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RESEARCH ARTICLE

AN ECHOCARDIOGRAPHIC STUDY OF LEFT VENTRICULAR FUNCTION DISTURBANCES IN CHRONIC SEVERE ANEMIA

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ABSTRACT

Background and Objectives: Anemia is a serious health problem in India. Anemia which is often untreated or inadequately treated is emerging as a potential contributor to the development and progression of cardiovascular disease. Hence the present study was undertaken to find out LV function changes in severely anemic patients by Echocardiography.

Methodology: Present study was conducted in Al-Ameen Medical College and Government district Hospital, Bijapur. 31 anemic patients (aged 18-40 yrs) and equal number of age and gender matched non anemic healthy individuals were volunteers. All anemic patients and controls were subjected for hemoglobin estimation and M mode 2D Echocardiography. Echocardiographic parameters- IVSTd, LVIDd, LVPWd, IVSTs, LVIDs, LVPWS, EDV, ESV, SV, CO, EF, FS were studied. Statistical analysis was done by Student's unpaired't' test.

Results: Statistically significant variations were found in parameters- Wt, BSA, BMI, PR, DBP, LVIDd, LVIDs, EDV, ESV, SV, CO, EF, FS in anemic patients compared to controls. Ht, SBP, IVSTd, LVPWd, IVSTs, LVPWs showed no variation.

Interpretation and Conclusion: The findings of increased LVIDd, LVIDs, EDV, ESV, SV, CO and decreased EF, FS, in anemic patients compared to controls may be as a consequence of hyperdynamic circulatory state leading to vascular and cardiac changes. These changes are mainly due to increased preload, decreased afterload, changes in cardiac geometry. These factors increases systolic wall stress resulting in eccentric LV hypertrophy and over time leads to LV systolic dysfunction.

INTRODUCTION

Anemia is very common in India especially in low socioeconomic group and is a serious health problem. It affects an estimated 50% of the population. Anemia which is often untreated or inadequately treated is emerging as a potentially common contributor to the development and progression of cardio vascular disease (CVD). (NAAC 2008) Extreme alterations in blood count as in anemia are known to cause circulatory changes and if these alterations persist, there occurs adaptations of cardiac geometry (Stritzke *et al.*, 2007). Anemia has a negative impact on physical work capacity in different age groups. Most of the cardiac dysfunction is due to abnormalities of left heart. Anemia significantly alters circulatory dynamics and so burdens circulatory system. The LV internal dimensions in systole and diastole, end systolic and end diastolic volume, and other performance indices are deranged in all anemic patients. Studies conducted to assess LV function by non invasive techniques show LV dysfunction in chronic severe anemia. Considerable impairment of LV function can occur before clinically recognizable congestive heart failure sets in. Hemodynamic changes brought about by this condition have consequences that could both predispose and aggravate existing cardiac disease. (NAAC 2008) Thus anemia represents an important treatable cause of cardiac morbidity and mortality. Echocardiography is a valuable non invasive diagnostic test for assessment of the cardiovascular system. Only few studies have assessed the left ventricular function by non invasive techniques. Hence this study is undertaken to assess the status of left ventricular function for detection of cardiac functional impairment, at an early stage by echocardiographic parameters.

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MATERIALS AND METHODS

The present study was conducted in the department of physiology Al-Ameen Medical College, Bijapur. Thirty one (31) patients (20 females, 11 males) with severe anemia (Hb ≤ 7gm%), between 18yrs to 40 yrs age visiting Al-Ameen medical college hospital, Bijapur and District Hospital Bijapur were selected. Equal number of age and gender matched individuals from Bijapur city were controls. Patients presenting with acute blood loss, pregnancy, hypertension, any underlying heart disease, COPD, patients with hyperdynamic circulatory

states like hyperthyroidism, beriberi, AV fistulas were excluded from the study. All anemic patients and controls underwent history taking and a thorough clinical examination. Their hemoglobin levels were estimated and were subjected for M mode two dimensional Echocardiography. Transthoracic Echocardiography was done using PHILIPS Envisor C (model no MCMD02AA) diagnostic Ultrasound System using 3.5 MHz transducer, probe (PA 4- 2) by physician experienced in Echocardiography. Measurements of the LV cavity dimension and wall thickness are derived from M-mode recordings and are made according to the recommendations of the American Society of Echocardiography (ASE) at end diastole and end systole. (Ronal *et al.,* 2001) Echocardiographic parameters studied were: Interventricular septum thickness at end diastole and end systole (IVSTd and IVSTs respectively), Left ventricular inner dimension at end diastole and end systole (LVIDd and LVIDs respectively), Posterior wall thickness at end diastole and end systole (LVPWd and LVPWs respectively). 2D echocardiography is significantly superior to M-mode approaches for the measurement of cardiac chamber volumes and EF. End diastolic volume (EDV), End systolic volume (ESV), Stroke Volume (SV) were obtained. Derived parameters of Systolic function includes: Left Ventricular Ejection Fraction (LVEF), Fractional Shortening (FS). Cardiac output (CO) was calculated as CO = HR x SV. Statistical analysis was done using student's unpaired 't' test (using Graph pad Prism 5 statistical software) to analyze the changes between the control group and anemic patients. A 'p' value <0.05 was considered statistically significant.

