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A STUDY ON THE PREVALENCE OF CARDIAC AUTONOMIC NEUROPATHY IN DIABETIC PATIENTS – A HOSPITAL BASED STUDY.

General Medicine

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ABSTRACT

Background: Diabetic Autonomic Neuropathy (DAN) is a serious and common complication of diabetes. Despite its relationship to an increased risk of cardiovascular mortality and its association with the multiple symptoms and impairments, the significance of diabetic autonomic neuropathy has not been fully appreciated. DAN can manifests in a spectrum of things, ranging from resting tachycardia and fixed heart rate (HR) to development of "silent" myocardial infarction.The prevalence of CAN is variable based on published studies and ranges from 2% to 91% in type I diabetes mellitus (T1DM) and 25% to 75% in type 2 diabetes (T2DM). This significant variability can likely be attributed to the lack of a uniform diagnostic criteria as well as underdiagnosis in the typical hospital setting.[2]

Aim And Objectives : To study the prevalence of cardiac autonomic neuropathy in hospital admitted diabetic patients.

Materials And Methods : 60 diabetic patients were taken for the study of which 48 were males and 12 were females.The study was carried out in tertiary care teaching hospital in North east India after clearance from institutional ethics committee. Subjects were divided according to duration of diabetes as Group I : 0 – 5 years(24 patients), Group II : 6 – 9 years(24patients), Group II I: 10 years or more(12 patients). Then special interest was taken to find out cardiac autonomic neuropathy and all the 5 tests were carried out in each of the patients to detect cardiac autonomic neuropathy and were divided into 3 groups. Group I (normal autonomic function test), group II (early DAN), group III (definitive DAN).

Results : In the present study it has been observed that out of 24 (40%) cases of diabetes mellitus in the 0 – 5 year duration group, 4 cases (16.7%) are having autonomic neuropathy, out of 24 cases in the duration group 6 – 9 years, 10 cases (41.7%) are having autonomic neuropathy and in the duration group ≥ 10 years, 8 cases out of 12 (66.7%) showing neuropathy. In the present study prevalence of diabetic autonomic neuropathy out of 60 number of patients taken it was seen as: 38 cases (63.3%) with normal autonomic function tests placed in group I, 12 cases (20%) with only cardiac parasympathetic damage or early DAN were placed in group II and 10 cases (16.7%) with both cardiac parasympathetic and sympathetic damage or definitive DAN were placed in group III. So out of 60 diabetic patients, 22 patients (36.7%) showed abnormal cardiovascular reflex in the present study.

Conclusion: It has been observed from the present study that duration of diabetes mellitus is directly proportional to development of cardiac autonomic neuropathy.

KEYWORDS

Diabetic Autonomic Neuropathy,Cardiovascular reflex,Diabetes Mellitus.

INTRODUCTION :

Diabetic Autonomic Neuropathy (DAN) is a serious and common complication of diabetes mellitus Despite its relationship to an increased risk of cardiovascular mortality and its association with the multiple symptoms and impairments, the significance of diabetic autonomic neuropathy has not been fully appreciated.[1] Cardiac autonomic neuropathy (CAN) is a serious complication of diabetes mellitus (DM) that is strongly associated with approximately five-fold increased risk of cardiovascular mortality. CAN manifests in a spectrum of things, ranging from resting tachycardia and fixed heart rate (HR) to development of "silent" myocardial infarction. The prevalence of CAN is variable based on published studies and ranges from 2% to 91% in type I diabetes mellitus (T1DM) and 25% to 75% in type 2 diabetes (T2DM).[2] This significant variability can likely be attributed to the lack of a uniform diagnostic criteria as well as under diagnosis in the typical hospital setting. Based on the Diabetes Control and Complications Trial (DCCT)/Epidemiology of Diabetes Interventions and Complications (EDIC) study, the prevalence of CAN in T1DM after 15 years was close to 60%.

So keeping in view of the magnitude of the problem how diabetic autonomic neuropathy can affect a diabetic patient especially in terms of cardiac problems leading to silent myocardial ischemia so we have decided to carry out this study to detect and to know the prevalence of diabetic autonomic neuropathy at an early stage and try to prevent cardiac death.

MATERIALS AND METHODS :

60 diabetic patients were taken for the study of which 48 were males and 12 were females.The study was carried out in tertiary care teaching hospital in North east India after clearance from institutional ethics committee.

Inclusion Criteria :

Diabetic patients admitted in a tertiary teaching health care institute were selected randomly with the duration of disease one year or more. The patients were selected irrespective of their age and sex.

