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Assessment of echocardiographic variables in severe anemic patients

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ABSTRACT

Background: Detection of left ventricular (LV) dysfunction in anemic patients using 2D strain echocardiography has been investigated inadequately. **Aims and Objectives:** This study was designed to compare the echocardiographic characteristics in patients with severe anemia to those without anemia using a 2D strain pattern. **Materials and Methods:** A cross-sectional study was conducted between April 2021 and March 2022. A total of 100 patients were incorporated in the case group, where patients with hemoglobin levels <7 g/dL, aged between 18 and 60 years, were included, whereas 100 patients with normal hemoglobin levels were included in the control group. Baseline clinical characteristics and echocardiographic parameters were studied. **Results:** The mean age of the case group was 38.32 ± 14.9 years and of the control group was 39.94 ± 14.3 years. In each group, majority of the patients were females (55%) and were from rural area. Mean hemoglobin level was 4.81 ± 1.42 g/dL in case group and 12.41 ± 0.9 g/dL in control group (P = 0.0024). Mean peak E velocity (P = 0.0002), mean peak A velocity (P < 0.0001) and mean isovolumetric relaxation time (P = 0.4612) represented statistically significant differences among case and control groups. The ejection fraction was 58% in the case and 56% in control group (P = 0.621). Stroke volume was 58 mL in the case and 52 mL in the control group (P = 0.653). LV dysfunction represented a significant difference between case and control group (Chi = 28.125; P = 0.0001). Furthermore, a statistically significant difference was observed between the global longitudinal strain score of the case and the control group (P = 0.0015). **Conclusion:** Using 2D strain imaging technique, LV dysfunction was detected in severely anemic patients who had no previously detected severe cardiovascular diseases.

Key words: Anemia; Cardiac functions; Echocardiography; Global longitudinal strain score; Left ventricular dysfunction; 2D strain imaging

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INTRODUCTION

Anemia is a common health problem worldwide and the prevalence of it is highest among the Indian population. Anemia is characterized by a reduction in the number of red blood cells and the oxygen-carrying capacity of hemoglobin.[1,2] The heart undergoes structural changes and develops functional impairment in response to the reduced hemoglobin levels in chronic anemia. Besides, in the general population, anemia is a risk factor for cardiovascular disease outcomes.[3] Furthermore, there are few previous data on the effect of low hemoglobin levels on left ventricular (LV) diastolic function in patients without overt heart disease.[4-7]

Strain imaging is the method of choice for the accurate quantification of ventricular function. It is an echocardiographic technique for the assessment of regional LV strains in the longitudinal, radial, and circumferential directions. Chronic anemia is usually accompanied by increased cardiac mass.[8] In addition, LV global longitudinal strain (GLS) has been shown to be a superior marker of LV dysfunction.[9] However, there is a lack of literature to understand the association between low hemoglobin levels and LV function and the use of a 2D strain pattern for the earliest detection of LV dysfunction in severe anemic patients based on the GLS score.

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Aims and objectives

This study was designed to compare the echocardiographic characteristics in patients with severe anemia to those without anemia using 2D strain pattern.

MATERIALS AND METHODS

Study setting and population

A cross-sectional study was conducted at a tertiary care center in India between April 2021 and March 2022. A total of 200 participants were included in the study, of which 100 patients with severe anemia (hemoglobin level <7 g/dL) were included in the case group, while 100 patients with normal hemoglobin levels were included in the control group.

Inclusion criteria were patients in the medical ward aged between 18 and 60 years and patients with hemoglobin levels <7 g/dL. Exclusion criteria were patients with chronic renal failure and chronic liver disease, pregnant females with anemia, and patients with other cardiac diseases such as ischemic heart disease, rheumatic heart disease, or infectious related disease.

Sample size

The sample size of the study was determined based on the weekly admission rate of patients with severe anemia to the general ward.

Methodology

Demographic details and the history of all the patients were documented. All the patients underwent physical, clinical, hematological, and peripheral smear examinations. Echocardiogram was recorded using Hewlett-Packard image point with 3.7, 5 MHz, and 2.0, 2.5 MHz probe.

Echocardiographic parameters such as LV mass, septal wall thickness, posterior wall thickness, LV end-diastolic diameter, mean peak E velocity, mean peak A velocity, mean E/A ratio, mean deceleration time, mean isovolumetric relaxation time, ejection fraction, stroke volume, LV dysfunction, and LV GLS were recorded.