RESULTS

Thirty one patients with severe anemia having hemoglobin concentration less than 7 gm/dl, between 18 and 40 yrs of age were selected for this study. Equal number of non anemic healthy individuals, matched for age and gender were the controls.

A. Physical parameters

Table No. 1 shows the mean ± SEM of age, Ht, Wt, BSA, BMI in anemic patients and controls. The mean value of height was numerically more in controls which was not statistically significant; (t=1.07, $p > 0.05$). The mean weight of anemic patients was found to be less than that of controls, with a statistically significant difference; (t = 4.277, $p < 0.0001$). The mean value of BSA and BMI of anemic patients was more as compared to that of controls. There was a statistically significant difference; (t = 3.451, $p < 0.01$) & (t = 4.46, $p < 0.0001$) respectively.

B. Physiological parameters

Table No. 2 Shows the mean ± SEM of Hb, PR, SBP, DBP in anemic patients and controls. The mean value of pulse rate of anemic patients was higher as compared to that of controls with a statistically significant difference; (t = 7.01, $p < 0.0001$). There was no statistically significant difference between the mean of SBP levels of anemic patients and controls; (t = 1.936, $p > 0.05$). The mean DBP level in anemic patients was lower as compared to the controls with a statistically significant difference; (t = 4.585, $p < 0.0001$). The mean ± SEM of hemoglobin in anemic patients was 4.958 ± 0.22 gm/dl; in controls 13.46 ± 0.13 gm/dl.

Table 1. Shows the mean ± SEM of Age, Ht, Wt, BSA, BMI in anemic patients and controls

Parameter	Anemic Patients (n = 31) Mean±Sem	Controls (n = 31) Mean±Sem	p value
AGE (yrs)	31.8 ± 1.33	30.3 ± 1.04	p > 0.05
Ht (cms)	155.1 ± 1.61	157.03 ± 0.83	p > 0.05
Wt (kgs)	45.94 ± 1.04	52.9 ± 1.25	p < 0.0001***
BSA (m^2)	1.014 ± 0.02	1.084 ± 0.01	p < 0.01**
BMI (kg/m^2)	19.15 ± 0.28	21.45 ± 0.44	p < 0.0001***

Table 2. Shows the mean ± SEM of Hb, PR, SBP, DBP in anemic patients and controls

Parameter	Anemic Patients (n = 31) Mean±Sem	Controls (n = 31) Mean±Sem	p value
Hb (gm/dl)	4.958 ± 0.22	13.46 ± 0.13	p < 0.0001***
PR (beats/min)	88.06 ± 1.08	78.83 ± 0.74	p < 0.0001***
SBP (mmHg)	109.29 ± 1.39	112.96 ± 1.28	p > 0.05
DBP (mmHg)	66.58 ± 1.38	74.64 ± 1.09	p < 0.0001***

Table 3. Shows the mean ± SEM of Echocardiographic parameters in anemic patients and controls

Parameter	Anemic Patients (n = 31) Mean±Sem	Controls (n = 31) Mean±Sem	p value
IVSTd (cms)	0.66 ± 0.01	0.635 ± 0.01	p > 0.05
LVIDd (cms)	4.76 ± 0.09	4.22 ± 0.06	p < 0.0001***
LVPWd (cms)	0.691 ± 0.01	0.66 ± 0.01	p > 0.05
IVSTs (cms)	0.981 ± 0.02	0.942 ± 0.01	p > 0.05
LVIDs (cms)	3.46 ± 0.012	2.86 ± 0.06	p < 0.0001***
LVPWs (cms)	1.015 ± 0.01	1.00 ± 0.01	p > 0.05
EDV (ml)	112.3 ± 5.98	75.9 ± 3.33	p < 0.0001***
ESV (ml)	46.92 ± 3.73	24.8 ± 1.65	p < 0.0001***
SV (ml)	65.25 ± 2.82	50.93 ± 1.88	p < 0.0001***
CO (Lts/ min)	5.8 ± 0.276	4.01 ± 0.16	p < 0.0001***
EF (%)	59.47 ± 1.25	67.48 ± 0.89	p < 0.0001***
FS(%)	27.93 ± 1.03	32.3 ± 0.82	p < 0.01**

