

**Original article**

**BLOOD PRESSURE RESPONSE TO SUSTAINED HANDGRIP TEST  
– A SINGLE TEST FOR DIAGNOSING AUTONOMIC  
NEUROPATHY IN PATIENTS OF CHRONIC KIDNEY DISEASE  
ON HAEMODIALYSIS**

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**Abstract**

**Introduction:** Cardiovascular autonomic dysfunction is a major complication of Chronic Kidney Disease (CKD) likely contributing to the high incidence of cardiovascular mortality in this patient population. The purpose of this study was to determine the frequency of autonomic neuropathy in patients with Chronic Kidney Disease on haemodialysis (HD) by using cardiovascular reflex tests.

**Objectives:** To assess the cardiovascular autonomic functions in patients of CKD on HD.

**Methods:** Following five tests were performed on 40 patients of CKD on HD

**Parasympathetic function tests:**

- Heart-rate response to Valsalva manoeuvre.
- Heart-rate variation during deep breathing.
- Immediate heart-rate response to standing.

**Sympathetic function tests:**

- Blood-pressure response to standing.
- Blood-pressure response to sustained handgrip.

**Results:** Thirty two of forty subjects (80%) had one or more abnormal tests. Among five tests the two most abnormal tests were heart-rate variation during deep breathing(n=28 , 70%) and the blood pressure response to sustained hand grip(n=24,60%).

**Conclusion:** In this study 20 out of 24 subjects who had abnormal blood pressure response to sustained hand grip also had one or more abnormal parasympathetic test. So

the blood pressure response to sustained hand grip test can alone be used to diagnose the autonomic neuropathy in patients of CKD on HD.

**Key words:** Chronic kidney disease; cardiovascular autonomic function tests; autonomic dysfunction; haemodialysis; isometric handgrip exercise.

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### **Introduction:**

The ultimate outcome of the visceromotor control (i.e. visceral homeostasis) is exerted by the division of nervous system called autonomic nervous system (ANS). Visceral nervous controls maintain a dynamic internal environment essential for proper functioning of all cells, tissues, organ systems and the individuals as a whole.<sup>1</sup> Classically the ANS consists of two main divisions, sympathetic and parasympathetic. Chronic Kidney Disease (CKD), with its high prevalence, morbidity and mortality, is an important public health problem. In India the reported prevalence of CKD in different regions ranges from 1% to 13%, and recently, data from the International Society of Nephrology's Kidney Disease

Data Center Study reported a prevalence of 17%.<sup>2</sup> Cardiovascular autonomic dysfunction is a major complication of CKD, likely contributing to the high incidence of cardiovascular mortality in this patient population.<sup>3</sup> This study was conducted to determine the status of cardiovascular autonomic nervous system in this patient population.

### **Materials and Methods:**

#### **Source of Data:**

40 Chronic Kidney Disease outpatients and inpatients on dialysis in Department of Nephrology and Department of Medicine at KIMS Hospital, Hubballi as subjects and 30 age matched healthy individuals as controls.

#### **Inclusion criteria:**

1. Age group: 20-60 years.

2. Patients meeting the criteria of chronic kidney disease as defined by KDIGO.<sup>5</sup>
3. Patients who are on drugs like blockers, nitrates, diuretics are asked to stop taking drugs one day prior to the day of test. Tests were done on next day of dialysis, so most of drugs would be eliminated and there would not be much long term effect of drugs.

**Exclusion criteria:**

1. Diabetes Mellitus.
2. CCF.
3. Ischemic heart disease.
4. Individual with severe respiratory disorders.

The tests were performed in the Department of Physiology, KIMS, Hubballi. Approval of institutional ethical committee was obtained prior to commencement of the study.

Informed written consent was obtained before the test procedures.

The instruments required are Electrocardiograph, sphygmomanometer and hand grip dynamometer.

**ECG Machine: (Hygeia):** The design of the electrocardiograph (ECG) used here complies with international

standard IEC 60601-1, GB 9706.1-2007 Medical Electrical Equipment.

The following cardiovascular autonomic function tests were performed as per Ewing and Clarke guidelines.<sup>6</sup>

• **Parasympathetic function tests:**

- i. Heart rate response to Valsalva manoeuvre.

