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Early Echocardiographic and Electrocardiographic Assessment of Neonates Born to Mothers with Iron-Deficiency Gestational Anaemia: A Comparative Cross-Sectional Study

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Research Article

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Abstract

Background

Iron-deficiency gestational anaemia (IDGA) is a major global health concern associated with adverse maternal and perinatal outcomes. However, evidence on early neonatal cardiovascular adaptation, assessed using echocardiography and electrocardiography, remains limited. This study evaluated neonatal cardiac structure, function, and electrophysiological parameters in term neonates born to mothers with IDGA.

Methods

This comparative cross-sectional study included 150 term neonates (≥ 37 weeks of gestation) evaluated at approximately 72 hours of life. Seventy-five neonates were born to mothers with iron-deficiency anaemia (haemoglobin < 11 g/dL with low ferritin), while 75 were born to non-anaemic mothers. Neonatal echocardiographic assessment was performed using standardized transthoracic imaging protocols, and electrocardiographic parameters were recorded using a standard 12-lead ECG. Multivariable linear regression analysis was performed adjusting for gestational age, birth weight, neonatal sex, and mode of delivery.

Results

Neonates born to anaemic mothers demonstrated significantly larger left ventricular internal dimensions during systole and diastole ($p < 0.001$) and lower fractional shortening (34.80% vs. 39.67%, $p < 0.001$). Ejection fraction was modestly lower in the anaemic group (66.42% vs. 69.33%, $p = 0.046$). Maternal anaemia remained independently associated with increased ventricular dimensions and reduced fractional shortening after adjustment. Electrocardiographic assessment demonstrated shorter PR interval and P-wave duration among neonates of anaemic mothers, whereas QTc prolongation was not independently significant after adjustment.

Conclusion

Iron-deficiency gestational anaemia was associated with subtle alterations in neonatal cardiac structure, systolic performance, and conduction parameters identified through early echocardiographic and electrocardiographic assessment. These findings may represent early cardiovascular adaptation to intrauterine iron deficiency and hypoxic stress.

What is Known

- Iron-deficiency gestational anaemia is highly prevalent worldwide and is associated with adverse maternal and neonatal outcomes, including preterm birth, low birth weight, and fetal growth impairment.
- Maternal iron deficiency and chronic intrauterine hypoxia may influence fetal myocardial development and cardiovascular adaptation.
- Echocardiography and electrocardiography are valuable non-invasive imaging tools for assessing neonatal cardiac structure, function, and electrophysiological parameters.

What is New

- Term neonates born to mothers with iron-deficiency gestational anaemia demonstrated subtle but measurable differences in cardiac structure and systolic performance on early neonatal echocardiography.
- Maternal anaemia was independently associated with larger left ventricular dimensions and lower fractional shortening after adjustment for neonatal and perinatal factors.
- Combined echocardiographic and electrocardiographic assessment identified early cardiovascular adaptations in neonates exposed to maternal iron deficiency, while most findings remained within accepted neonatal reference ranges.

Introduction

Iron-deficiency gestational anaemia (IDGA) is one of the most common medical disorders affecting pregnancy worldwide and remains a major public health concern, particularly in low- and middle-income countries[1]. In India, the prevalence of maternal anaemia continues to be high despite ongoing public health interventions and iron supplementation programmes, contributing substantially to maternal and neonatal morbidity[2].Iron deficiency during pregnancy has been associated with adverse obstetric and perinatal outcomes, including preterm birth, low birth weight, impaired fetal growth, and increased maternal and neonatal complications[3][4].These adverse effects are especially pronounced in resource-limited settings where nutritional deficiencies and healthcare disparities remain prevalent[5].

