

# Prevalence of Cardiovascular Autonomic Dysfunction in Type-2 Diabetes patients with Microalbuminuria in a Tertiary Level Hospital

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# Introduction....

The prevalence of cardiovascular autonomic dysfunction in diabetes is not precisely known; Abnormal cardiovascular function test suggest poor prognosis and increased incidence of silent myocardial infarction, cardiac arrest, sudden death, and inadequate response to stressful events, e.g., anaesthesia and surgery<sup>2,3</sup>. There are very few reports about the prevalence of cardiac autonomic neuropathy (CAN) along with correlation with other diabetic complications. To highlight the magnitude of the problem in Bangladeshi population, the present study was planned.

## Contd....

Several studies have suggested that impaired cardiovascular autonomic function and increased urinary albumin excretion are related in patients with diabetes. Most of these studies have been done in type 1 diabetes. Similar studies in type 2 diabetes were relatively small<sup>6</sup> .

For that reason, we planned to investigate the pattern of autonomic dysfunction and prevalence in patients with microalbuminuria and made an attempt to evaluate if there is an independent relation between increased urinary albumin excretion and subclinical autonomic neuropathy.

# Methods....

This observational study was done in the department of Medicine, Dhaka Medical College Hospital, Dhaka from August 2015 to January 2016.

- A total of 50 patients with diagnosis of type-2 DM were primarily enrolled for the study.
- Patients with proteinuria were excluded from the study and
- those with significant microalbuminuria were finally selected for analysis.

## Contd....

Cardiovascular autonomic function tests (CAFT) include tests for heart rate variability and responses to the certain maneuver were conducted. The following measures of cardiovascular autonomic function were used to detect cardiac autonomic neuropathy<sup>5</sup> :

<b>Autonomic test</b>	<b>Normal (Score 0)</b>	<b>Borderline (Score 1)</b>	<b>Abnormal (Score 2)</b>
Heart rate response to Valsalva manoeuvre (15 secs): ratio of longest to shortest R-R interval	>1.21	1.20-1.11	< 1.10
Heart rate response to deep breathing(6 breaths over 1 min): maximum - minimum heart rate	>15 beat/min	11-14 beat/min	< 10 beat/min
Heart rate response to standing after lying: ratio of R-R interval of 30th to 15th beats	>1.04	1.01-1.03	<1.00
Blood pressure response to standing: Fall in systolic BP (mm Hg)	<10 mm Hg	11-29 mm Hg	>30 mm Hg
Blood pressure response to sustained hand grip (rise in diastolic BP): highest diastolic BP during hand grip - mean of 3 diastolic BP before hand grip began (mm Hg)	>16 mm Hg	11-15 mm Hg	<10 mm Hg

Data were collected in structured case record form and were analyzed by using SPSS version 16.0.

# Results....

**Table-1: Base line characteristics of study population(n=50)**

total number of patient	50
Peak age(years)	40-60
Male:Female	2.22:1
Insulin:Oral medication	1.63:1
Mean duration of DM(years)	>12

## Contd....

A total of 50 patients were taken in the study; male were 34 and female were 16. Majority of the patients was between 41-50 years and mean duration of DM was more than 12 years.

Common symptoms were dizziness, abnormal sweating, impotence, bladder symptoms, constipation and nocturnal diarrhoea.



**Table- 2: Heart rate (HR) response in the study group (n=50)**

Variable	Frequency		Total
	<i>M (n=34)</i>	<i>F (n=16)</i>	
Heart rate response to Valsalva Maneuver (R-R interval)			
<0.5	7(20.58)	3(18.75)	10
0.6-1.10	8(23.53)	1(6.25)	9
1.11-1.15	12(35.29)	5(31.25)	17
1.16-1.20	5(14.70)	6(37.5)	11
>1.21	2(5.88)	1(6.25)	3
Heart rate response to Deep Breathing			
1-5	9(26.47)	6(37.5)	15
6-10	14(41.17)	8(50.0)	22
11-14	11(32.85)	2(12.5)	13
15-20	0	0	0
Heart rate response to standing			
<0.5	9(26.47)	6(37.5)	15
0.6-1.0	5(14.70)	3(18.75)	8
1.01-1.03	14(41.17)	6(37.5)	20
1.04-1.09	4(11.76)	1(6.25)	5
>1.10	2(5.88)	0	2