Ethical statement

The research protocol was approved by the institutional ethics committee (S.No./IEC/MC/2020/425) and the written informed consent was obtained from all the patients.

Statistical analysis

Data were analyzed using a commercially available statistical package for social sciences (Chicago, IL, USA) program, version 21.0. Correlation analysis was applied to correlate physical, clinical, and echocardiographic parameters. Continuous variables are expressed as mean and standard deviations, and discrete variables as counts and percentages. For categorical variables, the Chi-square test and Fisher exact t-test were used, and for continuous variables, the Student t-test was used where a $P<0.05$ was considered statistically significant.

RESULTS

The mean age in the case group was 38.32±14.9 years and in the control group was 39.94±14.3 years. Majority of patients were in the age group of between 18 and 30 years, covering 37% in the case group and 32% of patients in the control group. In each group, females were more prevalent than males (55% vs. 45%). Majority of patients were from rural area in both groups, including 76 (76%) patients in case and 69 (69%) patients in control and the maximum number of patient's socioeconomic status was below average. Hemoglobin level among the case group and control group was found to be statistically significant (P=0.0024). Among the patients in the case group, microcytic hypochromic anemia (38%) was the most prevalent, followed by macrocytic hyperchromic anemia (28%) and normocytic normochromic anemia (15%). In the case group, the mean hemoglobin level was 4.81±1.42 g/dL and the mean hemoglobin level in the control group was 12.41±0.93 g/dL (P=0.002). Clinical presentation such as palpitation was observed in 82 (82%) patients of case group and in two patients of the control group. Early fatiguability was observed in 96 (96%) patients of the case group and in one patient of the control group. Dyspnoea on exertion was experienced by 90 (90%) patients of case group and none in the control group. Demographic details, hematological profile and association according to the investigation parameters among the cases and control group are summarized in Table 1.

Echocardiographic characteristics such as mean peak E velocity (P=0.0002), mean peak A velocity (P<0.0001), and mean isovolumetric relaxation time (P=0.4612) represented statistically significant differences among case and control groups. However, LV mass, septal wall thickness, posterior wall thickness, LV end-diastolic diameter, and mean deceleration time showed no significant difference among case and control groups. Comparison of echocardiographic parameters using 2D strain pattern among case and control groups are demonstrated in Table 2. The ejection fraction was 58% in the case group and 56% in control group (P=0.621). Stroke volume was 58 mL in the case group and 52 mL in control group (P=0.653). LV dysfunction was present in 54 (54%) patients of case group and in 18 (18%) patients of the control group (P=0.0001).

The mean GLS score for LV function was −16.59±1.303% in the case group and was −19.23±0.633% in the control group (P=0.0015). The mean GLS score in the case group with hemoglobin levels of 2–5 g/dL was −15.98±0.98%, while those with hemoglobin levels of 5.1–7 g/dL was −17.3±1.28%. The mean GLS score of the control group with a hemoglobin level of more than 10 g/dL was −19.23±0.633%. A comparison of GLS score among case and control groups are demonstrated in Table 3.

DISCUSSION

In the present study, severe anemic patients (hemoglobin level <7 g/dL) and patients with normal hemoglobin levels were screened for clinical, hematological, and echocardiographic profiles using 2D strain pattern. In each group, females (55%) were found to be predominant over males (45%). Similarly in a previous study by Alvarez-Uria et al.,[10] 49.5% of patients with severe anemia

Table 1: Demographic details, hematological profile, and association according to the investigation parameters among the cases and control group

Parameters	Case (n=100) n (%)	Control (n=100) n (%)
Gender		
Female	55 (55)	55 (55)
Male	45 (45)	45 (45)
Age group		
18–30 years	37 (37)	32 (32)
31–40 years	15 (15)	14 (14)
41–50 years	18 (18)	31 (31)
51–60 years	30 (30)	23 (23)
Urban/Rural		
Rural	76 (76)	69 (69)
Urban	24 (24)	31 (31)
Socioeconomic status		
Average	29 (29)	21 (21)
Below average	71 (71)	79 (79)