According to the World Health Organization, gestational anaemia is defined as haemoglobin levels below 11 g/dL during pregnancy, with iron deficiency accounting for the majority of cases worldwide[6].Despite continued public health initiatives and antenatal supplementation programmes, many women enter pregnancy with depleted iron stores or progressively develop iron deficiency during gestation[7]. Although several investigations have demonstrated the association between maternal anaemia and adverse neonatal outcomes, including low birth weight and increased perinatal mortality[8] [9], the influence of maternal iron deficiency on neonatal cardiovascular adaptation remains insufficiently explored [10]. Iron plays a fundamental role in fetal growth and cardiovascular development by mediating oxygen transport, mitochondrial metabolism, myocardial energy homeostasis, and cellular differentiation [11]. Maternal iron deficiency may impair placental oxygen delivery and expose the fetus

to chronic intrauterine hypoxic stress, thereby influencing myocardial maturation and cardiovascular adaptation [12]. Experimental and translational studies have suggested that fetal hypoxia and iron deficiency can alter myocardial structure, ventricular performance, vascular tone, and cardiomyocyte development during critical stages of fetal growth [9, 11]. However, imaging-based evidence evaluating neonatal cardiac alterations associated with IDGA remains limited [13].

Recent advances in non-invasive cardiovascular imaging have significantly improved the evaluation of neonatal cardiac physiology and adaptation. Echocardiography has emerged as an essential imaging modality for assessing neonatal cardiac structure, ventricular performance, pulmonary haemodynamics, and myocardial function[14] [15]. Contemporary neonatal echocardiographic techniques facilitate the identification of subtle cardiovascular alterations that may not be clinically evident during routine neonatal examination[15]. Similarly, electrocardiography provides important information regarding neonatal cardiac conduction, autonomic regulation, and ventricular repolarisation [16]. Together, these imaging-based approaches enable comprehensive assessment of neonatal cardiovascular physiology and may improve understanding of fetal cardiovascular programming associated with maternal disorders during pregnancy.

Given the expanding role of imaging in maternal-fetal medicine and neonatal risk stratification, improved characterization of cardiovascular adaptation in neonates born to anaemic mothers may have important implications for early postnatal surveillance and long-term cardiovascular health assessment. Therefore, this study aimed to evaluate neonatal cardiac structure, systolic function, pulmonary haemodynamics, and electrophysiological parameters using echocardiography and electrocardiography in term neonates born to mothers with iron-deficiency gestational anaemia compared with neonates born to non-anaemic mothers. In addition, the study examined whether the observed imaging findings remained independently associated with maternal anaemia after adjustment for gestational age, birth weight, neonatal sex, and mode of delivery.

Methods

Study design and setting

This hospital-based comparative cross-sectional study was conducted at the Department of Obstetrics and Gynaecology in collaboration with the Departments of Neonatology and Cardiology at SRM Medical College Hospital and Research Centre, Chengalpattu, Tamil Nadu, India, between January and June 2025. The study evaluated early neonatal cardiovascular findings among term neonates born to mothers with and without iron-deficiency gestational anaemia (IDGA).

Study population

Term neonates (≥ 37 weeks of gestation) born during the study period were consecutively screened for eligibility and assessed at approximately 72 hours after birth. Maternal clinical and laboratory records

were reviewed to classify participants according to maternal haemoglobin and ferritin status.

Exposure definition and grouping

Maternal iron-deficiency gestational anaemia was defined as haemoglobin < 11 g/dL in association with low serum ferritin levels at delivery[17] [18]. Neonates born to mothers meeting these criteria were assigned to the anaemic group. Neonates born to mothers with haemoglobin ≥ 11 g/dL served as the non-anaemic comparison group [19] [20] [21]. Mild anaemia (haemoglobin 10.0–10.9 g/dL) was included within the anaemic category in accordance with World Health Organization criteria for anaemia in pregnancy.

Inclusion and exclusion criteria

Eligible participants included singleton term neonates born to mothers fulfilling the predefined haematological criteria. Neonates were excluded if they were born preterm (< 37 weeks of gestation), had congenital anomalies or structural heart disease, demonstrated haemodynamic instability, or required respiratory support beyond 48 hours of life. Mothers with hypertensive disorders of pregnancy, diabetes mellitus, cardiovascular disease, multiple pregnancy, or major systemic illness were also excluded. Cases with incomplete maternal or neonatal clinical records were not included in the final analysis.

