

**A STUDY OF AUTONOMIC FUNCTION TESTS IN PATIENTS WITH CHRONIC SEVERE ANEMIA**

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**ABSTRACT: AIM AND OBJECTIVES OF THE STUDY:** The present study is aimed at detecting the association of autonomic dysfunction occurs in chronic severe anemia. All patients with hemoglobin less than 6 gm % and symptoms referable to anemia for > 6 months duration were included in the study. Patients with cardiac, hepatic, renal disease, leprosy, hypertension, diabetes mellitus and those on sympathomimetic, parasympatholytic, antihypertensive drugs and also patients below the age of 13 year were excluded from the study. Sample size is 50. **RESULTS AND CONCLUSIONS:** A total of fifty patients were included in the study. Among them, 20 (40%) were males and 30(60%) were females with male to female ratio of 1:1.5. majority of the patients were in the age group of 21-30years with mean age of 33 years. Dimorphic anemia was the most frequent type of anemia in 56% of cases: microcytic hypochromic anemia 42% and macrocytic seen only in 2%. Resting tachycardia of more than 100 per min was observed in 62% cases. Most of the cases (86%) had prolonged QTc interval of more than 0.40sec. 44% cases had abnormal valsalva response, 60% had abnormal 30/15 ratio, inspiration and expiration ratio was abnormal in 38% cases, and postural hypotension was observed in 86% cases. Diastolic raise in blood pressure to sustained hand grip was abnormal in 78% cases. Atropine test was abnormal in 26% cases. Two or more autonomic function tests were abnormal in all the cases. All the cases had combined sympathetic and parasympathetic involvement. 42% cases had involvement of afferent limb of parasympathetic reflex arc. The common abnormality found in cases of chronic severe anemia are postural hypotension and abnormal heart rate response to valsalva and standing are due to blunting of carotid body chemoreceptor and baroreceptor indicating of both sympathetic and parasympathetic involvement.

**KEYWORDS:** Chronic severe anemia, Autonomic function tests, Valsalva maneuver, resting tachycardia, postural hypotension.

**INTRODUCTON:** Anaemia is very common world over, and it is one of the major public health problems in India. It is the cause of a lot of morbidity, mortality, poverty, and reduced work capacity in our country. In our hospital, approximately 12 percent of admissions are due to anemia. Anemia is associated with a decrease in red cell mass, hemoglobin and O<sub>2</sub> carrying capacity of blood. It is caused by varying etiologies which include conditions associated with decreased RBC production, excessive RBC destruction and blood loss or at times combination of these.

The decreased oxygen carrying capacity of blood in these patients as expected leads to various organ tissue dysfunctions as a result of hypoxia. This explains the different manifestations and consequences of anaemia. Autonomic nervous system innervates every visceral organ in body. It has a complex neuronal organization in brain, spinal cord and periphery, it is involuntary and

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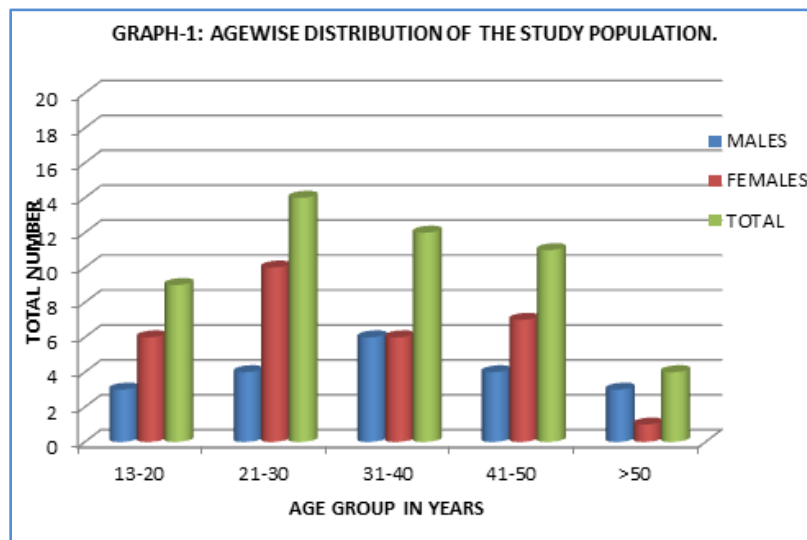
automatic. It is very essential in the vegetative aspects of life. It is of paramount important importance in maintaining life and many of its activities. The effect of chronic severe anemia on autonomic nervous system hasn't yet been studied extensively. This study was undertaken to study the autonomic abnormalities in patient with anemia.

