with diabetes and on the health care system. Diabetes mellitus (DM) leads to complications like macro- and micro vascular disorder such as diabetic retinopathy, nephropathy, neuropathy. Coronary involvement in diabetic patients is believed to be a consequence of microvascular as well as macrovascular complications. The aim of this study is to investigate the association of specific diabetic complications like retinopathy with left ventricular function. It is a cross-sectional study. Total of 50 cases of diabetes with and 25 for control group attending the outpatient department of tertiary care hospital, Jaipur were included from 2011-2013. Left ventricular ejection fraction (LVEF) with left ventricular dysfunction (LVEF<50%) were compared between the case and control group and development of diabetic retinopathy were studied. Patients' demographic variables were comparable between the two groups. Out of 50 diabetic patients 16 (32%) patients develop retinopathy and 34 (68 %) patients do not develop retinopathy. Among 16 patients with retinopathy 10 patients have systolic dysfunction (EF <50 %) and 6 patients have normal systolic function (EF >50 %). Mean LVEF was significantly lower in the patients having retinopathy. Frequency of cases with left ventricular dysfunction was significantly higher among the patients having diabetic retinopathy. The frequency of association between left ventricular dysfunction and diabetic retinopathy was significant. Left ventricular dysfunction and retinopathy significantly associated in diabetic patients. Percentage of impaired left ventricular function in patients with diabetic retinopathy is higher than the patients without retinopathy.*

Keywords: *Diabetic Retinopathy, Left Ventricular Ejection Fraction.*

I. Introduction

Diabetic retinopathy is one of the four leading causes of blindness in 20 to 74 year-old adults and a major cause of blindness all over the world. Prevalence of diabetesis up to 7% of the general population. It is estimated that 25% of the diabetic population has one or other form of diabetic retinopathy while 5% of the population suffers severe degrees of the disease. The prevalence of all types of diabetic retinopathy increases in the population parallel to the disease duration and onset age.[1-4] On the other hand, heart disease in diabetic retinopathy has shown to occur due to microvascular dysfunction. However, no simple and noninvasive evaluation of coronary microcirculation has been introduced and the existing studies suffer from technical flaws.[5-8]

Two decades ago, Framingham suggested that retinopathy symptoms may reflect a process of microangiopathy affecting the myocardium.[9] This hypothesis was confirmed by subsequent studies. In these studies, retinopathy signs with T-wave changes in ECG, coronary artery stenosis in the angiographic and histologic evidence of myocardial microvascular disease were associated.

Recent studies using photographic retinopathy grading have introduced stronger evidence on the relationship between this situation and cardiac dysfunction.[10,11] It has been recognized that diabetic retinopathy increases the risk of myocardial infarction, coronary artery disease and heart failure.[12-17] Due to the limitations and the importance of the previously performed studies, we decided to study the relationship between diabetic retinopathy and its severity in patients with left ventricular dysfunction.

II. Materials And Methods

After the approval of this Cross sectional study protocol by institutional ethical committee, a written informed consent was taken from the patients. This study of diabetic retinopathy and its association with left ventricular dysfunction in a selected group of diabetics (50) and control (25) group attending the outpatient department of NIMS hospital, Jaipur was from 2011-2013. The diabetic group of 50 patients, 32 male and 18 female was selected.

The criteria of inclusion for cases were 1. Age: 40-65 years. 2. Diabetes Mellitus diagnosed as per WHO criteria. For a control random sample of 25 patients 17 male and 8 female was selected. The criteria for

inclusion for the control group were Age, Sex, Body Mass Index and Blood Pressure were comparable to the study group., FBS < 126 mg/dl, PPBS < 200 mg/dl, Glycoslated Haemoglobin (HBA1c) < 6.5%, S .cholesterol < 240 mg/dl, S. Triglyceride < 150 mg/dl.

Diabetic patients and control subjects with the following conditions were excluded from this study. Age > 65 years, Morbid obesity (BMI > 30 kg/m2), SBP > 140 mm Hg, DBP > 90 mm Hg., S Creatinine > 1.2 mg/dl, Bl. Urea > 50 mg/dl, S cholesterol > 240 mg/dl, Smoking > 1 pack/day, Alcoholism. And if partients with History of Congestive heart failure, Valvular heart disease, Congenital heart disease, Previous angina, myocardial infarction, Cerebrovascular disease, Symptomatic peripheral vascular disease, Thyroid disease. If the resting ECG Shows, AV Block, BBB, LVH, Atrial fibrillation, Echo : abnormal regional wall motions were excluded from study. All the patients and the control subjects underwent a thorough clinical examination for symptoms restlessness, fatigue, pedal edema, chest pain.

Duration of diabetes was considered since it was first diagnosed. Control of diabetes was decided on basis of Glycolsylated Haemoglobin (HBA1c), measured by Ion Exchange High Performance Liquid Chromatography (HPLC).