Sample Size and Sampling

A total of 150 neonates were included in the study, comprising 75 neonates born to mothers with IDGA and 75 neonates born to non-anaemic mothers. Participants were enrolled consecutively during the study period. As this exploratory observational study was designed to evaluate early imaging findings, a formal a priori sample size calculation was not performed.

Data collection

Maternal demographic and antenatal variables were obtained from hospital medical records. Neonatal variables included gestational age, sex, birth weight, mode of delivery, and Apgar scores. Clinical and imaging assessments were performed at approximately 72 hours postnatally.

Echocardiographic assessment

All neonates underwent transthoracic echocardiographic evaluation using a GE Vivid E95 ultrasound system (GE Healthcare, Chicago, IL, USA) equipped with a 4–8 MHz paediatric sector transducer. Echocardiographic examinations were performed by experienced neonatologists trained in neonatal cardiac imaging to minimise inter-observer variability.

Standard two-dimensional, M-mode, and Doppler echocardiographic measurements were obtained in accordance with established paediatric echocardiography guidelines. Measurements were averaged over three consecutive cardiac cycles during sinus rhythm. Structural parameters included left ventricular internal dimensions during systole and diastole, interventricular septal thickness, and left ventricular posterior wall thickness. Functional assessment included ejection fraction, fractional shortening, mitral inflow velocity, aortic flow velocity, tricuspid annular plane systolic excursion (TAPSE), pulmonary artery acceleration time (PAAT), and PAAT/right ventricular ejection time ratio. Where appropriate, left ventricular dimensions were interpreted with consideration of neonatal body size and birth weight. Table 1.

Table 1
Echocardiographic parameters assessed

Category	Parameters assessed via 2D-ECHO
Left Ventricular Systolic Function	Ejection Fraction (EF, %)
	Fractional Shortening (FS, %)
	Tricuspid Annular Plane Systolic Excursion (TAPSE, mm)
	Left Ventricular Internal Diameter in Systole (LVIDs, cm)
Left Ventricular Diastolic Function	Left Ventricular Internal Diameter in Diastole (LVIDd, cm)
	Interventricular Septal Thickness (IVSd and IVSs, cm)
	Left Ventricular Free Wall Thickness (LVFW, mm)
	Aortic and Mitral Doppler Velocities (m/s)
Right Heart and Pulmonary Parameters:	Pulmonary Artery Doppler Velocity (m/s)
	Pulmonary Artery Acceleration Time (PAAT, ms)
	Right Ventricular Acceleration Time (RVAT, ms)
	Tricuspid Regurgitation (TR) Jet Velocity (m/s)

Electrocardiographic assessment

A standard 12-lead electrocardiogram (ECG) was recorded for all neonates at approximately 72 hours of life. ECG parameters included heart rate, P-wave duration, PR interval, QRS duration, and corrected QT interval (QTc). QTc values were calculated using Bazett's correction formula.[22] ECG recordings were interpreted according to established neonatal ECG standards by an experienced neonatologist blinded to maternal anaemia status.

Statistical analysis

Data were analysed using IBM SPSS Statistics version 22.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were presented as frequencies and percentages. Between-group comparisons were performed using independent sample t-tests for continuous variables and chi-square tests for categorical variables.

To evaluate the independent association between maternal anaemia and neonatal cardiovascular parameters, multivariable linear regression analysis was performed, adjusting for gestational age, birth weight, neonatal sex, and mode of delivery. Robust standard errors were applied where appropriate. A two-tailed p-value < 0.05 was considered statistically significant.

Ethical Considerations

The study was approved by the Institutional Ethics Committee of SRM Medical College Hospital and Research Centre (IEC No. 8539/IEC/2023). Written informed consent was obtained from parents or legal guardians prior to enrolment. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Results

Maternal Demographics

A total of 150 pregnant women were included in the study, of whom 75 (50.0%) were anaemic, and 75 (50.0%) were non-anaemic based on haemoglobin and maternal criteria. Anaemia prevalence varied across residential areas, being higher among women residing in urban areas (30/55; 54.5%), whereas rural participants showed equal distribution of anaemic and non-anaemic status (21/42; 50.0% each). In semi-urban areas, a lower proportion of women were anaemic (24/53; 45.3%).

