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RISK FACTORS FOR DIABETIC MICROVASCULAR COMPLICATIONS IN NEWLY DIAGNOSED TYPE 2 DIABETES MELLITUS

General Medicine

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ABSTRACT

Objective: Microvascular complications are seen to have been associated with diabetes type 2 cases. We carried out this study over subjects with newly diagnosed type II diabetes. Purpose was to find and report risk factors associated with micro vascular complications and to identify the clinical and biological characteristic changes associated.

Methods: 164 subjects were taken into the study (all having newly detected diabetes type 2). Standard evaluation tests in details were carried out over all the subjects to detect diabetic retinopathy (fundus examination), neuropathy (siemms monofilament test), and nephropathy (microalbuminuria).

Results: The occurrence of a microvascular complication of any form was 34.7%. Diabetic retinopathy ,diabetic nephropathy and neuropathy were prevalent in 5.5%, 11.6% and 12.8% cases respectively. The risk factors for developing any form of microvascular complication were increasing age , increasing systolic blood pressure and increasing hemoglobin . The risk factors for DR and diabetic nephropathy were increasing systolic blood pressure ,for diabetic nephropathy and increasing hemoglobin for retinopathy; Increasing age was the only risk factor for diabetic neuropathy . The risk factors for multiple microvascular complications (combination of any two) included poor glycemic control .

Conclusions: 34.7% of the subjects had some form of micro vascular complication; while the main risk factors correlated with diabetic microvascular complications were growing age,hypertension ,poor glycemic control and increased hemoglobin

KEYWORDS

INTRODUCTION

Type 2 diabetes mellitus and microvascular complication:

The microvascular complication of diabetes is long term complication of diabetes affecting small blood vessels including retinopathy , nephropathy and neuropathy. Retinopathy is divided into two main categories: non proliferative retinopathy and proliferative retinopathy. Non proliferative retinopathy related to venous loops, retinal hemorrhages , development of micro aneurysms ,hard exudates , and soft exudates . proliferative retinopathy is the presence of new blood vessels with or without vitreous hemorrhage.

Diabetic nephropathy is defined as the presence of persistent proteinuria greater than .5 gram per day . overt nephropathy is characterized by progressive decline in renal function resulting in end stage renal disease ,

Neuropathy : neuropathy is group of condition characterized by nerve dysfunction . the condition is classified according to the nerves affected. The classification of neuropathy includes focal , diffuse , sensory , motor , and autonomic neuropathy .

Symptoms of retinopathy are minimal until advance disease ensues with loss or blurring of vision. The earliest sign of nephropathy is hypertension along with the development of micro albuminuria. As nephropathy worsens, patient can develop edema, arrhythmias associated with hyperkalemia, and symptoms related to renal failure.

The pathogenesis of the microvascular complications in diabetes mellitus is not fully understood, and controversies exist about why they occur in some patients and not in others. There are also racial and ethnic differences in the prevalence of microvascular complications in diabetes (9).

This study was undertaken to define more clearly the risk factors influencing susceptibility to such complications in diabetic patients.

At our tertiary institute we mostly encountered diabetic patients with complications irrespective of the time of diagnosis and duration of diabetes in both indoor and outdoor patients .

MATERIALS AND METHODS

This descriptive observation study was carried out in the newly detected type 2 diabetic patients visiting or admitted in a tertiary care centre in North India for a period of six months . A total of 164 newly detected type 2 diabetic patients were studied at the hospital during this period .Consent of patients was obtained after explaining them about the purpose of the study, and the study protocol was approved by the local hospital ethics committee. The written consent was not required as the study was observational and not interventional. Diabetes was diagnosed as per American Diabetes Association (ADA) revised criteria . Glucose oxidase method was employed to measure blood glucose level. Glycosylated hemoglobin (GHb) was measured by ion exchange resin method with GHb kit. details of history, age, sex, socio economic status, rural or urban, duration of diabetes and treatment were recorded and complete clinical examination was carried out for subjects. in all the patients. The total serum cholesterol by CHOD-POD method, HDL cholesterol, LDL after protein precipitation by CHOD-POD method, and serum triglycerides were estimated. Height, weight, waist/hip size were also measured. The blood pressure was recorded, in the sitting position, in the right arm, to the nearest 2 mm Hg, using the mercury sphygmomanometer. Two readings were taken, 10 minutes apart, and their mean was taken as the blood pressure. Pregnant diabetic cases or gestational diabetes and type 1 diabetics were excluded from the study. Neuropathy was diagnosed by history of numbness, paraesthesias, tingling sensation, burning sensation and confirmed by touch sensation using 10gm monofilament, Painful peripheral neuropathy was diagnosed by history of pain worsening at night. Retinopathy was diagnosed by detailed fundus examination . At initial stage nephropathy was diagnosed by Micral test and was presumed to be present if microalbuminuria was detected. Further Nephropathy was diagnosed by elevated level of serum creatinine and blood urea, or presence of macroalbuminuria.

