Prevalence Of Cardiac Changes and Its Co-Relation with The Haemoglobin Level in Iron Deficiency Anaemia.

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Abstract
Aim: To study the cardiac profile in patients with iron deficiency anaemia and to evaluate in detail the electrocardiography and echocardiographic abnormalities in patients with iron deficiency anaemia.
Methods: All diagnosed cases of iron deficiency anaemia underwent electrocardiography and 2D-echocardiography studies, and statistical analysis was performed.
Results: A total of 150 patients with iron deficiency anaemia were enrolled in which females were 100 with a mean age of 36.17 ± 10.32 and males were 50 with a mean age of 36.8 ± 14.8 Out of all cases which turned out to be positive for electrocardiography showing ST-segment changes, majority had ST-segment depression. In t wave morphology changes, majority showed inversion. Among 50 cases of severe anaemia, 48 had echocardiography findings suggestive of enlarged cardiac chambers whereas only 58 cases out of 100 in moderate anaemia category showed similar findings. There was statistically significant association with severity of iron deficiency anaemia with abnormality in echocardiography parameters like left Ventricular mass, left ventricular internal dimension-systole, left ventricular internal dimension-diastole, right ventricular internal dimension-systole with significant 2 tailed Pearson Correlation coefficient p<0.01
Conclusion: Our study found that majority of the patients with iron deficiency anaemia is having electrocardiographic and echocardiographic changes. Cardiovascular complications of anaemia can be easily diagnosed with these investigations which ultimately help in making necessary plan for appropriate treatment.

Keywords: Anaemia, Electrocardiography, Echocardiography, heart failure.

Introduction

Anaemia and iron deficiency are important and common comorbidities that often coexist in patients with heart failure. Both conditions, together or independently, are associated with poor clinical status and worse outcomes. The prevalence of anaemia in patients with heart failure (defined as haemoglobin <13 g/dL in men and <12 g/dL in women) [1] is ≈30% in stable and ≈50% in hospitalized patients, regardless of whether patients have heart failure or ejection fraction or heart failure with preserved ejection fraction, compared with <10% in the general population (although prevalence increases with age, exceeding 20% in subjects ≥85 years old) [2-5]

Heart failure subjects shows resistance to erythropoietin in iron anaemia. [6]. Endothelial cells, smooth muscle cells and cardio-myocytes possess erythropoietin receptor and preclinical studies have established erythropoietin to be a pleiotropic cytokine with anti-apoptotic activity and tissue-protective actions in the cardiovascular system, We also have substantial evidence stating that erythropoietin therapy is safe and effective in reducing left ventricular hypertrophy, enhancing exercise performance and increasing ejection fraction in heart failure patients with anaemia. Most of the available literature have studied the effects of chronic anaemia of any aetiology on the cardiac function and have use M mode parameters for the same[7, 8].

The pathogenesis of heart failure involves cascade of inflammatory mechanisms, where there is increase in tumor necrosis factor-α, interleukin-6 and several other pro-inflammatory cytokines[6, 9] and C-reactive protein[10] and inversely related to haemoglobin level[11]. Opasich and colleagues[6] identified a specific cause of anaemia in only 43% of 148 patients with stable heart failure. Iron deficiency anaemia was seen in only 5% of patients. In the remaining 57% of patients, pro-inflammatory cytokine activation, inadequate erythropoietin production, or defective iron utilization was found despite adequate iron stores, indicative of anaemia of chronic disease. Therefore, an activated pro-inflammatory state and anaemia of chronic disease[12] could be the most frequent underlying cause of anaemia in heart failure. The association of haemoglobin level with mortality is not linear, and most of the increased risk occurs at low haemoglobin[13, 14]. Some studies have reported a J-shaped relationship between haemoglobin and mortality in the normal population[15] and patients with coronary artery disease[16], acute coronary syndromes[17], and heart failure[14, 18]. The lowest mortality risk was observed in the haemoglobin range of 13-16 g/dL, and the risk increased with haemoglobin concentrations below or above this range. There is a lack of sufficient data regarding left ventricular mass cavity dilation/ejection fraction, wall thickness and volume in iron deficiency anaemia. Hence, the aim of this study was to focus on these parameters based on clinical and echocardiographic findings in iron deficiency anaemia for early detection of heart failure.

Methodology

A total of 150 patients with iron deficiency anaemia, satisfying the inclusion criteria were recruited for the study. The study was conducted after taking a written and signed informed consent from the patients and it was being approved by the institutional ethical committee.