Patients were divided into two groups: 50 patients with diabetes (case group) and 25 patients without diabetes (control group). Indirect Ophthamoscopy was done for finding changes of diabetic retinopathy and arteriosclerosis. Retinopathy detection was made by an ophthalmologist and retina specialist. Left ventricular function was assessed by a consulting cardiologist. Two individuals were also unaware of the patient's retinopathy status. In this study, left ventricular dysfunction was defined as LVEF<50%.

Preliminary Data like Age, sex, weight, height, body mass index (BMI), Occupation was asked. And history of clinical symptoms like dyspnoea, chest pain, cough, palpitation, peripheral edema, fatigue, polyuria, polydypsia, urinary symptoms and previous illness like diabetes mellitus, its duration, treatment, hypertension, IHD were taken. family history of DM, CAD, hypertension and personal history of diet, habits like – smoking , alcohol were studied.

The obtained information is presented as the mean ± SD, frequency and percentage. SPSS statistical program version 15 was used. Quantitative variables were compared using Student T-test (Independent Samples). Qualitative variables (Categorical) were compared by Contingency tables using Chi-Squared test. P≤0.05 was considered statistically significant.

III. Results

The average age (range) of patients in case group was 55.60 ±6.73 (Male: 54.19±7.07, Female: 58.11± 5.39)(40-65)years and 54.88± 6.80 (Male: 54.47±7.36, Female: 55.75 ±5.78) (40- 65) years in the control group. There was no significant difference between two groups regarding patients'age (P= 0.665; Figure 1).

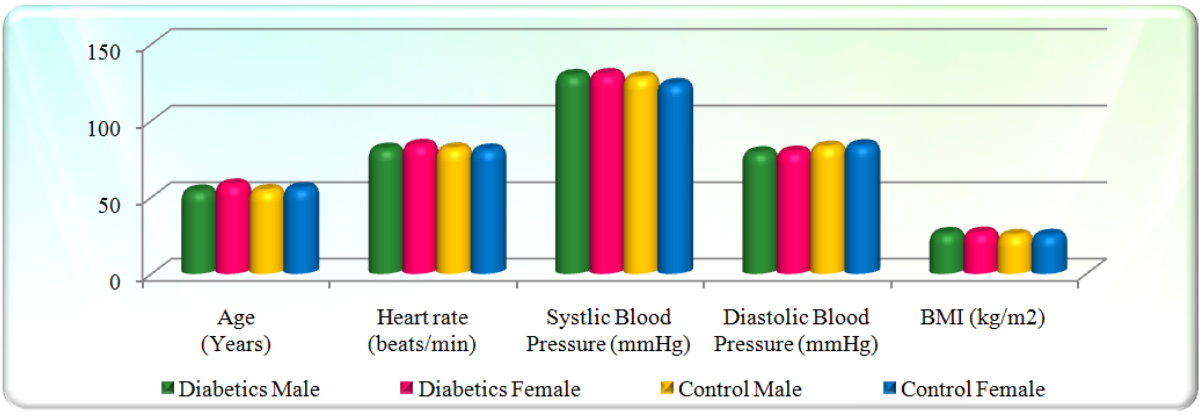
In two groups, demographic characteristics, Heart rate, Systolic blood pressure, Diastolic blood pressure, BMI were studied as shown in Figure 1.

Mean heart rate in diabetic patients is 82.40±6.46/min and in control subjects is 81.44±5.67/min. p value – 0.530. Mean systolic blood pressure (SBP) in diabetic patients is 129.84±6.95mmHg and in control subjects is 126.72±9.09 mmHg p-value -0.103. Mean diastolic blood pressure (DBP) in diabetic patients is 79.28±3.47 mmHg and in control subjects is 83.12±4.32 mmHg p value < 0.001.

Mean BMI in diabetic patients is 26.49±2.00 kg/m^2 and in control subjects is 25.20±1.68 kg/m^2 p value -0.007. Body mass index (BMI) is higher in diabetic patients as compared to control subjects - We found statistically significant difference in BMI and diastolic blood pressure ('p'<0.05)

The average duration of diabetes mellitus was significantly higher in case group (P<0.001). None of the patients had a history of alcohol consumption.

Fig 3.1.1 ***Comparison of Anthropometric & Clinical Data of Diabetic patients and Control***



In our study out of 50 diabetic patients 16 (32%) patients develop retinopathy and 34 (68 %) patients do not develop retinopathy. Among 16 patients with retinopathy 10 patients have systolic dysfunction (EF <50 %) and 6 patients have normal systolic function (EF >50 %) Among 18 patients with systolic dysfunction 10 (55.56%) have retinopathy and 8 (44.44%) do not have retinopathy among 32 patients with normal systolic function 6 (18.75%) have retinopathy and 26(81.25 %) do not have retinopathy. 'p' is 0.0074 ($p < 0.01$) (Chi – squre 7.172, Degree of freedom: 1).Odds ration is 5.417 (95% confidence interval: 1.497 to 19. 594). This suggest, patients with abnormal systolic function has 5 times more chances of developing retinopathy than the patients with normal systolic function. (Table 1)