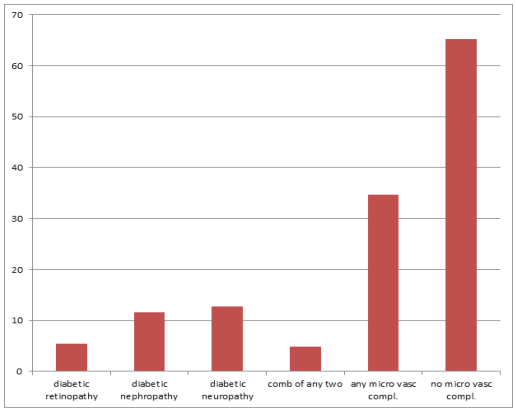
Statistical Analysis: multivariate regression analysis was done for finding the scientific risk factor's association with various microvascular complications. Logistic regression analysis was used to find out strength of association of risk factors with specific complication.

Results

Out of 164 subjects the finding of presence of different microvascular complications was as follows:-

N(total number of subjects having diabetes type)		164
Category	Number of case	%
Any Microvascular complication	57	34.7
Diabetic retinopathy	9	5.5
Diabetic nephropathy	19	11.6
Diabetic neuropathy	21	12.8
Combination of any two	8	4.8

CHART -1
Percentage



Risk factors associated with different microvascular complications

2×2 contingency table had been created to evaluate the association of various risk factors with different types of microvascular complications . out of all the factors tested only four factors namely age, systolic blood pressure,HbA1c and hemoglobin presented statistical significance to one or more type of complication hence only these which had a valid statistical significance associated with any type of the microvascular complication has been described below in form of 2×2 contingency table.

Age as the risk factor: all the subjects were divided into two age groups the first group having its all members with age>50(group1) and the second group with age ≤50(group 2)

Table 1

GROUP	ANY MICRO VASCULAR COMPLICATION (NO.)	NO MICRO VASCULAR COMPLICATION(NO.)	TOTAL
1	34	39	73
2	23	68	91
TOTAL	57	107	164

Odds ratio(CI at 95%)=2.57(1.33-4.98) , P=.005, χ^2 =8.1
Thus the relation found statistically significant affirming age to be the risk factor for any type of microvascular complication.value of χ^2 Which is 8.1 Is Greater than the table value for degree of freedom 1 and P=.005 .thus data is statistically significant.

Similarly 2×2 contingency table for those with and without D/R,D/neph,D/neuro and combination of any two worked out below:-

Table 2

group	D/R	NO D/R	D/NEPHRO	NO D/NEPHRO	D/NEURO	NO D/NEURO	COMB OF ANY TWO	NO COMB OF ANY TWO	TOTAL (EAC PAIR)
1	4	69	9	64	18	55	3	70	73
2	5	86	10	81	3	88	5	86	91
TOTAL	9	155	19	145	21	143	8	156	164
	.99 (.25-3.85), P=1		1.13(.43-2.97),P=.8, $\chi2$ =.07		9.6(2.70-34.11), P<.0001, $\chi2$ =16.55		.73(.17-3.19), P=.73		

Here except diabetic neuropathy there is no statistical significance of age vs. other form of complications .while age is highly statistically significant with the complication cases of diabetic neuropathy(9.6(2.70-34.11), P<.0001, χ^2 =16.55 which is greater than the table value for P<..0001

Systolic BP as the risk factor:-

The values of systolic BP were categorized in two groups, first group having value ≥140(group 1),second group having value< 140(group 2)