Inclusion criteria

1. Patients above the age of 18 years
2. Patients with moderate (Hb= 7-9.9) and severe (Hb<7) iron deficiency anaemia.

Exclusion criteria

1. Patients of chronic renal failure, chronic liver disease, anaemia in pregnancy, dimorphic anaemia and other cardiac diseases like ischemic heart disease, rheumatic heart disease.
2. Anaemia due to any other pathophysiology other than iron deficiency.

Complete blood picture, peripheral smear study, RBC indices (MCV, MCH, MCHC), serum iron (cut off values in microgram/dl–37.0 for females, 49.0 for males), serum ferritin (cut off values in ng/ml–6.24 for females <50yrs, 11.1 for females >50yrs, 17.9 for males) serum transferrin (cut off value in microgram/dl - >400) levels were done for all the patients. Electrocardiography (ST-segment, T-wave changes) and echocardiography (LVIDs, LVIDd, RVIDs, RVIDd, LV mass, LA(d)) was then performed to correlate with severity of iron deficiency anaemia.

Frequency tables and measures of central tendency (mean) and measures of dispersion (Standard Deviation) were calculated. Correlation was assessed using the chi-square test for comparing mean of different group independent sample t-test and ANOVA were applied. Karl Pearson correlation coefficient was calculated for measuring linear relationship between Hb level and other echocardiograhy variables (LVIDs, LVIDd, RVIDs, RVIDd, LV mass, LA(d)). P<0.05 was considered as significant.

Results

A total of 150 patients with iron deficiency anaemia were enrolled in which females were 100 with a mean age of 36.17 ± 10.32 and males were 50 with a mean age of 36.8 ± 14.8. Majority of cases had moderate anaemia that is haemoglobin between 7.0- 9.9 gm/dl. (66.6%) and rest had severe anaemia that is haemoglobin below 7.0 gm/dl (33.3%).

Severe anaemia was predominantly associated with ECG changes, with a significant association between severity of haemoglobin levels and ECG abnormalities. Similarly, out of all cases which turned out to be positive for ECG showing ST-segment changes, majority had ST-segment depression in their ECG. In t wave morphology changes, t wave inversion was the commonest finding.

Among the 50 cases of severe anaemia, 48 cases had ECHO findings suggestive of enlarged cardiac chambers whereas only 58 cases out of 100 in moderate anaemia category showed similar findings. There was statistically significant association with severity of iron deficiency anaemia with abnormality in ECHO parameters like LVIDs, LVIDd, RVIDs, RVIDd, LV mass, LA(d), with significant 2 tailed Pearson Correlation coefficient p<0.01

Figure 1: Association between sex and age group.

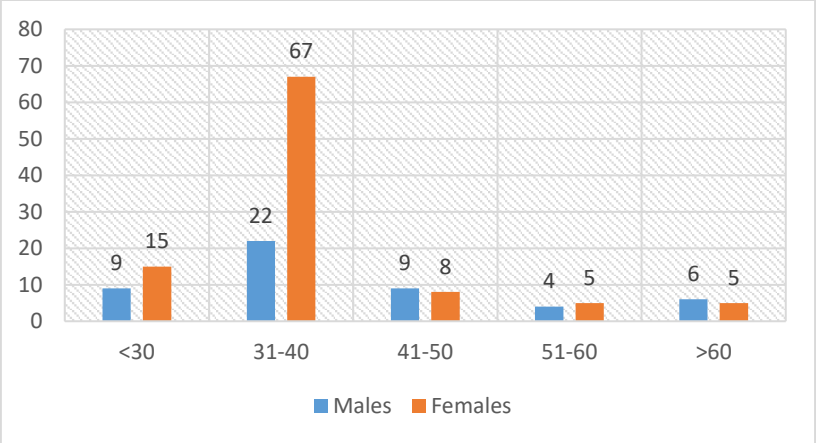

Figure 2: Association between anaemia and ECG changes.