Across maternal age groups, anaemia was most frequently observed among women aged 25–30 years (33/59; 55.9%), followed by those aged > 30 years (23/47; 48.9%) and 18–24 years (19/44; 43.2%). With respect to parity, primigravida women showed a slightly higher prevalence of anaemia (40/76; 52.6%) compared with multigravida women (35/74; 47.3%).

Haemoglobin stratification demonstrated complete concordance with group allocation: all women with Hb > 11 g/dL were categorised as non-anaemic (75/75; 100%), whereas all women with Hb < 11 g/dL were categorised as anaemic (75/75; 100%), confirming the internal consistency of the anaemia classification. Table 2 **Maternal Demographics**

Table 2
Maternal Demographics

Characteristic	Category	Anaemic (%)	Non-anaemic (%)	Total
Residential Background	Rural	21 (50.0%)	21 (50.0%)	42
	Semi Urban	24 (45.3%)	29 (54.7%)	53
	Urban	30 (54.5%)	25 (45.5%)	55
Maternal Age	18–24 years	19 (43.2%)	25 (56.8%)	44
	25–30 years	33 (55.9%)	26 (44.1%)	59
	More than 30 years	23 (48.9%)	24 (51.1%)	47
Parity	Primigravida (= 1)	40 (52.6%)	36 (47.4%)	76
	Multigravida (> 1)	35 (47.3%)	39 (52.7%)	74
Haemoglobin group	Hb > = 11 g/dL	0 (0%)	75 (100%)	75
	Hb < 11 g/dL	75 (100%)	0 (0%)	75

Legend: Data represent the distribution of maternal participants according to residential background, age group, parity, and haemoglobin category. Haemoglobin levels defined study categorisation, with the anaemic group including mothers with Hb < 11 g/dL and low ferritin and the non-anaemic group including mothers with Hb ≥ 11 g/dL.

Neonatal Demographics

Comparative analysis between neonates born to anaemic and non-anaemic mothers demonstrated a significant difference in gestational age at delivery. Anaemic mothers had a higher proportion of full-term deliveries (39–40 weeks) compared with non-anaemic mothers, and the difference in mean gestational age was statistically significant ($t = 3.452$; $df = 148$; $p = 0.001$).

The mode of delivery did not differ significantly between groups. Vaginal delivery occurred in 39 anaemic and 36 non-anaemic mothers, while caesarean section was performed in 36 anaemic and 39 non-anaemic mothers ($\chi^2=0.240$; $df = 1$; $p = 0.624$)

Birthweight distribution differed significantly between groups ($t = -3.557$; $df = 148$; $p = 0.001$). Because infant size differed between groups, the main interpretation of cardiac dimensions is based on analyses adjusted for birth weight and gestational age rather than on unadjusted absolute dimensions alone. Neonates born to anaemic mothers were more frequently represented in the higher birth-weight categories, particularly 3.5-4.0 kg (18 vs 2), whereas neonates of non-anaemic mothers were predominantly clustered in the 2.5-3.0 kg category (48 vs 28). The distribution of low birth weight (1.5–2.5 kg) was comparable between the two groups.

APGAR Scores at birth did not differ significantly between the two groups (chi-square = 0.718, df = 2, p = 0.698).

Table 3 **Neonatal Demographics**

Table 3
Neonatal Demographics

Characteristic	Measure	Patient group		Total (n)		
		Anaemic (n = 75)	Non – Anaemic (n = 75)		Statistical Test value	p-value
Gestational Age	**Weeks, mean (SD)**	37.84 ± 0.75	38.40 ± 1.18	-	t = -3.452, df = 148	0.001*
Birth Weight	**Kg, mean (SD)**	3.10 ± 0.53	2.84 ± 0.34	-	t = 3.557, df = 148	0.001*
Type of delivery	**Vaginal**	39	36	75	χ^2 value = 0.240, df = 1	0.624
	LSCS	36	39	75		
Gender of the baby	**Male**	33	45	78	χ^2 value = 3.846, df = 1	0.050
	Female	42	30	72		
Weight of Baby	**1.5–2.5 kgs**	8	8	16	t value = -3.557, df = 148	0.001
	2.5–3.0 kgs	28	48	76		
	3.0–3.5 kgs	21	17	38		
	3.5–4.0 kgs	18	2	20		
APGAR score	**0–3 score**	18	20	38	χ^2 value = 0.718, df = 2	0.698
	4–6 score	30	25	55		
	7–10 score	27	30	57		