Hematological profile of case and control group

Parameters	Case	Control
	Mean±SD	Mean±SD
Age (years)	38.32±14.9	39.94±14.3
Hemoglobin (g/dL)	4.81±1.42	–
MCV (μm³)	85.45±21.0	–
MCH (pg)	28.39±8.8	–
Cholesterol (mg/dL)	188.08±37.1	–
Urea (mg/dL)	26.43±14.8	Urea (mg/dL)
Creatinine (mg/dL)	0.67±0.49	Creatinine (mg/dL)

Association according to the investigation parameters among case and control groups

Parameters	Case	Control	t-value	P-value
	Mean±SD	Mean±SD		
Age (years)	38.32±14.9	39.94±14.3	0.811	0.42
Hemoglobin (g/dL)	4.81±1.42	12.41±0.9	44.714	0.002
Urea (mg/dL)	26.43±14.8	23.86±5.9	−1.526	0.13
Creatinine (mg/dL)	0.67±0.4	0.75±0.4	1.157	0.25

Table 2: Comparison of echocardiographic parameters using 2D strain pattern among case and control groups

Echocardiographic findings	Case	Control	t-value	P-value
Left ventricular mass (g)	216	186	0.175	0.525
Septal wall thickness (mm)	7.3	9.56	0.195	0.510
Posterior wall thickness (mm)	7.6	10.6	0.203	0.490
Left ventricular end diastolic diameter (mm)	55.6	44.4	0.165	0.575
Mean peak E velocity (m/s)	0.8±0.12	0.89±0.11	3.9	0.002
Mean peak A velocity (m/s)	0.38±0.02	0.289±0.01	28.77	<0.001
Mean E/A ratio	2.0	1.9		
Mean deceleration time (ms)	169±40.1	190±46.5	0.740	0.461
Mean isovolumetric relaxation time (ms)	79±12.8	81±14.2	2.418	0.017

Table 3: Comparison of GLS score among case and control groups

Groups	Minimum GLS score	Maximum GLS score	Mean GLS score±SD	
Case	−19	−14	−16.59±1.303	
Control	−20	−18	−19.23±0.633	
Association of GLS score among cases and controls				
Parameter	**Case**	**Control**	**t-value**	**P-value**
GLS score	−16.59±1.303	−19.23±0.633	−18.344	0.0015
Distribution of GLS score among case and control groups based on hemoglobin level				
Groups	**Hemoglobin level (g/dL)**	**Mean GLS score±SD**		
Case	2–5	−15.98±0.98		
	5.1–7	−17.3±1.28		
Control	More than 10	−19.23±0.633		

GLS: Global longitudinal strain

were females. The mean age of patients in case group was 38.32±14.9 years and the mean age of the control group was 39.94±14.3 years (P=0.42). Similarly, in a previous study by Cho et al.,[11] the mean age of the anemic patients was 35±11 years and in the control group was 35±11 years (P=0.999). Anemic patients were more prevalent in rural area (76%) as compared to urban area (24%). Perhaps, the low socioeconomic status, low serving of iron-rich foods, lack of adequate nutrition information, and a high number of illiterates among rural residents as compared to urban residents could be the reason behind the predominant prevalence of anemia among rural residents. Similarly in a study by Tesfaye et al.,[12] the prevalence of anemia among rural residents was 20.1% and 46.6% among urban residents.

The most common clinical symptom observed in our study was early fatiguability (96%) followed by dyspnoea on exertion (90%), and palpitation (82%). Previous study by Dunn et al.,[13] also found similar results where fatigue was the most common symptom of severe anemia.

In our study, majority of severely anemic patients had microcytic hypochromic anemia followed by macrocytic hyperchromic, normocytic normochromic, normocytic hypochromic, microcytic normochromic, and normocytic hyperchromic anemia. A previous study by Alvarez-Uria et al.,[10] reported a higher prevalence of microcytic anemia followed by the highest prevalence rates of normocytic anemia, which was found to be increased with age in male adults and in females after menopause. In our study, the mean hemoglobin level in the control group was 12.41±0.933 g/dL, whereas, in anemic patients, the mean hemoglobin was 4.81±1.42 g/dL. These findings were consistent with the previous finding of Cho et al.,[11] who reported hemoglobin level as 5.8±1.4 g/dL in patients with anemia and 13.0±0.9 g/dL in patients without anemia.