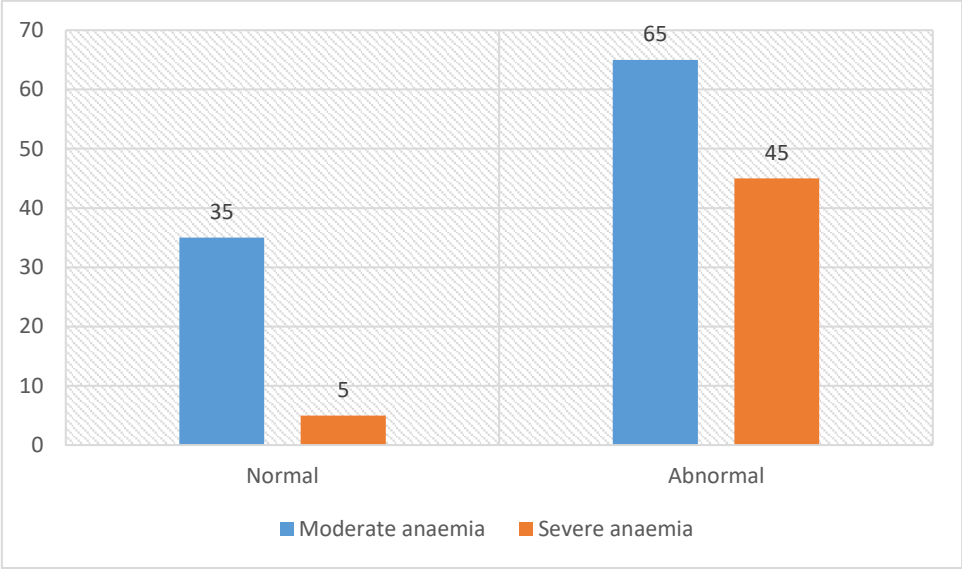

Figure 3: Association between HB and ST-segment.

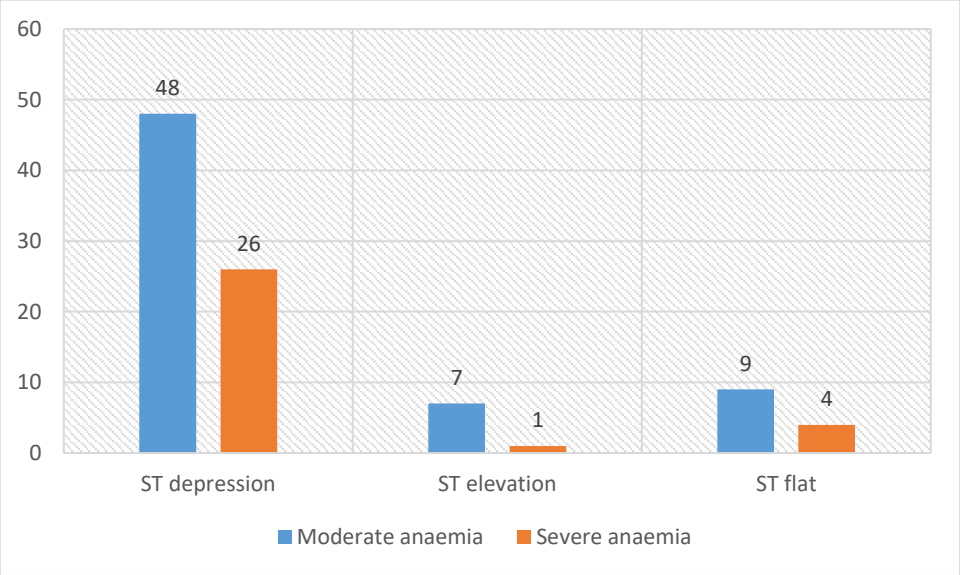

Table 1: Correlation table for haemoglobin and different studied variables.

Variables	Statistical analysis	Values
Age	Pearson Correlation	-0.341**
	Sig. (2-tailed)	0.003
	N	150
Heart rate	Pearson Correlation	-0.512**
	Sig. (2-tailed)	0.001
	N	150
LVIDs	Pearson Correlation	-0.887**
	Sig. (2-tailed)	0.001
	N	150
LVIDd	Pearson Correlation	-0.761**
	Sig. (2-tailed)	0.001
	N	150
RVIDd	Pearson Correlation	-0.678**
	Sig. (2-tailed)	0.001
	N	150
LV Mass	Pearson Correlation	-0.691**
	Sig. (2-tailed)	0.001
	N	150
LA	Pearson Correlation	-0.769**
	Sig. (2-tailed)	0.001
	N	150

Discussion

Females are predominantly involved in iron deficiency anaemia. Blood loss due to menstruation, poor intake, mal-absorption, and pregnancy related factors are the widely distributed factors for the same[19]. Severe anaemia causes inadequate oxygen delivery to tissues, which in the heart could cause myocyte dysfunction. Additional disease- specific factors may also contribute, including microinfarctions due to coronary vascular disease, and reduced myocyte iron stores in iron- deficiency anaemia[20].