Legend: Continuous patient characteristics for gestational age and birth weight are presented as mean (SD). Data represent the distribution of neonates born to anaemic and non-anaemic mothers across mode of delivery, gender, birth weight, and APGAR score ranges.

Comparative Echocardiographic Outcomes

Echocardiographic evaluation performed at approximately 72 hours of life revealed significant differences in left ventricular morphology and function between neonates born to anaemic and non-anaemic mothers (Table 4). Absolute left ventricular internal dimensions were larger in the anaemic

group during systole (LVIDs: 1.31 ± 0.30 cm vs. 0.97 ± 0.13 cm, p < 0.001) and diastole (LVIDd: 1.86 ± 0.27 cm vs. 1.52 ± 0.19 cm, p < 0.001). The absolute differences need to be understood through comparison with adjusted regression models because the groups had different gestational age and birth weight measurement results.

Table 4
Echocardiographic parameters of neonates born to mothers at ~ 72 hours of life

Parameter	Non-Anaemic (mean ± S.D)	Anaemic (mean ± S.D)	t-value	p-value
IV septum thickness (mm)	4.73 ± 1.05	4.37 ± 0.91	2.247	0.026
LV free wall thickness (mm)	2.88 ± 0.63	2.63 ± 0.46	2.718	0.007
TAPSE (mm)	8.93 ± 1.01	9.00 ± 0.90	-0.493	0.622
Pulmonary artery Doppler (m/s)	0.84 ± 0.17	0.80 ± 0.09	2.027	0.044
Ejection fraction (%)	69.33 ± 9.22	66.42 ± 8.48	2.015	0.046
Fractional shortening (%)	39.67 ± 7.56	34.80 ± 6.94	4.103	< 0.001
LVIDs (cm)	0.97 ± 0.13	1.31 ± 0.30	-8.903	< 0.001
LVIDd (cm)	1.52 ± 0.19	1.86 ± 0.27	-8.764	< 0.001
IVSs (cm)	0.42 ± 0.09	0.38 ± 0.09	2.941	0.004
IVSd (cm)	0.37 ± 0.08	0.40 ± 0.08	-1.648	0.101
Aortic Doppler (m/s)	0.67 ± 0.16	0.57 ± 0.11	4.167	< 0.001
Tricuspid regurgitation (m/s)	0.74 ± 0.32	0.81 ± 0.37	-1.278	0.203
Mitral Doppler (m/s)	0.52 ± 0.13	0.60 ± 0.19	-3.049	0.003
PAAT (ms)	99.05 ± 24.52	94.92 ± 17.67	1.182	0.239
RVAT (ms)	474.44 ± 97.40	444.12 ± 79.86	2.085	0.039
PAAT/RVAT ratio	0.21 ± 0.06	0.22 ± 0.06	-0.382	0.703
Pulmonary vascular tone	0.20 ± 0.05	0.21 ± 0.05	-0.728	0.468

Legend: Data are presented as mean values. Statistical analysis was performed using the independent t-test. A p-value < 0.05 was considered statistically significant. Significant differences were observed in interventricular septal thickness, left ventricular free wall, ejection fraction, fractional shortening, left ventricular internal dimensions (LVIDs and LVIDd), pulmonary artery Doppler velocity, aortic flow velocity, mitral inflow velocity, and right ventricular acceleration time (RVAT).