**MATERIALS AND METHODS:** The study was hospital based study, conducted on patients admitted to Vijayanagar institute of medical science, Bellary. A total of 50 patients of chronic severe anemia patients were randomly selected and subjected to autonomic function tests. The cases which were selected are those who had hemoglobin less than 6 gm % and symptoms referable to anaemia for > 6 months duration.

Patients with cardiac, hepatic, renal disease, leprosy, hypertension, diabetes mellitus and those on sympathomimetic, parasympatholytic, antihypertensive drugs and also patients below the age of 13 year were excluded from the study. All patients were subjected to heart rate variation to Valsalva maneuver (valsalva ratio):

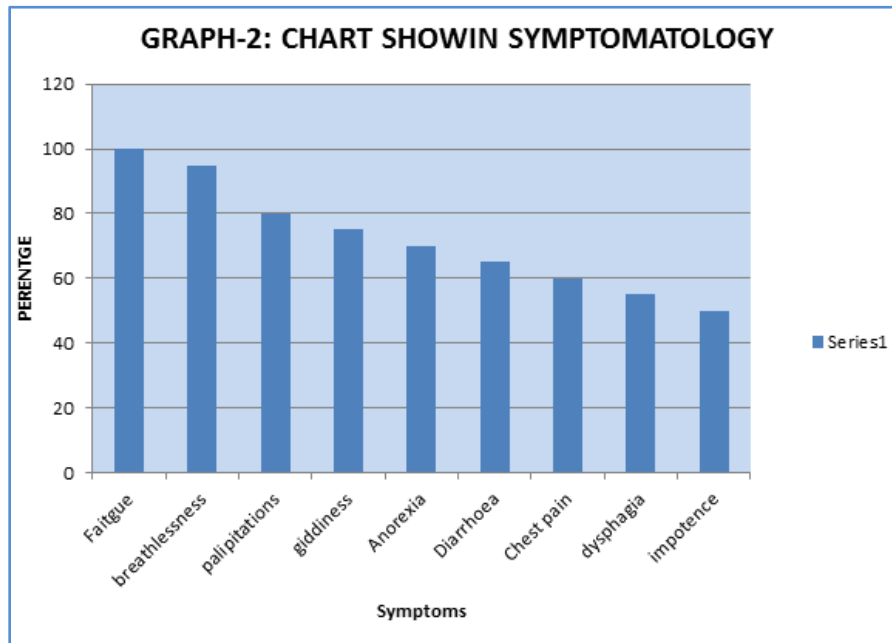
The test was performed by asking the patient to sit quietly and then to blow mercury manometer up to 50 mm of Hg and to maintain mercury Colum at that level by controlled blowing into mouth piece connected to the manometer for 15 sec, continuous ECG is recorded during the procedure and fifteen seconds after the release of pressure. This test was performed 3 times at 1 minute interval. The ratio of longest R-R interval after the maneuver to shortest interval during a maneuver was expressed as valsalva ratio. A valsalva ratio of 1.21 or greater is normal. 1.11 to 1.20 is borderline and 1.10 or less is abnormal.

**RESULTS:** A total of fifty patients were included in the study. Among them, 20 (40%) were males and 30(60%) were females with male to female ratio of 1:1.5. majority of the patients were in the age group of 21-30years with mean age of 33 years (GRAPH-1).