**Table- 2(b): Heart rate response and autonomic score of study subject (n=50)**

Heart rate	Number of Patients		
	Normal	Borderline	Abnormal
Heart rate response to Valsalva Maneuver	3	28	19
Heart rate response to Deep Breathing	0	13	37
Heart rate response to standing	7	20	23

## Contd...

Regarding the heart rate response to Valsalva Maneuver, abnormal response was observed in 19 subject; majority were male 8(23.53). Borderline response was detected in 28 subjects and normal were only in 3 subjects, of whom maximum were female 1(6.25). In case of heart rate response to Deep Breathing, abnormal heart rate was found in 37 patients. In this series, female subjects 8(50.0) were affected more than male 14(41.17). No patients were detected with normal heart rate response during Deep Breathing. Heart rate response to standing showed that 23 patients had abnormal heart rate with female 6(37.5) predominance. Borderline heart rate was found in 20 subjects. So, overall abnormal heart rate was found in 19, 37, 23 number of cases respectively.

**Table-3(a): Blood pressure response in the study group (n=50)**

Variable	Frequency		Total
	M (n=34)	F (n=16)	
BP response to standing: fall in systolic BP(mm of Hg)			
<5	1(2.94)	0	1
6-10	2(5.88)	0	2
11-20	9(26.47)	3(18.75)	12
21-29	11(32.35)	8(50.0)	19
>30	11(32.35)	5(31.25)	16
BP response to sustained handgrip: rise in diastolic BP (mm of Hg)			
<5	2(5.88)	3(18.75)	8
6-10	14(41.17)	7(43.75)	21
11-15	12(35.29)	5(31.25)	17
16-20	2(5.88)	1(6.25)	3
>20	1(2.94)	0	1

**Table-3(b): Blood pressure response and autonomic score of study subject (n=50)**

Blood pressure	Number of Patients		
	Normal	Borderline	Abnormal
BP response to standing (fall in systolic BP)	3	31	16
BP response to sustained handgrip (rise in diastolic BP)	4	17	29

## Contd...

BP response to standing demonstrated that total 3 patients had normal systolic BP. In this series maximum were male subjects 2(5.88). Borderline BP response was detected in 31 cases. Among them 5(31.25) were female. Abnormal BP response was found in 16 subjects of whom 11(32.35) were male. BP response to sustained handgrip represented that 29 patients had abnormal BP response with female predominance . Borderline BP response was found in 17 subjects and among them 12(35.29) were male and 5(31.25) were female.

**Table- 4: Abnormal cardiovascular autonomic function test in the study group (n=50)**

<b>Abnormal reflex</b>	<b>Number of case (%)</b>
One abnormal CV reflex	13(26%)
Two abnormal CV reflexes	22(44%)
Three abnormal CV reflexes	5(10%)
Total number of patients having abnormal CV reflexes	40(80%)

**Table-5: Abnormal parasympathetic and sympathetic function in the study group (n=50)**

Type of autonomic neuropathy	Number of case	Percentage
Parasympathetic neuropathy	40	80%
Sympathetic neuropathy	43	86%

. \*Parasympathetic neuropathy = at least one of the three tests of parasympathetic function being abnormal

\* Sympathetic neuropathy = at least one of the two tests of sympathetic function being abnormal