The larger ventricular dimensions were accompanied by lower fractional shortening (34.80 ± 6.94% vs. 39.67 ± 7.56%, p < 0.001) and a modestly lower ejection fraction (66.42 ± 8.48% vs. 69.33 ± 9.22%, p = 0.046). Interventricular septal thickness and left ventricular free wall thickness were also lower in the anaemic group. These differences indicate early physiological adaptation rather than overt neonatal cardiac dysfunction.

Doppler assessment showed higher mitral inflow velocity in neonates born to anaemic mothers (0.60 ± 0.19 m/s vs. 0.52 ± 0.13 m/s, p = 0.003). while aortic flow velocity was significantly lower. Right ventricular systolic function, assessed by TAPSE and most pulmonary vascular indices (PAAT, PAAT/RVAT ratio and Pulmonary vascular tone), did not differ significantly between groups.

Table 4 **Echocardiographic parameters of neonates born to mothers at ~ 72 hours of life.**

Blood Pressure and Electrocardiographic Parameters

Electrocardiographic assessment demonstrated significant differences in atrial and atrioventricular conduction parameters between groups, while baseline heart rate remained comparable. Neonates born to anaemic mothers exhibited shorter P-wave duration (62.44 ± 11.77 ms vs. 69.60 ± 12.62 ms, p < 0.001) and PR interval (79.49 ± 15.74 ms vs. 99.88 ± 13.73 ms, p < 0.001).

The QTc interval was longer in the anaemic group in unadjusted analysis (442.80 ± 35.90 ms vs 429.97 ± 38.52 ms; p = 0.037) whereas QRS duration did not differ significantly between groups (p = 0.356). In adjusted analysis, QTc prolongation was not independently associated with maternal anaemia.

Table 5 **Comparative analysis of neonatal blood pressure and electrocardiographic parameters between offspring of anaemic and non-anaemic mothers (Independent t-test results**

Table 5
Comparative analysis of neonatal electrocardiographic parameters between offspring of anaemic and non-anaemic mothers

Parameter	Non-anaemic (n = 75)	Anaemic (n = 75)	p-value
Heart rate (bpm)	120.05 ± 18.19	121.52 ± 15.35	0.594
P-wave duration (ms)	69.60 ± 12.62	62.44 ± 11.77	< 0.001
PR interval (ms)	99.88 ± 13.73	79.49 ± 15.74	< 0.001
QTc interval (ms)	429.97 ± 38.52	442.80 ± 35.90	0.037
QRS duration (ms)	72.12 ± 13.84	70.10 ± 12.74	0.356
Legend: Data are presented as mean +/- SD.			

Regression Analysis

Multivariable linear regression analysis was performed to evaluate the independent association between maternal anaemia and neonatal cardiac structural and electrical parameters, adjusting for gestational

age, birth weight, neonatal se, mode of delivery, maternal age group, and parity. **(**Table 6**) Multivariable regression analysis adjusting for gestational age, birth weight, sex, and mode of delivery (Anaemic and Non-anaemic group)**.

Table 6
Multivariable regression analysis adjusting for gestational age, birth weight, sex, and mode of delivery (Anaemic and Non-anaemic group)

Outcome	Adjusted β (anaemia vs non-anaemia)	95% CI	p-value
LVIDd (cm)	0.32	0.24 to 0.41	< 0.001
LVIDs (cm)	0.34	0.26 to 0.43	< 0.001
Fractional shortening (%)	-5.21	-7.89 to -2.53	< 0.001
Ejection fraction (%)	-3.02	-6.30 to 0.27	0.072
PR interval (ms)	-20.43	-25.95 to -14.91	< 0.001
P-wave duration (ms)	-7.50	-11.73 to -3.27	< 0.001
QTc interval (ms)	7.49	-7.04 to 22.02	0.312
Legend: Regression models adjusted for gestational age, birth weight, sex, and mode of delivery.			

Maternal anaemia remained a significant independent predictor of left ventricular enlargement, with positive associations observed for both diastolic (LVIDd: β = 0.32 cm, 95% CI: 0.24–0.41, p < 0.001) and systolic dimensions (LVIDs: β = 0.34 cm, 95% CI: 0.26–0.43, p < 0.001). A significant reduction in fractional shortening was independently associated with anaemia (β = -5.21%, 95% CI: -7.89 to -2.53, p < 0.001), while the association with ejection fraction did not reach statistical significance (p = 0.072).