Exclusion Criteria :

Patients with history of coronary disease, old/acute patients of myocardial infarction, hypertension, overt nephropathy were excluded from the study.

Subjects were divided according to duration of diabetes as :
Group I : 0 – 5 years(24 patients),
Group II : 6 – 9 years(24patients),
Group II I: 10 years or more(12 patients).

Then special interest was taken to find out cardiac autonomic neuropathy and all the 5 tests were carried out in each of the patients to detect cardiac autonomic neuropathy and were divided into 3 groups :
Group I (normal autonomic function test),
group II (early DAN, only cardiac parasympathetic damage)
group III (definitive DAN , both cardiac parasympathetic and more widespread sympathetic damage).

The Following Battery Of Tests Were Done For Detection Of Diabetic Autonomic Neuropathy :

TEST REFLECTING PARASYMPATHETIC FUNCTIONS:

I. Heart rate response to Valsalva manoeuvre :

The test was performed by the patient in sitting position blowing into a mouth piece connected into a mercury sphygmomanometer and were trained to maintain an expiratory pressure of 40 mm of Hg for 15 seconds. After training each subject three Valsalva manoeuvres were performed separated by a rest period of one minute. During each manoeuvre heart rate was recorded continuously throughout the strain period and 15 seconds following release of strain by means of ECG in standard lead II.

The result is expressed as Valsalva ratio (*Ratio of longest R-R interval following strain and shortest R-R interval during manoeuvre*).

Average of three Valsalva ratios were taken as final value.

Interpretation

Normal = 1.21

Borderline = 1.11 to 1.20
Abnormal ≤ 1.10

II. Heart Rate Variation During Deep Breathing :
In this test, the patient was on sitting position and was connected with an ECG machine. After three minutes rest, one minute heart rate was recorded while patient was on quiet breathing. Then after two minutes interval heart rate was recorded during one minute while the patient was taking deep breath at 6 breaths per minute; (5 seconds in and 5 seconds out). The maximum and minimum R-R interval during each breathing cycle were measured and were converted to beats per minute. The results was then expressed as the difference between maximum and minimum heart rate.

Interpretation
Normal ≥ 15 beats
Borderline = 11 – 14 beats
Abnormal ≤ 10 beats

III. Immediate Heart Rate Response To Standing :
In this test in the patient lied quietly in bed for three minutes and then was asked to stand up and remain motionless for two minutes. ECG was recorded 16 beats before to 40 beats after standing. R-R interval at around 15th beat and 30th beat were measured and expressed in 30:15 ratio.

Interpretation
Normal ≥ 15 beats
Borderline = 11 – 14 beats
Abnormal ≤ 10 beats

TEST FOR SYMPATHETIC FUNCTION:
IV. Blood Pressure Response To Standing :
In this test, blood pressure was measured in lying down position and after minute of standing. Difference of systolic blood pressure of lying down and standing position was measured.

Interpretation
Normal ≤ 10mmHg
Borderline = 11 – 29 mmHg
Abnormal ≥ 30 mmHg

V. Blood Pressure Response To Sustained Hand Grip :
In the test the patient was asked to grip a sphygmomanometer maximally with the dominant art for few seconds and repeated twice. The highest value of three contraction was taken as maximum voluntary contraction (MVC). Hand grip was then maintained steadily at 30% MVC. Blood pressure was measured beforehand grip (*three times*) and during hand grip in non exercising arm (*three times at one minute's interval*).

The result is expressed as difference of highest diastolic pressure during hand grip and average of three blood pressure beforehand grip.

Interpretation
Normal ≥ 16 mmHg
Borderline = 11-15 mmHg
Abnormal ≤ 10 mmHg

These five tests are very simple to perform and total time requirement is very less (about 30 minutes).

RESULTS AND OBSERVATIONS :
The present study was carried out with a total of 60 patients admitted in a tertiary teaching health care system in north eastern part of india irrespective of their sex and age.All the patients had undergone battery of tests for detection of diabetic autonomic neuropathy to know the prevalence of it in diabetic patients.

Table I Showing The Distribution Of Patients According To Age Group

Age in years	No. of cases	Percentage (%)
30 - 39	10	16.7
40 - 49	18	30.0
50 – 59	20	33.3
≥60	12	20.0

From this table it is observed that age varied from 30 years to more than 60 years. It is seen that maximum number of cases were in the age group of 50 – 59 (33.3%) followed by 40 – 49 (30%) cases (Fig. 1).