For the heart rate response to the Valsalva manoeuvre, the ratio of the longest R-R interval to the shortest R-R interval was checked during forced exhalation into the mouthpiece of a manometer against 40 mmHg for 15 seconds

- ii. Heart rate variation during deep breathing

(Expiration/Inspiration ratio). The expiration/inspiration (E/I) ratio was calculated as the mean of the longest R-R interval during expiration divided by the mean of the shortest R-R interval during inspiration, while the patient lay quietly and breathed deeply with an electrocardiogram that

recorded heart rate variation over six breathing cycles.

**iii. Immediate Heart rate response to standing (30:15 ratio).**

The ratio of postural change was the ratio of the longest R-R interval during beats 20-40 after standing to the shortest R-R interval during beats 5-25 after standing.

**• Sympathetic function tests:**

**i. Blood pressure response to standing.**

Blood pressure in response to standing from lying down posture.

**ii. Blood pressure response to sustained handgrip.**

Blood pressure variation before and during a sustained handgrip was recorded.

**Table 1:** Normal, borderline, and abnormal values in tests of cardiovascular autonomic function

Test	Normal	Borderline	Abnormal
Valsalva ratio	≥ 1.21	1.11 – 1.20	≤ 1.10
E:I	≥ 1.21	1.11 – 1.20	≤ 1.10
30:15	≥ 1.04	1.01 – 1.03	≤ 1
Fall in SBP	≤ 10 mmHg	11 – 29 mmHg	≥ 30 mmHg
Rise in DBP	≥ 16 mmHg	11 – 15 mmHg	≤ 10 mmHg

The results are categorized into following groups:<sup>6</sup>

- 1. Normal**
- 2. Early parasympathetic damage** with results of one of the three tests of parasympathetic function abnormal;
- 3. Definite parasympathetic damage** with results of at least two of the tests of parasympathetic function abnormal;
- 4. Combined parasympathetic and sympathetic damage,** where in addition to abnormal parasympathetic test results findings in one or both of the sympathetic tests are abnormal. For the purpose of the above mentioned classification, the borderline tests were interpreted as normal.

**Study Design and Statistical Analysis:**

It is a cross sectional study in which the statistical analysis was done by using the SPSS Software version 20.

Statistical analysis done by Unpaired Student’s t-test.

P value < 0.05 was taken as significant.

**Results:**

**Table 2:** Parasympathetic function tests of controls and patients of CKD on dialysis:

Variab les	Controls Mean±S D (n=30)	CKD on Dialysis Mean±S D (n=40)	t value	P value
Valsalv a ratio	1.48±0.2 26	1.42±0.3 44	0.829 7	0.409 6
E:I ratio	1.57±0.1 85	1.15±0.1 84	9.429	<0.0001
30:15 ratio	1.4±0.17 4	1.17±0.1 63	5.6758	<0.0001

The above table shows that the difference in Valsalva ratio between the above two groups is not statistically significant and the difference in E:I ratio and 30:15 ratio is statistically significant.

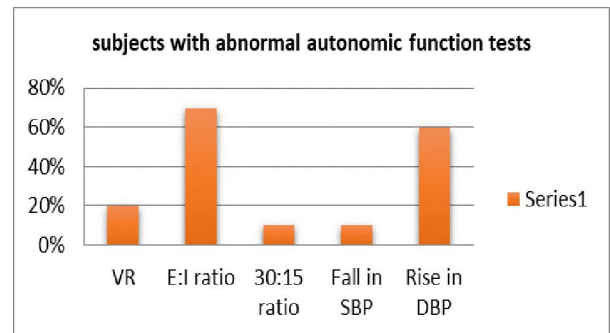
	CKD on dialysis
Normal	08(20%)
Early parasympathetic dysfunction	00(0%)
Definite parasympathetic dysfunction	08(20%)
Combined autonomic dysfunction	20(50%)
Only sympathetic dysfunction	04(10%)
Total	40(100%)

**Table 3:** Sympathetic function tests of controls and patients of CKD on dialysis:

Variables	Controls Mean±S D (n=30)	CKD on Dialysis Mean±S D (n=40)	t value	P value	Significa nce
Fall in SBP immediat ely after standing	5.2±1.54	10.3±8.5 64	3.217 3	0.002	HS
Rise in DBP on sustained handgrip	17.27±1. 92	9.8±5.76 1	6.813 2	<0.00 01	VHS