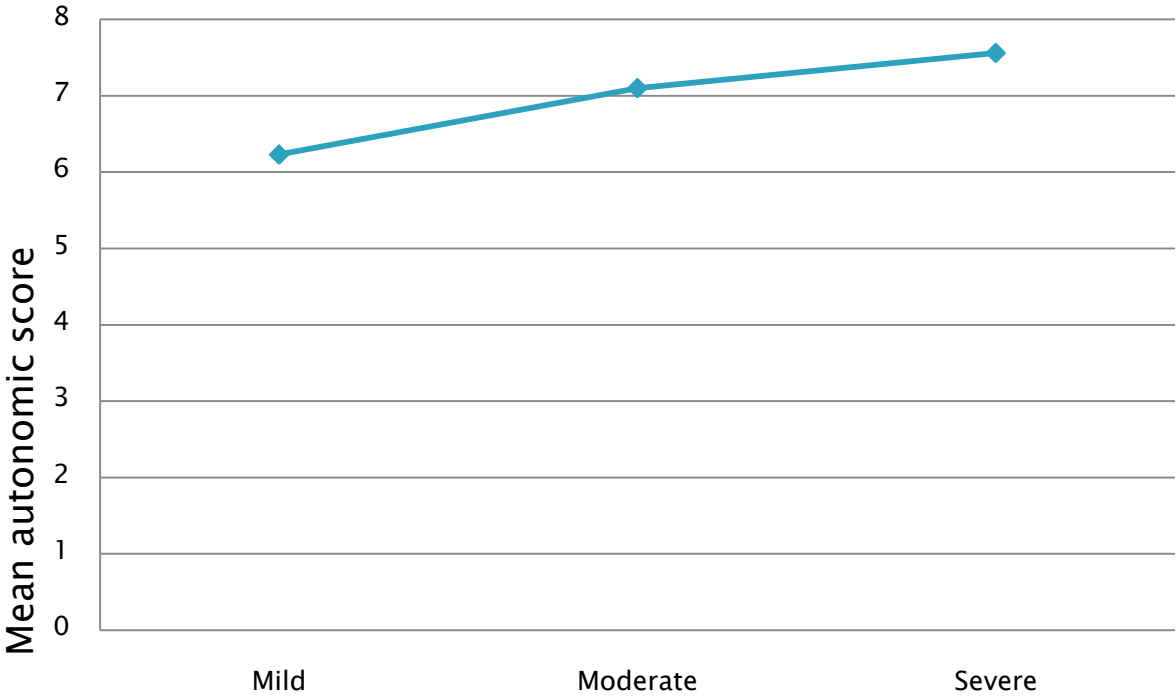
**Table-6: Association of Heart rate (HR) response with different grade of microalbuminuria (n=50)**

Variable	Grade of microalbuminuria			Total
	<i>Mild (n=19)</i>	<i>Moderate (n=24)</i>	<i>Severe (n=7)</i>	
Heart rate response to Valsalva Maneuver (score)				
0 (normal)	3(15.78)	0	0	3
1 (borderline)	15(78.94)	12(50.0)	1(14.28)	28
<b>2 (abnormal)</b>	1(5.26)	12(50.0)	<b>6(85.71)</b>	19
Heart rate response to Deep Breathing (score)				
0 (normal)	0	0	0	0
1 (borderline)	10(52.63)	3(12.5)	0	13
<b>2 (abnormal)</b>	9(47.36)	21(87.5)	<b>7(100.0)</b>	37
Heart rate response to standing (score)				
0 (normal)	5(26.31)	2(8.3)	0	7
1 (borderline)	14(73.68)	4(16.6)	2(28.57)	20
<b>2 (abnormal)</b>	0	18(75)	<b>5(71.42)</b>	23

## Contd...

Finding showed that severe grade of microalbuminuria patients is associated with abnormal to borderline dysfunction. In case of heart rate response to valsalva maneuver, 6(85.71) patients with severe microalbuminuria had abnormal heart rate and 15(78.94) patients with mild microalbuminuria had borderline heart rate response. All cases of severe microalbuminuric patients had abnormal heart rate response to Deep Breathing, followed by 21(87.5) patients with moderate microalbuminuria. Heart rate response to standing showed that 14(73.68) patients with mild microalbuminuria had borderline heart rate response , 18(75) patients with moderate microalbuminuria and 5(71.42) patients with severe microalbuminuria had abnormal heart rate response.

**Figure-1: Heart rate response (parasympathetic function) in DM case with different grade of microalbuminuria (n=50)**



## Contd....

Cardiovascular autonomic dysfunction is associated with microalbuminuria in patients with type 2 diabetes mellitus. In this table mean heart rate score was higher (7.56) in type 2 DM with severe microalbuminuria patients. A positive correlation was observed between the parasympathetic function and the severity of microalbuminuria. Mean score was 6.23 in type 2 DM with mild microalbuminuria, 7.1 was in type 2 DM with moderate microalbuminuria and 7.566 was in type 2 DM with severe microalbuminuria patients.