Table II Showing The Distribution Of Patients According To Sex

Sex	No. of cases	Percentage (%)
Male	48	80
Female	12	20
Total	60	

From this table, it has been observed that out of 60 (sixty) cases, 48 (80%) cases are male and 12 (20%) cases are female. In this study male out numbered female (Fig. 2).

Fig 1: A pie diagram showing the distribution of patients according to age group in %

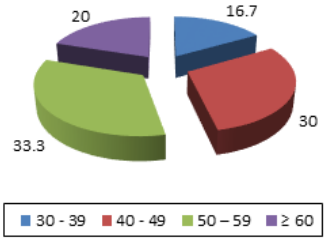


Fig 2: Pie diagram showing the distribution of patients according to sex in %

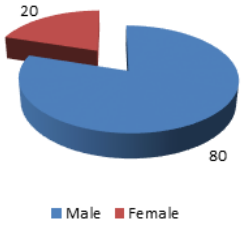


Table III Showing The Duration Of Diabetic Condition

Duration in years	No. of cases	Percentage (%)
0 - 5	24	40
6 – 9	24	40
≥10	12	20

Duration of diabetes varied from 1 year (one) to 24 years (twenty five). From table III, it is seen that maximum number of cases found in the duration of 0 – 5 years and 6 – 9 year group (40% each).

Table IV Showing Various Manifestations Of Diabetic Autonomic Neuropathy

Manifestation	Number of cases	Percentage (%)
Sweating abnormality	18	30.0
Postural hypotension	18	30.0
Impotence	10	16.7
Diabetic diarrhoea	06	10.0
Bladder disturbance	05	08.3
Dependent oedema	04	06.7
Trophic ulcer	04	06.7

From table IV, it is observed that sweating abnormality and postural hypotension are the most common symptoms relating to diabetic autonomic neuropathy (30% case) followed by impotence (16.7%). Whereas symptoms like diabetic diarrhoea, bladder disturbance, dependent oedema and trophic ulcer also occurs but less frequently. (Fig. 3).

Fig 3: Bar diagram showing various manifestations of diabetic autonomic neuropathy

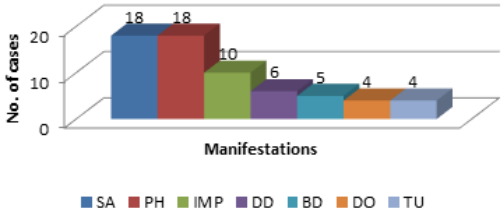


Table V Showing Prevalence Of Autonomic Neuropathy

Group	No. of cases	Percentage (%)
I	38	63.3
II	12	20.0
III	10	16.7

Table V showing that out of 60 cases, 38 cases are found in group I (those with normal autonomic function tests), 12 cases are in group II (only cardiac parasympathetic damage), 10 cases are in group III (those with abnormalities of autonomic function tests suggestive of cardiac parasympathetic and more widespread sympathetic damage). Out of 60 cases 22 cases (36.7%) are found to have abnormal response to cardiovascular reflexes.

Table VI Showing Abnormal Autonomic Function Test

Test		Abnormal results (%)	No. of cases with borderline results (%)	Total abnormal result	Percentage (%)
1	Hear rate response to Valsalva manoeuvre	10 (45%)	12 (54.5%)	23	36.7
2	Heart rate variation during deep breathing	10 (50%)	10 (50%)	20	33.3
3	Immediate heart rate response to standing	5 (31.3%)	11 (68.8%)	16	26.7
4	Blood pressure response to standing	4 (28.6%)	10 (71.45%)	14	23.3
5	Blood pressure response to sustained hand grip	2 (25%)	6 (75%)	8	13,3

From table VI, it is obvious that 22 cases out of 60 cases have shown abnormal Valsalva ratio (36.7%). Out of 22 cases 10 (45%) had definite abnormal result (Valsalva ration ≤ 1.10) and 12 (54.5%) cases showed borderline result (valsalva ration 1.11 – 1.2). 20 cases (33.3%) showed abnormal results in the test heart rate variation during deep breathing. Out of 20 cases equal number of cases showed definite abnormal and borderline results. In the test immediate heart rate response to standing, 11 cases (68.8%) and 5 cases (31.3%) showed borderline and definite result respectively, total being 26.7%.

Blood pressure response to standing in 14 cases i.e. 23.3% showed abnormal result. Out of that 4 cases (28.6%) showed definite abnormal result and 10 (71.45%) cases showed borderline result.

Out of 8 (13.3%) total abnormal cases in the test blood pressure response to sustained hand grip, 2 cases (25%) showed de definite abnormal result and 6 cases (75%) showed borderline result.