TABLE 3.1.2 Association of left ventricular Systolic function and retinopathy in Diabetic Patients

Systolic function (EF %)	**Retinopathy**					
	Present		**Absent**		**Total**	
	No.	**%**	**No.**	**%**	**No.**	**%**
Abnormal (EF < 50 %)	10	55.56	8	44.44	18	100.00
Normal (EF ≥ 50 %)	6	18.75	26	81.25	32	100.00
Total	16	32.00	34	68.00	50	100.00

IV. Discussion

In this study, the relationship between diabetic retinopathy and left ventricular dysfunction in diabetic patients was evaluated.

Accordingly, we found that 16 patient's developed diabetic retinopathy among which 10 (55.56%) patients having the mean LVEF lower **(EF < 50 %) than** in patients without diabetic retinopathy, which were 6 (18.75%). The percentage of impaired left ventricular function in patients with diabetic retinopathy was significantly higher (55.56%).

It has previously been shown that the cardiac disease and retinopathy in patients with diabetes mellitus is due to microvascular dysfunction. In other words, the underlying pathophysiology in coronary artery disease and diabetic retinopathy is the same.[5-8]

Two and half decades ago, Framingham Heart Study shown that retinopathy symptoms may reflect a microangiopathic process in which the myocardium is also involved.[9] which was later approved by the other studies. In these studies, retinopathy signs were associated with changes of T-wave in ECG, coronary artery stenosis in the angiographic and histo-pathological evidence of myocardial microvascular disease.[10,11]

Recent studies by using photographic retinopathy grading, shows stronger evidence on the relationship between retinopathy and cardiac dysfunction. It shows that the diabetic retinopathy increases the risk of myocardial infarction, coronary artery disease and heart failure.

The study done by, Frati et al. included diabetic patients without cardiovascular symptoms. Which shows that left ventricular dysfunction has a significant relation with duration of diabetes and microvascular disease including diabetic retinopathy.[18]

Annonu et al. have done study in 66 patients with type 1 diabetes without cardiovascular diseases. Which have demonstrated that left ventricular dysfunction is associated with the duration of diabetes and diabetic retinopathy.[19]

Wong and colleagues studied 627 patients with type 2 diabetes. After 7 years, the risk of heart failure was more than 2 times higher in patients with retinopathy than those without retinopathy.[13]

In Fuller and colleagues study, 1126 patients with type 1 diabetes and 3179 patients with type 2 diabetes were studied. After 12 years, in patients with type 2 diabetes, diabetic retinopathy increased the risk of heart disease up to 1.5 to 2 times higher. The increased risk was also observed in women with type 1 diabetes while in men with type 1 diabetes, the risk of heart disease was more than 2 times.[14]

Cheung and colleagues studied 1021 middle-aged patients with type2 diabetes with normal renal function and no symptoms of coronary artery disease and heart failure. Retinopathy severity, incidence of heart failure and mortality associated with the severity of retinopathy were evaluated. 12.8% of these patients had diabetic retinopathy. After 9 years, 10.1% of the patients developed heart failure. The incidence of heart failure in patients with retinopathy was significantly higher (cumulative incidence of 6.12% vs. 5.8%). After controlling other risk factors, increased the risk of heart failure by 2.5 times found in diabetic retinopathy.[12]

Klein and colleagues studied 996 patients with type 1 diabetes. Twenty years later, a significant relationship between severity of retinopathy and heart disease was reported. [16]

In the study done by Mishra and colleagues,73 diabetic patients without symptoms of heart disease were under gone for Echocardiographic systolic and diastolic function assessment separately. There were significantly higher numbers of diabetic retinopathy cases in patients with left ventricular dysfunction and significantly associated with duration of diabetes mellitus.[20]

Aguilar and colleagues studied 531 patients with type 2 diabetes. In this study it was demonstrated that increase in these verity of retinopathy increased left ventricular mass and left atrial dimension and LVEF, independent of confounding variables.[17]

Our results are similar as shown in previous study. In our study, left ventricular dysfunction was significantly higher in the patients with diabetic retinopathy. We have studied the correlation between left ventricular dysfunction and the type and severity of diabetic retinopathy. Reaven and colleagues showed that coronary calcium has a direct relationship with diabetic retinopathy.[21]

The results of our study are similar to previous reports in this field. However, for further evaluation more studies with larger sample size are required.

V. Conclusion

In our study, 55.56% of diabetic patients with retinopathy had left ventricular dysfunction. While, in patients without diabetic retinopathy and with left ventricular dysfunction was seen in only 44.44% of cases. Percentage of impaired left ventricular function in patients with diabetic retinopathy is higher than the patients without retinopathy. In order to reach conclusive results, further studies with larger sample size are recommended.

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