Table 3

GROUP	MVC	NO MVC	D/R	NO D/R	D/NEPH	NO D/NEPH	D/NEURO	NO D/NEURO	ANY TWO	NO COMB.	TOT. (PAIR)
1	25	28	6	47	12	41	3	50	4	49	53
2	32	79	3	104	7	104	18	93	4	107	111
TOTAL	57	107	9	155	19	145	21	143	8	156	164
	2.20(1.11-4.34),P=.02, $\chi2$ =5.32		4.59(1.10- 19.15),P=.03		4.34(1.60-11.81), P=.003, $\chi2$ =9.34		.31(.08-1.10),P=.3		2.18(.52-9.09) P=.4		

The confidence intervals in the cases of Diabetic neuropathy and combination of any two contain the value 1 also the value of P is far greater than .05 hence pose no statistical significance, while cases of any microvascular complication ,diabetic retinopathy and diabetic nephropathy have statistical significance. Leading to the inference that systolic blood pressure is a risk factor to the prevalence of any microvasular complication, diabetic retinopathy and diabetic nephropathy.

HbA1c as the risk factor:-

The values of HbA1c were categorized in two groups ,those having their HbA1c value above 10% were kept in the first group(group 1) and rest were in group 2. 2×2 contingency table study was carried out to establish the correlation with different types of microvascular complications and increased value of the HbA1c.-

Table 4

GROUP	MVC	NO MVC	D/R	NO D/R	D/NEPH	NO D/NEPH	D/NEURO	NO D/NEURO	ANY TWO	NO COMB.	TOT. (PAIR)
1	8	9	1	16	2	15	1	16	4	13	17
2	49	98	8	139	17	130	20	127	4	143	147
TOTAL	57	107	9	155	19	145	21	143	8	156	164
	1.77(.64-4.8),P=.25, $\chi2$ =1.27		1.08(.12-9.25,P= 1		1.01(.21-4.85), P=1		.39(.04-3.15),P=.47		11.0(2.46-49.18) P=.004		

The above table clearly shows that there is no statistical significance in cases of any microvascular complication, diabetic retinopathy , diabetic nephropathy and diabetic neuropathy as in each case the value of P is large and value of 1 is contained in the 95% CI, but there exists statistical significance in cases of combination of any two. Thus establishes the fact that HbA1c is potential risk factor for the combination of any two microvascular complications.

Hemoglobin as risk factor:- on the basis of hemoglobin percentage the number of subjects was divided into two groups . viz those having their Hb\p; (gram) value >13.5 kept in group 1 and those having H b ≤13.5 kept in group 2. 2×2 contingency table study was carried out to establish or reject the correlation:-

Table 5

GROUP	MVC	NO MVC	D/R	NO D/R	D/NEPH	NO D/NEPH	D/NEURO	NO D/NEURO	ANY TWO	NO COMB.	TOT. (PAIR)
1	33	40	8	65	14	59	9	64	2	71	73
2	24	67	1	90	5	86	12	79	6	85	91
TOTAL	57	107	9	155	19	145	21	143	8	156	164
	2.3(1.19-4.43),P=.01, $\chi 2$ =6.33		11.09(1.35-90.74),P=.01		4.08(1.39-11.94), $\chi 2$ =7.4,P=.006		.92(.36-9.33),P=1, $\chi 2$ =.03		.39(.07-2.03) P=.30		

It is evident from the 2×2 contingency table that except in cases of diabetic neuropathy and combination of any two the rest had statistical significance if Hb was considered a factor hence establishing the fact that Hb is a risk factor in cases of any microvascular complication (value of χ^2=6.33 greater than table value for degree of freedom 1 and P=.01),diabetic retinopathy and diabetic nephropathy(value of χ^2=7.4 greater than table value for degree of freedom 1 and P=.006 .

DISCUSSION

This study was conducted on 164 patients of type 2 diabetes. Retinopathy was present in 9(5.5%) patients. our observation of association of retinopathy with hypertension has also been recorded by works of Rema et al and Klein et al previously (2,3). We also observed that poor glycemic control is associated with increased incidence of diabetic retinopathy and any other microvascular complication simultaneously and these results were consistent with findings of works of Rema et al,Klein et al and Knuiman et al (2,3,4). we observed evidence of nephropathy in 19 (11.6%) out of 164 patients. Ronald Klein et al (3) in his study found that frequency of microalbuminuria was 29.2% in those taking insulin and 22.0% in those not taking insulin. A lower prevalence of proteinuria (19.7%) was found in the study conducted by Ramachandran et al (1999) (5). Gupta et al (1991) (6) from New Delhi reported prevalence of microalbuminuria in 26.6% patients .

