

Analysis of the Clinical Profile of Diabetes Mellitus and its Association with Autonomic Dysfunction

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Abstract

Background: Diabetes is known to man for centuries but yet to be fully understood. This relative lacuna of knowledge makes man wish to search for simple and reliable and versatile tests that not only help in primary and secondary prevention of most of the complications but also in the primordial prevention of the disease on the whole. **Material & Methods:** The present prospective study including 50 Diabetic patients which were selected by simple random sampling. Institutional Ethics Committee Clearance was obtained and written informed consent was obtained from all the patients. **Results:** Among 9 cases with sexual impotence 4 cases had autonomic dysfunction. Among 7 cases with retrograde ejaculation 5 cases had autonomic dysfunction ($p < 0.01$). The mean atonic urinary bladder in cases with autonomic dysfunction was 10 (66.67%) ($p < 0.0001$). Among 14 cases with gustatory sweating 9 cases had autonomic dysfunction ($p < 0.001$). Among 12 cases with delayed gastric emptying 8 cases had autonomic dysfunction ($p < 0.005$). Among 4 cases with nocturnal diarrhea 2 cases had autonomic dysfunction ($p > 0.05$). Among 29 cases with constipation 12 cases had autonomic dysfunction ($p < 0.05$). Among 8 cases with eye pupillary changes, 7 cases had autonomic dysfunction ($p < 0.001$). Among 4 cases with vascular dizziness 4 cases had autonomic dysfunction ($p < 0.05$). Among 10 cases with skin absent sweating 6 cases had autonomic dysfunction ($p < 0.05$). Among 14 cases with numbness 10 cases had autonomic dysfunction ($p < 0.0001$). Among 20 cases with weakness of muscles 7 cases had autonomic dysfunction ($p > 0.05$). **Conclusion:** Among the genitourinary system, atonic urinary bladder and retrograde ejaculation were common dysfunctions. Among the gastrointestinal system, gustatory sweating, constipation, and delayed gastric emptying were common dysfunctions. Numbness was commonly associated with diabetic autonomic dysfunction.

Keywords: Diabetes, Autonomic Dysfunction, Diabetic Complications.

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Introduction

Diabetes mellitus is a common metabolic disorder with alarmingly increasing worldwide incidence. It has raised over the past two decades from an estimated 30 million cases in 1985 to 177 million in 2000 and is estimated to cross a global estimate of 300 million by 2030[1]. India leads the world today with the largest number of diabetics in any given country. In the 1970s the prevalence of diabetes among urban Indians was reported to be 2.1% and this has now risen to 12.1%[2].

India is the diabetic capital of the world. Thus, diabetes is a growing menace in our society, with a growing worldwide incidence. To beat it all, though diabetes can be easily detected and diagnosed overall, its actual hold over the various systems in the form of complications is seldom fully recognised. Most people link diabetes to major manifestations of the eyes or heart that they overlook its grasp on the nerves, and the dreaded neuropathic complications[3].

Diabetes is known to man for centuries but yet to be fully understood. This relative lacuna of knowledge makes man wish to search for simple and reliable and versatile tests that not only help in primary and secondary prevention of most of the complications but also in the primordial prevention of the disease on the whole. It is sad to note that the various manifestations and complications of diabetes mellitus are still difficult to detect, and most of the sufferers usually end up in the final stages or a disabled form especially neuropathy[4].

It is proclaimed that these bedside methods of assessments calculate the prevalence of autonomic neuropathy in diabetes in a range of 10-100%[5]. Thus it is very evident to make an effort to study autonomic manifestations in diabetes mellitus, and to use the bedside clinical tests to detect early diabetic dystonomia, and the varied relations and effects autonomic failure has on other

complications in diabetes[6]. The present study highlights the direct bearing of diabetic autonomic neuropathy on morbidity and mortality of diabetics, in the form of silent cardiac arrests and the dreaded 'death in bed' syndrome. The significance and need of this study of autonomic manifestations in diabetes mellitus are thus emphasized.

Materials & methods

The present prospective study was conducted at Dr. D.Y. Patil Medical College, Hospital & Research Centre, Pimpri, Pune. Fifty Diabetic patients were enrolled for the study by simple random sampling. Institutional Ethics Committee Clearance was taken before the start of the study and written informed consent for the study purpose was obtained from all the patients. Patients with age more than 60 years, severe anemia, liver diseases, congestive cardiac failure, cardiac arrhythmias, renal failure, pregnant females, electrolyte imbalance, central or peripheral neuropathies due to cause other than diabetes and exposure to lead, drugs (like INH) and drugs affecting the autonomic function were excluded from the study. The selected fifty Diabetic patients were questioned about the presence of symptoms reported to be related to autonomic neuropathy, viz. postural giddiness, disturbances of bladder sphincter, nocturnal polyuria, diarrhea, constipation, impotence, and bouts of localized sweating. All the patients were subjected to a detailed clinical examination by pretested proforma. The cases were subjected to five non-invasive autonomic functions tests to assess cardiovascular autonomic reflexes as recommended by Ewing-Clarke which are tests reflecting Parasympathetic functions (heart rate variation during deep breathing, immediate heart rate response to standing, heart rate response to Valsalva Manoeuvre), and tests reflecting Sympathetic functions (blood pressure response to standing, blood pressure response to sustained handgrip).