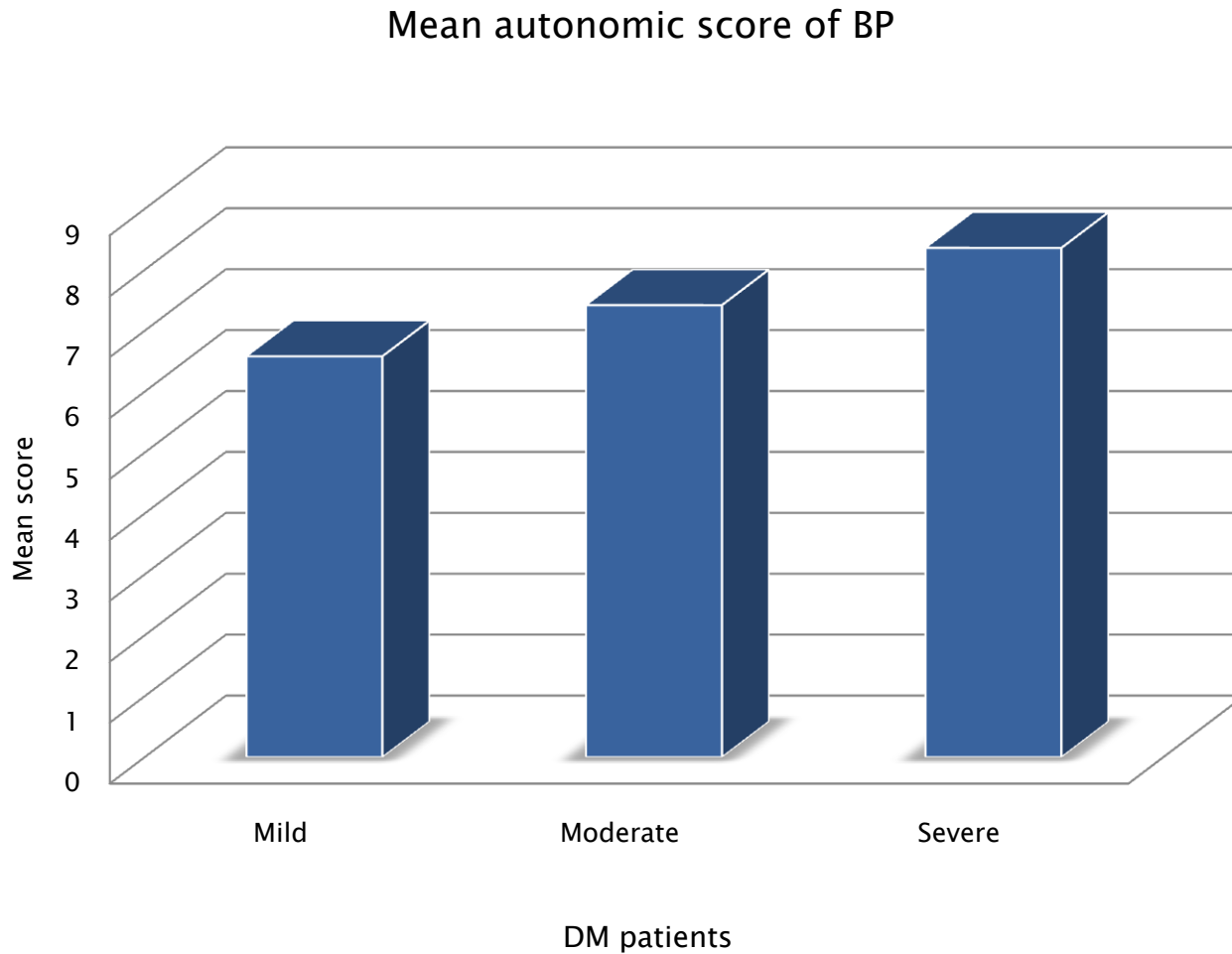
**Table-7: Association of blood pressure response with different grade of microalbuminuria (n=50)**

Variable	Grade of microalbuminuria			Total
	<i>Mild (n=19)</i>	<i>Moderate (n=24)</i>	<i>Severe (n=7)</i>	
BP response to standing (score)				
0 (normal)	2(10.52)	1(4.16)	0	3
1 (borderline)	16(84.21)	13(54.16)	2(28.57)	31
<b>2 (abnormal)</b>	1(5.26)	10(41.66)	<b>5(71.42)</b>	16
BP response to sustained handgrip (score)				
0 (normal)	3(15.78)	0	1(14.28)	4
1 (borderline)	13(68.42)	4(16.6)	0	17
<b>2 (abnormal)</b>	3(15.78)	20(83.3)	<b>6(85.71)</b>	29