The risk factors for developing DR and nephropathy among subjects with newly diagnosed diabetes, in the present study, were higher systolic blood pressure and higher hemoglobin. High systolic blood pressure (undiagnosed longstanding) per se can produce changes mimicking DR and nephropathy. In contrast to this study, other studies have found anemia as a risk factor for DR and nephropathy Qiao et al (7). Agrawal et al., (8) demonstrated that poor glycemic control (HbA1c > 8) was significantly associated with nephropathy [odds ratio 4.46 (CI: 3.80-5.23)], neuropathy [odds ratio 2.73 (CI: 2.29-3.27)] and retinopathy [odds ratio 2.64 (CI: 2.21-3.12)]. A Ramachandran et al (5) has showed that high blood pressure is significantly associated with diabetic vascular complications (retinopathy, nephropathy and cardiovascular disease).

In conformity to the present study similar results were found by Conway et al(9) that proliferative diabetic retinopathy can be predicted by a higher hemoglobin level . Their study tells about the factors related to increased hemoglobin as testosterone, hypoxia, growth factors, and viscosity, possibly responsible for the proliferative diabetic retinopathy.

In this study no case had been that of proliferative diabetic retinopathy yet both types of reports like presence of proliferative diabetic retinopathy and absence of the same (de Fine Olivaris et al)(10) presence (Lee et al)(11) have been found in results.

2×2 contingency table clearly showed that amongst all the known risk factors only age was found effective risk factor for diabetic neuropathy among cases of newly diagnosed diabetes type 2 .Similar results were found by Barbosa et al (12) and Al-Mahroos et al(13).In this study no correlation was found between HBA1c and Diabetic neuropathy and as the cases examined were newly diagnosed diabetes type 2 cases it appears that increasing age is the only risk factor for diabetic neuropathy with little or no relation to the duration of diabetes and glycemic control. Similar results were reported by Belmin,et al(14). Ravid et al(15) showed in 49 normotensive subjects with type 2 diabetes and microalbuminuria (mean 143 mg/24h (range 30-290) that improved blood pressure control with enalapril prevented an increase in urine albumin excretion and gave a slower decline in renal function.

In this study out of 164 patients of type 2 diabetics, neuropathy was present in 21 (12.8%) patients.these results were consistent with findings of Knuiman et al (1986) (4) who found that sensory neuropathy is strongly related to both age at diagnosis and duration of diabetes

Our study was representative of a cross sectional population,although the results could be extrapolated to the rest of urban India.but different pattern of lifestyle, delay in diagnosis, different diagnostic approach and delay in onset of intervention may lead to variations. Thus the findings of the study cannot be generalized to all subjects with diabetes.

These relationships are independent of the effect of other variables.

CONCLUSION:

The microvascular complications in newly detected diabetic type2 cases were higher in people with more age, high systolic blood pressure,increased value of hemoglobin & poor glycaemic control. A strong association of hypertension with nephropathy also found (mohan et al)(16). Systolic blood pressure also associated with high prevalence of diabetic nephropathy; however diastolic blood pressure had no significant contribution to nephropathy. Similar result also observed by Rema et al (2) and Ramachandra et al (5) .

Poor glycemic control reflected by a need of insulin therapy was found to be associated with the presence of microangiopathies (UKPDs prospective study)(17). Process of care and temporary reversion to traditional lifestyle and diet did not influence glycemic control, although it worked in reducing hypertension.(17)

Type 2 diabetes mellitus has rapidly become a global health problem with rapid worldwide increasing population growth, aging, urbanization and increasing prevalence of obesity and physical inactivity indicating the urgent need to prevent diabetes and its complications rather than simply treat it, once established. Patients should be educated for lifestyle changes such as weight control, increased physical exercise, and smoking cessation, which are potentially beneficial in preventing diabetes mellitus and coronary artery disease. Furthermore, the morbidity and mortality caused by diabetes mellitus can be reduced by secondary prevention through regular screening, early detection, and appropriate treatment of chronic complications. In many developing countries in Asia, the limited health care resources must be rationally allocated to programmes of proven efficacy. This is a tough challenge indeed, and the decisions made will influence the quality of diabetes care in Asia.

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