Autonomic dysfunction when present was classified using the criteria of Ewing and Clarke[7]. The data were analyzed using MS Excel 2010, Epi Info v7, and SPSS v22.

Results

In the present study out of a total of 50 patients, the majority 16 (32%) are in the age group 41 to 50 years, followed by 30% who are in the age group 31 to 40 years and 11 (22%) are in the age group of 51 to 60 yrs. Only 8 (16%) are in the 21 to 30 yrs.

Both males (25) and females (25) were equal in number in the study group. Constipation (58%) was a common symptom among the study group, followed by weakness of muscles (40%), numbness, gustatory sweating and retrograde ejaculation (28%), atonic urinary bladder (26%), delayed gastric emptying (24%), skin absent sweating(20%), eye pupillary changes (16%), sexual impotence (18%) and nocturnal diarrhea (8%). (Table 1)

Table 1: Presenting complaints wise distribution of cases in the study group

Presenting complaints	No of cases	Percentage
Sexual impotence	9	18
Retrograde ejaculation	7	28
Atonic urinary bladder	13	26
Gustatory sweating	14	28
Delayed gastric emptying – Vomiting	12	24
Nocturnal diarrhoea	4	8
Constipation	29	58
Eye pupillary changes	8	16
Vascular dizziness	4	8
Skin-absent sweating	10	20
Numbness	14	28
Weakness of muscles	20	40

The majority 9 (18%) had early cardiac autonomic dysfunction, followed by 4 (8%) had definite, 1(2%) had atypical and severe cardiac autonomic dysfunction respectively. 35 cases did not have cardiac autonomic dysfunction in the study group.

Among 9 cases with sexual impotence 4 cases had autonomic dysfunction and 5 did not have autonomic dysfunction. Among 7 cases with retrograde ejaculation 5 cases had autonomic dysfunction and 2 did not have autonomic dysfunction (p<0.01).

Mean atonic urinary bladder in cases with autonomic dysfunction was 10 (66.67%) and 3 (8.57%) with no autonomic dysfunction, which is statistically highly significant (p<0.0001). Among 14 cases with gustatory sweating 9 cases had autonomic dysfunction and 5 did not have autonomic dysfunction(p<0.001). Among 12 cases with delayed gastric emptying 8 cases had autonomic dysfunction and 4 did not have autonomic dysfunction(p<0.005). (Table 2)

Table 2: Association between Presenting complaints and autonomic dysfunction in the study group

Genitourinary autonomic symptoms	Autonomic dysfunction		Z Value	P-Value
	Yes	No		
Sexual impotence	4 (50)	5 (29.41)	0.99	>0.05
Retrograde ejaculation	5 (62.50)	2 (11.76)	2.70	<0.01
Atonic urinary bladder	10 (66.67)	3 (8.57)	4.45	<0.0001
Gustatory sweating	9 (60)	5 (14.29)	3.27	<0.001

Delayed gastric emptying – Vomitting	8 (53.33)	4 (11.43)	3	<0.005
Nocturnal diarrhoea	2 (13.33)	2 (5.71)	0.79	>0.05
Constipation	12 (80)	17 (48.57)	2.35	<0.05
Eye pupillary changes	7 (46.67)	1 (2.86)	3.32	<0.001
Vascular dizziness	4 (26.67)	0	2.33	<0.05
Skin-absent sweating	6 (40)	4 (11.43)	2.08	<0.05
Numbness	10 (66.67)	4 (11.43)	4.15	<0.0001
Weakness of muscles	7 (46.67)	13 (37.14)	0.62	>0.05

Among 4 cases with nocturnal diarrhea, 2 cases had autonomic dysfunction and 2 did not have autonomic dysfunction ($p > 0.05$). Among 29 cases with constipation 12 cases had autonomic dysfunction and 17 did not have autonomic dysfunction ($p < 0.05$). Among 8 cases with eye pupillary changes 7 cases had autonomic dysfunction and 1 did not have autonomic dysfunction ($p < 0.001$). Among 4 cases with vascular dizziness 4 cases had autonomic dysfunction ($p < 0.05$). Among 10 cases with skin absent sweating 6 cases had autonomic dysfunction and 4 did not have autonomic dysfunction ($p < 0.05$). Among 14 cases with numbness 10 cases had autonomic dysfunction and 4 did not have autonomic dysfunction ($p < 0.0001$). Among 20 cases with weakness of muscles 7 cases had autonomic dysfunction and 13 did not have autonomic dysfunction ($p > 0.05$). (Table 2)