Table VII Showing Relationship Of Autonomic Neuropathy With Duration Of Diabetes

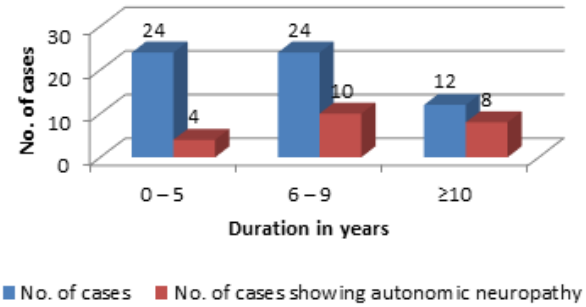
Duration in years	No. of cases	No. of cases showing autonomic neuropathy	Percentage (%)
0 – 5	24	4	16.7
6 – 9	24	10	41.7
≥10	12	8	66.7

Table VII is showing that out of 24 (40%) cases of diabetes mellitus in the 0 – 5 year duration group, 4 cases (16.7%) are having autonomic neuropathy, our of 24 cases in the duration group 6 – 9 years, 10 cases (41.7%) are having autonomic neuropathy. In the duration group ≥ 10 years, 8 cases out of 12 (66.7%) showing neuropathy. From this table, it is clear that autonomic neuropathy is directly proportional to the duration of diabetes (Fig 4).

Table – VIII Showing Distribution Of Sex In Diabetes Autonomic Neuropathy

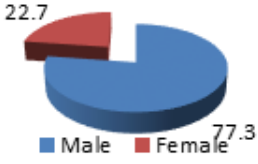
Sex	No. of cases with DAN	Percentage (%)
Male	17	77.3
Female	05	22.7
Total	22	

Fig 4: Bar diagram showing relationship of diabetic autonomic neuropathy (DAN) with duration of diabetes



From the table it has been observed that out of 22 patients who are having diabetic autonomic neuropathy (DAN) 17 patients (77.3%) are male and 5 patients (22.7%) are female. Here also male outnumbered the female (Fig. 5).

Fig 5: Pie diagram showing distribution of sex in diabetic autonomic neuropathy in %



DISCUSSION:

Out of 60 diabetic patient studied in the present study maximum number of patients were seen in the age of 50-59 years.

Out of all the patients who had symptoms of autonomic neuropathy complaint of sweating abnormality and postural hypotension was found in highest number. 18 cases i.e. 30% of cases was complaining of sweating abnormality. Balachandran J, Chandrashekhar (1984) found that 38% of their diabetic subjects have sweating abnormality.[4]The present study finding of 30% is somewhat comparable to that of Balachandran J, Chandrashekhar S (1984).

Another important symptom was postural hypotension. It also constituted 30% in the present study i.e. 18 cases. LOW et al in 1975 found 44% of cases in their series of study had postural hypotension.[5] In 1984, Chandrashekhar S. Balachandran J et al found postural hypotension in 76% cases. Oxford community diabetes study found 14.5% of patient had postural hypotension (D. Ziegler 1996).The finding of 30% postural hypotension is comparable to that of LOW et al 4but it is less comparable to that of Chandrashekhar et al.

About 16.7% of patients i.e. 10 patients complained of impotence in the present study. Various authors have given different data regarding the incidence of impotence. In 1967, Bahl et al noted in their study that 14.03% of their cases had impotence. Hosking et al (1979) found it was 20%.[6] Masaharu Takanami et al (1997) in their study found 44% of their patients had impotence.[7] The present study finding of 16.7% is comparable to that of Bahl et al (1967).

Diabetic diarrhoea was found in 10% of the cases. Rundle (1945) found 15% had diarrhoea,either continuous or recurrent.[8] Friedman and Schiller (1983) found diarrhoea in 18% of their cases. Balachandran J, Chadrashekhar S et al (1984) found 42% of their cases had diabetic diarrhoea. The present study finding of 10% is somewhat comparable to the study of Rundle. The high incidence of diarrhoea in the study of Balachandran J et al (1984) might be due to some associated co-morbid conditions.

In the present study prevalence of diabetic autonomic neuropathy was seen as: 38 cases (63.3%) with normal autonomic funding placed in group I, 12 cases (20%) with only cardiac parasympathetic damage placed in group II and 10 cases (16.7%) with both cardiac

parasympathetic and sympathetic damage were placed in group III. So out of 60 diabetic patients, 22 patients (36.7%) showed abnormal cardiovascular reflex.

From this study it has been observed that autonomic neuropathy is not uncommon complication of diabetes mellitus.