C. Echocardiographic parameters

Table No. 3 Shows the mean ± SEM of Echocardiographic parameters in anemic patients and controls. The mean value of IVSTd was numerically more in anemic patients as compared to the controls with a statistically significant difference; (t = 1.692, $p > 0.05$). The mean value of LVIDd in anemic patients was 0.54 cms more as compared to that of controls. This difference was found to be highly statistically significant; (t = 5.064, $p < 0.0001$). The mean value of LVPWd was found to be numerically more in anemic patients as compared to that in controls with no statistically significant; (t = 1.886, $p > 0.05$). No statistically significant difference was found for means of IVSTs; (t = 1.889, $p > 0.05$). The mean of LVIDs in anemic patients was 0.6 cms more than that of controls. This difference was found to be statistically significant; (t = 4.85, $p < 0.0001$). No statistically significant difference was found for means of LVPWs (t = 1.002, $p > 0.05$). In anemic patients the mean value of EDV was more when compared with that of controls by 36.4ml. This difference was highly statistically significant; (t = 5.328, $p < 0.0001$). The mean of ESV in

anemic patients was more when compared with that of controls with a statistically significant difference; (t=5.413, p < 0.0001). In anemic patients the mean of SV and CO was higher as compared to that of controls. This difference was found to be statistically highly significant; (t=4.22, p < 0.0001) and (t=5.55, p < 0.0001) respectively. In anemic patients the mean value of EF and FS were lower when compared with that of controls. This difference was statistically significant; (t=5.201, p < 0.0001) and (t = 3.33, p < 0.01) respectively. Statistically significant variations were found in the mean value of parameters viz- LVIDd, LVIDs, EDV, ESV, SV, CO, EF, FS in anemic patients as compared to controls.

DISCUSSION

In the present study the means of Wt, BSA, and BMI of anemic patients were found to be lower than that of controls with a statistically significant difference (p < 0.05). This difference is probably due to poor nutritional status of anemic patients. It was found that the pulse rate was significantly faster in anemic patients when compared with controls (Bahl *et al*., 1992). Singh K, and Singh PI, conducted a study and observed that there was an elevation of heart rate in anemics. (Singh K and Singh PI 1994) Our finding of an elevated pulse rate in anemic patients suggest the possibility of increased activity of sympathetic part of autonomic nervous system due to reduced oxygen delivery to the tissues. (Singh K and Singh PI 1994; Aessopos *et al.*, 2004) There was no significant difference in the mean ± SD of SBP of 31 chronic severe anemia patients and controls. (Bahl *et al*., 1992) The systolic blood pressure did not differ significantly between patients with sickle β thalassemia and healthy controls (Moyssakis *et al.*, 2005). Our findings are similar to other studies. In 41 elderly patients with chronic severe anemia, DBP were lower in the patient group when compared with controls (Athanasios *et al*. 2004). DBP in anemic patients was 68 ± 10 mmHg and 82 ± 5 mmHg in controls, this difference was significantly lower in the patients compared with the normal subjects (Bahl *et al*, 1992). Our results are consistent with other studies. The lower DBP levels in anemic patients in our study may be due to decrease in the systemic vascular resistance. Inadequate tissue oxygenation resulting from anemia appears to be the initial trigger for a number of specific hemodynamic adjustments. This leads to systemic arterial vasodilatation and reduced vascular resistance (NAAC 2008).

In a study, LVIDd in controls was 4.4 ± 0.39 cms and in anemic patients with and without tachycardia, 4.8 ± 0.56 cms and 4.63 ± 0.36 cms respectively. The study showed that LV internal dimensions in diastole are deranged in all anemic patients (Panwar *et al*., 1991). In 2004, Ahmed *et al.* determined the echocardiographic abnormalities in patients with sickle cell disease (SCD). Their findings included dilated atrium in 14 (37%), dilated ventricle in 5 (13%), ventricle hypertrophy in 5 (13%), and ventricle dysfunction in 3 (9%) patients. (Ahmed *et al*., 2004) The findings of our study are in agreement with other studies. In chronic severe anemia the LV preload is significantly higher and after load is lower due to reduced systemic vascular resistance. The decreased after load may be due to peripheral vasodilatation related to anemia. (Hayashi *et al*., 1999) With decreased afterload, the venous return (preload) and left ventricular filling increase, leading to increased LV end-diastolic fiber length. Our finding of an increased LVIDd can be attributed towards the role of Frank Starling mechanism in the hyper dynamic state of chronic anemia. Our finding of an increased LVIDs is also in accordance with other studies mentioned above. It may be due to the result of increased volume overload which in the long term causes hemodynamic alterations leading to gradual development of cardiac enlargement and LV hypertrophy. This LVH is eccentric, characterized by increased LV internal dimensions (Metivier *et al*., 2000).