Discussion

The present study was conducted to find out the clinical profile and autonomic dysfunction in diabetic patients and the association of presenting complaints with autonomic dysfunction. Total study subjects were 50 cases, which were enrolled based on inclusion and exclusion criteria. Presenting symptoms among diabetic autonomic dysfunction distribution showed that constipation (58%), weakness of muscles (40%), gustatory sweating (28%), atonic urinary bladder (26%), delayed gastric emptying (24%), numbness (28%), skin absent sweating (20%) was commonly seen in the study group. JL Noronha et al determined the frequency and pattern of autonomic neuropathy in diabetic patients. Among 33 cases in the study, seventeen

patients had one or more symptoms. Nine patients complained of nocturnal polyuria. Eight had impotence. Seven had postural giddiness and only 2 had constipation. Disturbances of bladder sphincter, diarrhea, or bouts of localised sweating were not seen in any patient [8]. Prabhakar Rao et al intended to detect the prevalence of QTc prolongation in diabetic patients as well as its relationship with cardiac autonomic neuropathy. Postural dizziness (54%), Impotence (46%), Gustatory sweating (32%), Atonic urinary bladder (18%), Gastric atony (20%), Constipation (18%), and Diabetic diarrhea (12%) were the symptoms in the study cases [9].

Among genitourinary autonomic symptoms, retrograde ejaculation was significantly seen in cases with autonomic dysfunction compared with no autonomic dysfunction. Sexual impotence was not significant among the cases with autonomic dysfunction in the study group. A similar finding was also observed in a study conducted by Ziaei-Rad et al who investigated the prevalence of sexual dysfunctions (SD) among diabetic patients in Iran and examined whether glycemic control has a role in SD. Among 15 cases with retrograde ejaculation, 9 were among uncontrolled diabetes with autonomic dysfunction group and 6 were among the controlled group and the difference was significant between the two groups [10].

The atonic urinary bladder was significantly higher among cases with autonomic dysfunction as compared to cases without autonomic dysfunction in the study group. Buck A-C et al assessed the frequency and extent of autonomic and

peripheral neuropathy in 60 subjects with diabetes mellitus. Objective evidence of neuropathic bladder dysfunction was detected in 43 of them (71.7%) out of the total 60 cases in the study. The commonest abnormality was a hypotonic, insensitive large capacity bladder, which was usually asymptomatic. Less frequently (15%) this was complicated by bladder decompensation and sphincter involvement, resulting in excessive residual urine and infection; some of these had bladder paralysis with chronic painless retention of urine (7%) which resembled our study finding[11].

Among gastrointestinal autonomic symptoms, gustatory sweating, constipation, and delayed gastric emptying were significantly seen in cases with autonomic dysfunction compared with no autonomic dysfunction. Nocturnal diarrhea was not significant among the cases with autonomic dysfunction in the study group. Massimo Pozzi et al evaluated in 18 diabetic patients, 11 with and 7 without evidence of autonomic neuropathy, as revealed by common cardiovascular tests alterations indicative of autonomic nervous involvement of the gastrointestinal tract independently of the presence of suggestive symptoms. Data confirmed that delayed gastric emptying of indigestible solids is a frequent finding in diabetic subjects and was highly significant[12].

Among other system autonomic symptoms, eye pupillary changes, vascular dizziness, and absent sweating in the skin were significantly altered in autonomic dysfunction with diabetes in the study group. A similar finding was observed in a study conducted by Mansour A et al, who examined the utility of the sympathetic skin response (SSR) as a measure of impaired autonomic function among diabetic patients in Saudi Arabia. The SSR was present in all healthy subjects, and 32 diabetic patients. Among 16 patients with autonomic neuropathy, the SSR was absent in 14 and present in 2, while 4 of 34 patients lacking evidence of autonomic neuropathy had

absent SSR. There was a strong association between absent SSR and autonomic neuropathy ($p < 0.001$)[13]. Hee Jung Kwon and Hye Young Kim screened for diabetic autonomic neuropathy of the pupil using 0.5% apraclonidine and 0.1% pilocarpine. Patients who had a positive pupillary test had a significantly higher rate of positive cardiac autonomic dysfunction tests ($p = 0.032$). The authors concluded that Pupillary autonomic neuropathy was related to the duration of diabetes and the degree of DM retinopathy[14].

Among neurological autonomic symptoms, numbness was significantly seen in cases with autonomic dysfunction compared with no autonomic dysfunction. Weakness of muscles was not significant among the cases with autonomic dysfunction in the study group. Peripheral neuropathy was significantly seen in cases with autonomic dysfunction compared with no autonomic dysfunction. A similar finding was also observed in a study conducted by Wang DD et al who investigated the prevalence of diabetic peripheral neuropathy (DPN) in a Saudi population. The prevalence of DPN in this population was 19.9%. In the multivariable analyses, longer duration of diabetes [odds ratio (OR) for every 5-year increase, 2.49, 95% CI, 1.75-3.53], abdominal obesity, and higher levels of fasting blood glucose, creatinine, and white blood cell count were associated with higher odds of DPN[15].

Conclusion

We concluded from the present study that among the genitourinary system, atonic urinary bladder and retrograde ejaculation were common dysfunctions. Among the gastrointestinal system, gustatory sweating, constipation, and delayed gastric emptying were common dysfunctions. Numbness was commonly associated with diabetic autonomic dysfunction.

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