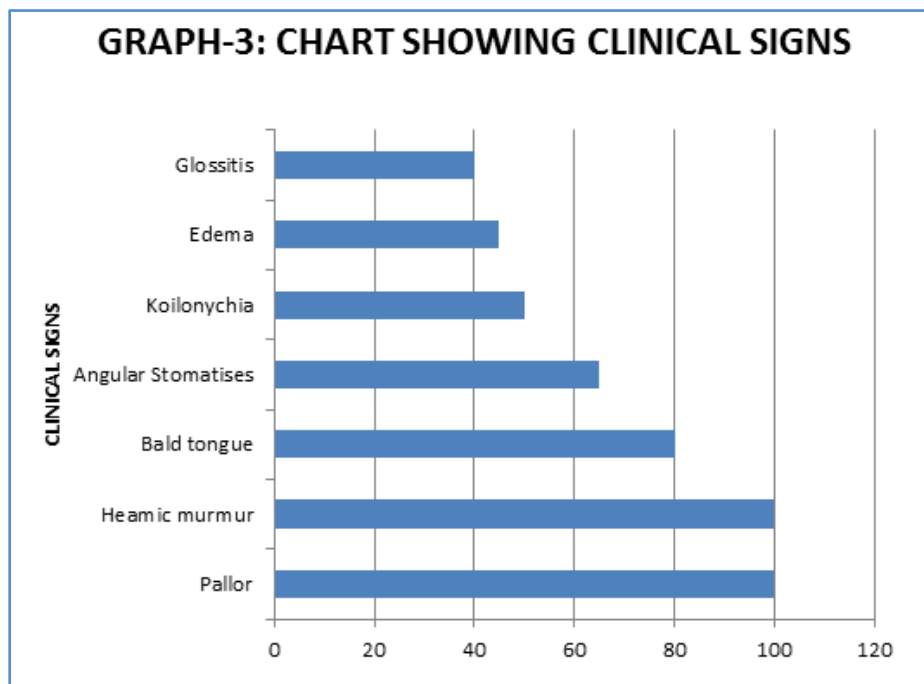


Majority of the patients presented with easy fatigability and breathlessness. Symptoms with which these patients in the present study presented are shown in GRAPH-2.

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The most common clinical signs were pallor and hemic murmur and least frequently occurring signs were edema and glossitis. (GRAPH-3)



Hemoglobin concentration varied from 1.5 gm% to 6 gm% in this study. The mean hemoglobin of chronic severe anaemia in this study was 5gm%. The maximum numbers of cases were in 4.5-6 gm% range. (TABLE-1)

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Hemoglobin	No. of cases			Percentage		
	Male	Females	Total	Males	Females	Total
1.5-3 gm%	5	7	12	10	14	24
3.0-4.5 gm%	6	5	11	12	10	22
4.5-6.0 gm%	9	18	27	18	36	54

**Table 1: Pattern of haemoglobin distribution in the study group**

The most common type was dimorphic anemia in 28 cases and in 1 case it was macrocytic anemia showing megaloblastic change in the bone marrow. In 21 cases it was microcytic hypochromic anemia. In 80% of the cases it was nutritional, chronic blood loss in 16% and Hook worm in 4% of patients. 31 (62%) of the patients had resting heart rate of 100/minute or more and 19 (38%) had less than 100/minute.

QTc interval prolongation was seen in 43 (86%) of cases in this study. In the present study the 30/15 ratio was the most common abnormal parasympathetic test. The tests for parasympathetic affection done were valsalva ratio, inspiration/Expiration ratio, 30/15 ratio and atropine test. (TABLE-2) Parasympathetic system was affected in 2/3<sup>rd</sup> of cases, of these tests 30/15 ratio was the most sensitive test and it was found abnormal in 66% of cases in this study.

Autonomic function test	Normal	Definite	Borderline	Total	Percentage
Valsava ratio	28	09	13	22	44
Inspiration/Expiration ratio	31	08	11	19	38
30/15 ratio	17	26	07	33	66
Atropine test	37	-	-	13	26
Diastolic raise in blood pressure to sustained hand grip exercise	11	21	18	39	78
Systolic fall in BP on standing	07	04	39	43	86

**TABLE 2: AUTONOMIC FUNCTION STUDY OF THE CASES**

The tests indicating sympathetic involvement were; systolic fall of blood pressure on standing and raise in diastolic blood pressure to sustained hand grip exercise. These tests were abnormal in more than 75% of cases in the present study. They were equally sensitive test as per present study. All the 50 cases showed combined involvement of sympathetic and parasympathetic system. Overall abnormality of autonomic function is given in TABLE-3.