Severe anemia leads to hyperdynamic circulation and chronic volume overload state and causes significant changes in echocardiographic parameters. In the present study, the LV mass was higher in case group (216 g) as compared to control group (186 g). Our results were consistent with a previous study by Sarin et al.,[14] where the mean LV mass in anemic patients was 193.4±63.51 g and in control group was 155.38±40.27 g. In our study, LV end-diastolic diameter was 55.6 mm among case group and 44.4 mm among the control group. Our findings were comparable with a previous study by Cho et al.,[11] where the LV end-diastolic diameter in patients with anemia was 51.8 mm and was 47.2 mm in patients without anemia. The increased LV end-diastolic diameter may be attributed to the Frank starling mechanism in the hyperdynamic condition of anemic patients.

In this study, the ejection fraction among the cases group was 58% and among the control group was 56%. Ejection fraction was found to be raised nonsignificantly (P=0.621) due to increased preload, better myocardial contractility, and decreased afterload. Our finding was consistent with a previous study by Sarin et al.,[14] where the ejection fraction in patients with anemia was 74.5±10.1% and in patients without anemia was 71.32±8.29%.

Stroke volume in our study was found to be 58 mL in case group and 52 mL in the control group. This increase in the stroke volume in anemic patients could be due to an overall increase in sympathetic and inotropic activity, which places the myocardium under more strain, perhaps causing remodeling of the myocytes and vasculature. Similarly, in a previous study by Cho et al.,[11] the association of anemia with augmented cardiac indices and stroke volume has been demonstrated where the stroke volume was reported as 76.1±14.8 mL in anemic patients and 67.9±12.7 mL in patients without anemia. In this study, the mean peak E velocity in case group was 0.8±0.12 m/s and 0.89±0.11 m/s in control group, while mean peak A velocity was 0.38±0.02 m/s in case group and 0.28 9±0.01 m/s in control group. These findings were comparable with

a similar study by Cho et al.,[11] where the mean peak E velocity in anemic patients was reported as 1.0±0.2 m/s and in the control group was 0.8±0.2 m/s and the mean peak A velocity in anemic patients was 0.7±0.2 m/s and was reported as 0.6±0.1 m/s in patients without anemia. The mean E/A ratio in our study was 2.0 in the case group and 1.9 in control group. Similar findings were reported in a previous study by Sengupta et al.,[5] where E/A ratio in patients with sickle cell anemia was 2.11±12.13 and in control group was 1.16±1.35.

In our study, on comparison among case and control groups, LV dysfunction was found in 54% of anemic patients (case group) and in 18% of patients with normal hemoglobin levels (control group). Whereas LV dysfunction was absent in 46% of patients of the case group and absent in 82% of patients of control group (P<0.0001). Therefore, this study confirms that there is a strong correlation between severely anemic patients and LV dysfunction and the use of 2D strain echocardiography would be beneficial for the detection of LV dysfunction before the LV anatomical changes appear. Furthermore, based on the GLS score, LV dysfunction was detected in severely anemic patients. GLS expresses longitudinal shortening as a percentage. It is derived from speckle tracking and analyzed by post-processing of apical images of the LV. The GLS score of −16% is considered abnormal, the GLS score of >−18 is normal and the GLS score −16%–18% is borderline.[15] In the present study, the mean GLS score in the case group was −16.59±1.303%, while in the control group, the mean GLS score was −19.23±0.633%. Similarly, in a previous study by Eroglu et al.,[9] LV GLS score in patients with heart failure was −9 and in control group mean LV GLS score was −20. Also, it has been reported by Eroglu et al.,[9] that worsening GLS is an indicator of an advanced degree of systolic dysfunction.

Limitations of the study

This study has some limitations. First, a smaller sample size. Second, the evaluation of diastolic function by 2D strain echocardiography is not precise because it permits only an indirect measure of diastolic function in relation to ventricular filling.

CONCLUSION

In conclusion, LV dysfunction is frequently observed in patients with severe anemia as compared to the patients without anemia. Use of 2D strain imaging technique (echocardiography) may help detecting LV dysfunction in patients with severe anemia. Thus, suggests the need for the timely management of anemia to prevent associated cardiac dysfunction.

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Author's Contribution:
SG- Implementation of study protocol, data collection, data analysis, manuscript preparation and submission of article; **HG-** Concept, design, clinical protocol, manuscript preparation, editing, and manuscript revision; **RPP-** Design of study, statistical analysis and interpretation; **TVD-** Literature review, manuscript revision, review manuscript.

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