I.A.D.O. Brien et al (1986) found 17.3% diabetics had abnormal cardiovascular reflexes. Bielefeldt-K', Reis-HE (1989) found that 40.6% diabetics and autonomic neuropathy.[9] In Oxford community diabetes study the prevalence of autonomic neuropathy was 20.9% with definite abnormal result found in 16.8% (Diabetes news 1996). In EURODIAB IDDM complication study prevalence of definite and early autonomic neuropathy was found to be 7.7% and 9.2% respectively in 130 newly diagnosed patients. Richard Migisha et al 2019 in southwestern Uganda Cardiac autonomic neuropathy was detected in 52.5% of the participants on the basis of one or more abnormal cardiovascular autonomic reflex tests. Qi Pan et al 2019 in Beijing China in their study found that 62.6% of their diabetic patients were having cardiac autonomic neuropathy. Strauss RH et al (1997) found prevalence of definite autonomic neuropathy in 16.4% and early or borderline was 27.9%. The present study findings of 36.7% diabetic autonomic neuropathy cases is somewhat comparable to the find of Bielefeldt-K, Reis-HE (1989), as well as somewhat to the study of Strauss RH et al (1997).

In the present study diagnosis of diabetic autonomic neuropathy were based on the five tests on cardiovascular reflexes. Out of 60 (sixty) diabetic patients, 22 i.e. 36.7% patients showed abnormal response of heart rate to Valsalva manoeuvre. Out of 22 cases, 10 cases had Valsalva ratio of 1:1 or less suggesting definite abnormal result. Other 2 cases had Valsalva ration of 1:1 or less suggesting definite abnormal result. Other 12 cases had Valsalva ratio between 1.11-1.20 suggesting borderline abnormality. Different authors had given various data regarding abnormality of Valsalva manoeuvre. Sharpey Schafer (1960) found 20.5% of 330 diabetics had abnormal Valsalva ratio. Since then abnormal Valsalva ratio have been reported in 7 to 12% of diabetes (Gluck Z et al 1979; Sund K vist G 1981) and 40 to 70% of diabetics (Bennet et al, 1976, Ewing DJ et al 1973), RC Gupta et al (1994) found 26% of patient had abnormality of heart rate response to Valsalva manoeuvre. The present study finding of 36.7% is somewhat comparable to the studies of Ewing et al (1973) and Bennet T et al (1976).

The present study showed 20 patients out of 60 diabetics (33.3%) had abnormal heart rate variation during deep breathing. Out of these 20 patients, abnormal results and borderline results constituted 10 patients each. Hilsted (1979) found 40% of patients in his study had abnormal heart rate variation during deep breathing. Dyrberg (1981) found it was about 27%. Masaoka et al (1981) found somewhat higher percentage of cases had abnormal variability during deep breathing. According to her it was 50%. O'Brien I.A.D. (1986) found in their study, 21.7% had abnormal heart rate variation during deep breathing. The present study though does not correlate directly with the find of other authors, but has some similarity with the findings of Dyrberg (1981) and R.C. Gupta et al (1994).

Immediate heart rate response to standing were being found abnormal in 16 patients (26.7%). Information regarding the prevalence of abnormal heart rate response to standing is very less. In 1978, Ewing et al found all of the cases who were having symptoms of autonomic neuropathy associated with abnormal heart rate response to standing was 43%. !.A.D.O' Brien et al (1986) found this abnormality was about 10%. R.C. Gupta et al (1994) found as high as 56% patients had abnormal response of heart rate to standing. The present study have some correlation with the finding of O' Brien et al 1986.

In this study, fall of systolic blood pressure on standing found in 14 patients (23.3%). Out of this 14 patients, 4 patients had fall of blood pressure more than 30 mmHg. The rest 10 patients showed fall of systolic blood pressure in between 11 – 29 mm of Hg, suggesting borderline result.

Out of 50 diabetic patients (13.3%) had abnormal response to sustained hand grip in the present study.

In the present study, 66.7% of patients had diabetic autonomic neuropathy who were having this disease for 10 years or more than that. This high prevalence is most probably due to inadequate glycemic control.

In the present study out of 22 patients who showed evidence of diabetic autonomic neuropathy 17 cases (77.3%) were male and only 5 cases (22.7%) were female.

CONCLUSION:

Duration of diabetes is directly linked to the development of Cardiac Autonomic Neuropathy and silent myocardial ischaemia which is evident from the study. In the present study, 36.7% of the study subjects showed evidence of autonomic neuropathy.

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