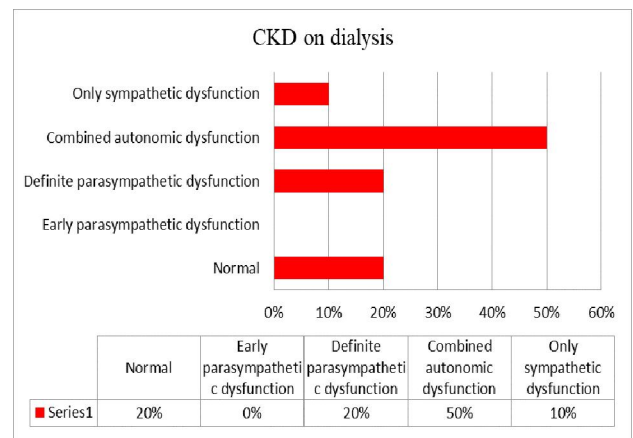
The above table shows that the difference in fall in SBP immediately after standing and rise in DBP on sustained handgrip is statistically significant between the above two groups.

**Thirty two (80%)** out of forty patients of CKD on dialysis had one or more abnormal autonomic function tests.



Among the five tests, the two most abnormal tests were the heart rate variation during deep breathing(70%) and the blood pressure response to hand grip exercise(60%).

**Table 4:** Number of patients with different patterns of autonomic dysfunction



8 subjects (20%) had definite parasympathetic dysfunction and **20 subjects (50%)** had combined autonomic dysfunction.

**Discussion:**

**Combined form of autonomic dysfunction** was seen in 50% subjects. Among 80% of patients of CKD on dialysis who had one or more abnormal autonomic function tests, 20% had definite parasympathetic dysfunction, 50% had combined autonomic dysfunction and 10% had only sympathetic dysfunction. Combined form of autonomic dysfunction was observed in 50% of the cases clearly suggesting involvement of both the divisions of autonomic nervous system. This is in concordance with study by Stamboulis E et al,<sup>7</sup> where 62% of chronic hemodialysis patients had combined autonomic dysfunction. These results are also in concordance with studies by Sahin M et al,<sup>8</sup> Sanya EO,<sup>9</sup> Solders G,<sup>10</sup> Heidbreder,<sup>11</sup> Thapa L et al,<sup>12</sup> Vita G et al.<sup>13</sup>

Among the five tests, the two most abnormal tests were the heart rate variation during deep breathing (**70%**) and the blood pressure response to hand grip exercise (**60%**). According to

previous studies parasympathetic dysfunction occurs much earlier than sympathetic dysfunction.<sup>3</sup>In this study 20 out of 24 subjects (**83%**) who had abnormal blood pressure response to sustained hand grip also had one or more abnormal parasympathetic test. So the blood pressure response to sustained hand grip test can alone be used to diagnose the autonomic neuropathy in patients of CRF on HD.

In patients with renal failure on hemodialysis (HD) cardiovascular disease is a major cause of death.<sup>13</sup> Bleyer et al. estimate approximately 42% of death on dialysis is of cardiovascular etiology, of which 22.4% are related to cardiac arrest or arrhythmia.<sup>14</sup> The autonomic nervous system (ANS) controls a variety of fundamental physiological processes in the human body including regulation of breathing, heart rate, blood pressure, temperature, gastrointestinal motility<sup>15</sup>, bladder, and sexual function.

The autonomic and peripheral nervous system dysfunction is a well-known complication of chronic uremia and nearly 70 % of uremic patients fulfill electrodiagnostic criteria for polyneuropathy including autonomic

neuropathy (AN). <sup>4</sup>Cardiac autonomic nervous system dysfunction (CAND) leading to depressed arterial baroreflex sensitivity (BRS) has been associated with an increased risk of ventricular arrhythmias and sudden death in patients with CKD on maintenance hemodialysis (MHD). Autonomic dysregulation, which is common among patients on HD even without diabetes, may contribute to dysrhythmias and an increased risk of sudden death.<sup>4</sup>

Among the five tests, the two most abnormal tests were the heart rate variation during deep breathing and the blood pressure response to handgrip exercise. Sahin M, et al.<sup>17</sup> also found these two tests to be abnormal in his study suggesting that performing only one test instead of all five tests has a high sensitivity and is more practicable in terms of determining autonomic neuropathy.

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