Electrocardiography (ECG) and 2D Echocardiography (ECHO) were utilized to study the cardiovascular system. In our study, we correlated haemoglobin levels with ECG changes pertaining to ST-T segment, T wave and QT interval and volume overload changes by 2D Echocardiography. Changes seen in our study were ST segment depression and T wave flattening and inversion. Earlier studies have reported decreased QRS amplitude, T-wave flattening and minor degrees of atrioventricular conduction disturbances[21]. Many studies have reported changes in ECG like ST segment depression, flat or inverted T waves, but without corresponding changes in QRS complex[22, 23]. The total prevalence of electrocardiographic changes in 150 patients was 76%, which was similar to high incidence of electrocardiographic changes of 62% in 183 patients reported by Mohit Khatri et al[24].

In patients with moderate anaemia, ST segment depression was seen in (47) 49.4%, ST elevation was seen in 6(6.3%) and 8(8.4%) who had flat ST segment. T wave inversion was seen in 31(32.6%) and there was only 1 patient with tall T wave and 2 had flat T wave.

In patients with severe anaemia, 10 (52.6%) had ST depression and only 1 had ST elevation and 2(10%) had flat ST segment. T wave inversion was seen in 6(31.5%).Similar findings were observed Neha H. Pandya et al [25]. In ST segment changes were present in Lead I, II, III, avF, V4 -V6 and T wave changes were present in Lead V4 - V6. They also found 17 cases which had ST segment changes and the association of anaemia with ST segment changes was significant and further 8 cases having T wave abnormality which was found to be significant[25]. One additional ECG change we noted in our study was Left Ventricular Hypertrophy (LVH)

that indicates cardiac enlargement. Patients with severe anaemia shows cardiac enlargement without other aetiologies and the severity was directly proportional to the haemoglobin level[26] In anaemia there is a need to improve the oxygen delivery, for which the cardiac output should increase. Hence we observed an increased heart rate and stroke volume in anaemic patients. To accommodate this greater output, there is an increase in LV chamber size, both systolic and diastolic[27].

The LVIDs in anaemic patients were significantly higher compared to non-anaemic population. Left ventricular end systolic volume and systolic radius/thickness ratio was also significantly increased in anaemia [28, 29]. Compared to non-anaemic population, the anaemic patients had significant increase in LVIDd. These findings reflect the changes in end diastolic volume in severe anaemia and are suggestive of a chronic volume overload state, a known feature of chronic severe anaemia. The RVIDs and RVIDd was also increased in severe anaemic patients. The septal thickness in systole and diastole did not show any significant changes. This represents the increase in preload, which is seen in chronic severe anaemia. This finding suggests a role for the Frank Starling mechanism in the hyperdynamic state of chronic anaemia[30].

The LV mass is significantly increased in patients with severe anaemia ($P<0.001$). The mean LV mass was 241.54 gm ± 11.23 in cases of severe anaemia and 172.17 gm ± 38.98 in cases of moderate anaemia indicating hypertrophy. Trivedi et al[31] studied left ventricular mass in normal Indian population and found that the left ventricular mass in men was found to be 124 ± 32gm in males whereas in women it was 93 ± 37 gm.

The percentage of fractional shortening and ejection fraction did not show significant differences. This finding in conjunction with increased end diastolic volume suggests that Starlings forces play an important role in the compensatory mechanisms seen in chronic severe anaemia[32]. In patients with chronic severe anaemia the increased preload and a decreased afterload (decreased blood pressure, hyperkinetic circulatory state) are the basic compensatory mechanisms. Due to these changes, the indices of left ventricular function are set at a higher level in the compensated state. Decompensation, therefore, probably occurs at a higher level of these indices as compared to normal individuals.

In our study, multiple linear regression analysis between haemoglobin levels and various ECHO parameters studied showed that with every 1gm% fall in haemoglobin the LV mass increased by 12.97 and chances of this occurring was 53.47% which is statistically significant. Similarly, LVIDs, LVIDd, RVIDs, RVIDd and LA(d) increased by 0.197, 0.269, 0.150, 0.156, 0.274 respectively.

Conclusions

ECG and ECHO can be used to diagnose cardiovascular complications of iron deficiency anaemia. Severe anaemia is associated with increase in left ventricular mass, left ventricular internal dimension- systole, left ventricular internal dimension-diastole, right ventricular internal dimension-systole, right ventricular internal dimension-diastole. Each 1g/dl decrease in haemoglobin was associated with 8% increase in risk of LV hypertrophy. Assessing cardiovascular complications in iron deficiency anaemia helps in timely and proper diagnosis and treatment planning.

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