No. of abnormal test	No. of cases	Percentage
Nil	0	0
1	0	0
2	8	16
3	22	44
4	11	22
5	3	6
All abnormal	3	6

**TABLE 3: TOTAL NUMBER OF AUTONOMIC FUNCTION ABNORMALITIES IN STUDY POPULATION**

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**DISCUSSION:** In the present study the easy fatigability, dyspnea, giddiness, palpitation and anorexia were most common symptoms. The symptomatology is so diverse that any symptom can occur. The symptoms are related to the severity and to the duration of anaemia. The most common symptom is fatigue, present in 100% of case on the present study. The type of anemia varied from study to study. In the present study dimorphic anaemia was present in 56% of cases where as it almost seen in 54% in the Vijaya Deepak study.<sup>[1]</sup>

The incidence of which was almost similar to the present study. Microcytic hypo chromic anaemia was present in 42% of cases which is comparable to the incidence in the study of Vijaya Deepak<sup>[1]</sup> where it was 46%. Macrocytic anemia was seen in 02% of cases in the present study. The incidence of macrocytic anaemia varied from 0-33.3% in various studies. The incidence in the present study correlated with the study of Vijaya Deepak.<sup>[1]</sup> In the present study resting heart rate of more than 100 per minute was observed in 62% of cases, 38% of cases shows heart rate of less than 100/minute.

Usually resting tachycardia is an indicator of autonomic neuropathy, however it is a poor guide for present or absence of autonomic dysfunction especially so in anemic individuals. The Prolonged QTc interval of more Than 0.40 Sec was seen in 86%. The QTc prolongation is an indicator of autonomic neuropathy and may also be due to myocardial ischemia in anaemia subjects. Other studies have not mentioned the resting heart rate and QTc interval. In the present study all the cases had involvement of autonomic nervous system. All of them had two or more abnormal autonomic function tests. All the cases showed involvement of both sympathetic and Para sympathetic nervous system. Usually involvement of both sympathetic & parasympathetic system is observed in autonomic neuropathies as in chronic alcoholism, diabetes and leprosy.

The present study suggests that is the case even in chronic severe anemia (CSA) related autonomic neuropathy. This is because degeneration occurs in both vagus and splanchnic nerves.<sup>[2]</sup> The result of the present study suggests that autonomic dysfunction occurs in case of chronic severe anaemia. Similar observation was made in the study done by Nand.<sup>[3]</sup> In another similar study done by Vijaya Deepak and others In JJM College, Davanagere also suggested involvement of autonomic dysfunction in cases of chronic severe anaemia. The comparison of autonomic function abnormalities of our study to various studies are given in TABLE-4.

Sl. No.	Contents	Present Study %	Nand, Khosla <sup>[3]</sup> %	Vijaya Deepak <sup>[1]</sup> %
1	Valsalva ratio	44	50	40
2	Inspiration expiration Ratio	38	30	30
3	30/15 ratio	66	60	50
4	Systolic fall in blood Pressure to sustained hand exercise	78	—	—
5	Atropine ratio	26	26.6	20
6	All the above autonomic function tests abnormal	06	16.6	10
7	One or more tests abnormal	100	100.0	92
8	Two or more autonomic function tests abnormal	100	--	--

**TABLE 4: COMPARATIVE STUIES**

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Chronic hypoxemia in anemia makes the baroreceptors insensitive and blunts its functioning. This could be the cause for postural hypotension in anemia. This blunting of baroreceptor leading to postural hypotension is reported in other disease also. There are reports in the literature of the effect of chronic tissue hypoxia on cardiovascular reflexes or autonomic functions in human being. In one study an attempt was made to determine the importance of carotid body chemoreceptors in control of cardiovascular response to acute hypoxia.

It is concluded that carotid bodies were essential for normal response during hypoxia.<sup>[4]</sup> In cases of chronic severe anaemia there is decrease in oxygen carrying capacity of blood, leading to chronic tissue hypoxia which at times can cause irreversible damage to tissues. The observation made in the present study suggests the involvement of afferent limb of parasympathetic reflex arc which consists of carotid body chemoreceptors, tenth cranial nerve and cardiovascular receptors in medulla.

Abnormal heart rate response to standing and Valsalva maneuver may be partly due to involvement of carotid body chemoreceptors which might have been blunted like baroreceptors. Although the exact nature of various factors responsible for blunting or insensitivity of carotid body baroreceptor and chemo receptor is a matter of speculation. Thus the common abnormality found in cases of chronic severe anaemia are postural hypotension and abnormal heart rate response to Valsalva and standing are due to blunting of carotid body chemoreceptor and baroreceptor indicating of both sympathetic and parasympathetic involvement.

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