## Contd....

Finding showed that severe grade of microalbuminuric patients is associated with abnormal to borderline dysfunction. In BP response to standing, 5(71.42) patients with severe microalbuminuria had abnormal BP response and 16(84.21) patients with mild microalbuminuria had borderline response. In case of BP response to sustained handgrip, almost all cases with severe microalbuminuria and 20(83.3) patients with moderate microalbuminuria had abnormal BP response.

**Figure-2: Blood pressure (BP) response (Sympathetic Function) in DM case with different grade of microalbuminuria (n=50)**



## Contd....

Present study demonstrated that cardiovascular autonomic function (sympathetic function) is related to the presence of microalbuminuria. In this figure mean BP score was 6.58 in type 2 DM patients with mild microalbuminuria, 7.42 was in type 2 DM patients with moderate microalbuminuria and 8.36 was in type 2 DM patients with severe microalbuminuria. Microalbuminuria is a strong and independent indicator of increased cardiovascular risk among individuals with diabetes.



## Discussion....

Present study demonstrated that, 40(80%) patients had parasympathetic dysfunction and 43(86%) patients had sympathetic dysfunction which is consistent to the study done by Basu AK in which parasympathetic and sympathetic abnormality were 52% and 20% respectively.

## Contd....

In this study, common risk factors were HTN, smoking, obesity and dyslipidaemia and it is consistent with the study done by Deepak N Parchwani et al. in which age, triglycerides, blood pressure and HbA1c were significantly related to the presence of microalbuminuria.

This study also showed that, cardiovascular autonomic dysfunction is related to the presence of microalbuminuria which is consistent with other international study<sup>6</sup>.

## Conclusions....

Evaluation of cardiovascular reflexes in type 2 DM patients with paucity of related symptoms constitutes an important feasible and reproducible bedside clinical technique and correlates with abnormal albumin excretion. It should be included as a routine in work-up of patients with type 2 DM as it often uncovers autonomic neuropathy even in asymptomatic state.

## Limitations of the study

- Small sample size.
- It was a single centre study. So this may not reflect the overall picture of the country.
- Sample were taken by purposive method in which question of personal biasness might arise.

**Conflict of interest:** None

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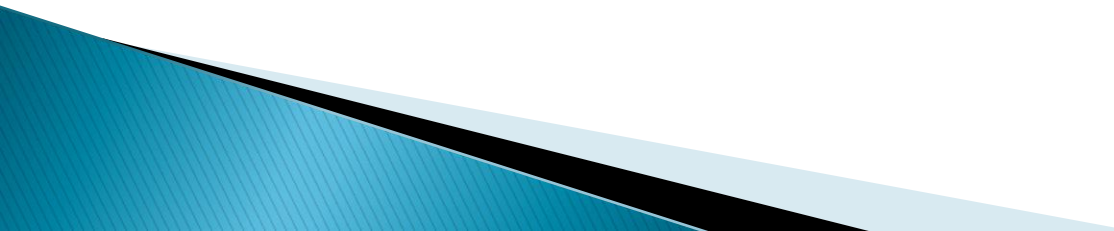
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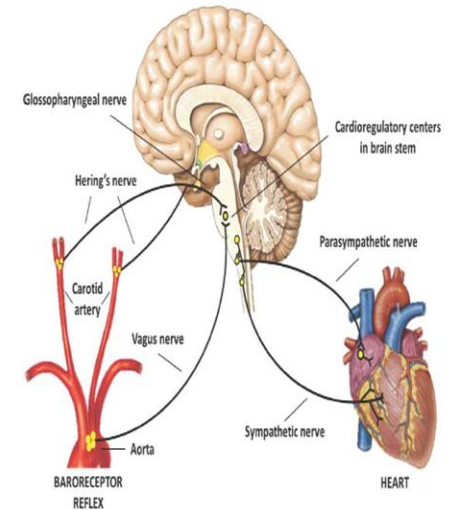
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