Panwar *et al*. (1991), observed that EDV index in anemic patients was more than controls. Panwar *et al*. (1991) EDV index in anemic patients was significantly lower as compared to controls and after Iron therapy the values were similar to that of controls (Riku Hayashi *et al*., 1999). Our finding of an increased EDV in anemic patients may be attributed towards hyperdynamic state in chronic anemia. As the preload increases the left ventricular filling increases leading to increased LV end-diastolic volume in order to maintain a high stroke work. (Metivier *et al*., 2000) The ESVi in thalassemia patients was 36.9±10.8ml/m^2 and in controls 28.15±2.6 ml/m^2 with a statistical significance (Bosi *et al*. in 2003). The finding of an increased ESV in anemic patients in our study may be due to early feature of onset of impaired LV function in these patients. Chronic anemia is known to cause systolic dysfunction especially when the hemoglobin concentration falls below 6 gm/dl. Changes in hemodynamic parameters were observed before and after treatment in 14 subjects with IDA. These results were compared with those of normal subjects. In the anemic patients, LV stroke volume (SV) increased, which was accompanied by an increase in LV preload (Takahashi *et al*., 1990). The increased SV in anemic patients may be attributed towards hyperdynamic state in chronic anemia which causes an increased LV preload and reduced after load. (Hayashi *et al*., 1999) The increase in SV is associated with increase in LVIDd in our study. It may be due to the Frank Starling mechanism that operates in the hyper dynamic state of chronic anemia.

In patients with severe anemia (Hb 5.7 ± 0.6 g/dl), cardiac index was higher (4.8 ± 0.4 L/min/m^2 < 0.01) compared with the other group (Hb 9.8 +/- 1.7 g/dl; CI 3.9 ± 1.1 L/min/m^2). It was found that the increase of cardiac index caused by anemia correlated with increased stroke volume and heart rate and lowered pulmonary and peripheral resistance (Schafer *et al*., in 2002). Higher cardiac index is observed in anemic patients when compared to controls. (Bahl *et al*., 1992; Moyssakis *et al*., 2005) It was found that the cardiac index decreased in patients with IDA after therapy when compared with before therapy. (Hayashi *et al*., 1999) Our finding of an increased CO in anemic patients is in agreement with other studies mentioned above. The increased CO in anemic patients is probably due to reduced oxygen supply to the tissues found in chronic anemia that causes hemodynamic mechanisms to operate to compensate for anemia. Increased CO is the main hemodynamic factor mediated by lower afterload, increased preload and positive chronotropic effects. (Bosi *et al*., 2003) In the present study probably the increased heart rate and stroke index overcame the significant decrease in LV contractility and

resulted in an increased cardiac output. EF and FS of anemic patients was found to be significantly lower in severe anemia patients when compared with that of controls. (Bahl *et al*., 1992; Panwar *et al*., 1991; Mara Ferrara *et al*., 2004) Our finding of lower EF and FS in anemic patients is similar to that of other studies. The EF and FS which are considered to be indices of systolic function being lower in anemic patients may indicate that the systolic function in these patients is slightly compromised.

Conclusion

Our findings of increased LVIDd, LVIDs, EDV, ESV, SV, CO, and decreased EF, FS in anemic patients are as a consequence of hyperdynamic circulatory state leading to vascular and cardiac changes which are mainly due to increased preload, decreased afterload, positive chronotropic effects, and changes in cardiac geometry. These changes may be attributed to ventricular remodeling that occurs following sustained hemodynamic overloading of the heart which may be due to volume overload. Chronic anemia causes a long lasting volume overload which results in ventricular dilatation. The increased preload conditions found in anemic patients may be attributed to the Frank Starling mechanism that is operating in hyperdynamic state of chronic anemia. The stress of volume overload over prolonged period weakens the left ventricle and leads to LV systolic dysfunction as indicated by altered echocardiographic parameters in our study.

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