From an electrophysiological perspective, maternal anaemia was independently associated with shorter PR interval (β = -20.43 ms, 95% CI: -25.95 to -14.91, p < 0.001) and P-wave duration (β = -7.50 ms, 95% CI: -11.73 to -3.27, p < 0.001). No significant independent association between anaemia and the QTc interval was observed after adjustment (p = 0.312).

Discussion

This study demonstrates that iron deficiency gestational anaemia (IDGA) is associated with subtle but measurable alterations in neonatal cardiac structure, function, and electrophysiological parameters. Using echocardiographic and electrocardiographic evaluation, evidence of ventricular remodelling, mild systolic and diastolic functional changes, and altered cardiac conduction was identified in term neonates born to anaemic mothers.

Contrary to large epidemiological and meta-analytic evidence linking maternal anaemia with low birth weight and growth restriction [23][24]. Neonates in the anaemic group in this study showed a higher proportion of birth weights in the 3.5-4.0 kg range. Anaemia itself is unlikely to promote foetal

macrosomia; rather, these findings may reflect residual confounding by unmeasured maternal factors such as gestational weight gain, nutritional supplementation, or metabolic status. Therefore, the birth-weight finding should not be interpreted as a causal effect of anaemia. Context-dependent associations have been reported in hospital-based cohorts, particularly in settings with routine iron supplementation and adequate caloric intake [25][26], with compensatory effects of micronutrient supplementation also described [27][28] [29].

Structural echocardiographic assessment revealed reduced interventricular septal and left ventricular free wall thickness with increased left ventricular internal dimensions in neonates exposed to maternal anaemia, suggesting a pattern consistent with eccentric cardiac remodelling. Because infant size differed between groups, the adjusted regression results and indexed/ z-score approach are more appropriate for interpretation than unadjusted absolute dimensions alone. This pattern is consistent with compensatory adaptation to chronic intrauterine hypoxaemia rather than hypertrophic growth. Experimental and clinical studies have demonstrated impaired myocardial maturation and attenuated wall thickness under iron-deficient and hypoxic conditions [30][31][31], with similar remodelling reported in anaemia-exposed and growth-restricted neonates [32].

Mild reductions in left ventricular systolic function, reflected by lower ejection fraction and fractional shortening, were observed in the anaemic group. These findings are consistent with prior experimental and neonatal studies showing reduced myocardial contractility under iron-deficient and hypoxic states without overt cardiac failure [33][34][35]. Altered pulmonary haemodynamic indices, including reduced right ventricular acceleration time and pulmonary artery velocity, suggest mildly increased pulmonary vascular resistance, as described in experimental models of maternal anaemia [36][37][38]. Although the absence of significant changes in PAAT/RVAT ratios indicates these changes were likely modest and potentially reversible [39].

Electrocardiographic analysis demonstrated shortened PR interval and P-wave duration with modest QTc prolongation in neonates of anaemic mothers, suggesting altered atrioventricular conduction and ventricular repolarisation. Similar electrophysiological changes have been attributed to hypoxia-related autonomic imbalance and myocardial oxidative stress in neonatal studies [40][41]. Multivariable regression confirmed maternal anaemia as an independent predictor of neonatal cardiac remodelling and functional alterations, with fractional shortening emerging as a sensitive marker of early systolic change.

These findings support the concept of early cardiovascular programming in neonates exposed to maternal anaemia through chronic intrauterine hypoxia and hemodynamic adaptation [42][43][44].

Although limited by its cross-sectional design, lack of iron biomarker assessment, and single-centre setting, this study underscores the importance of optimising maternal iron status during pregnancy to reduce early neonatal cardiovascular adaptations

Conclusion

The study found that pregnant women who experienced iron deficiency gestational anemia displayed mild differences in their newborns' left ventricular dimensions and fractional shortening and selected ECG conduction parameters at around 72 hours after birth. Maternal anaemia showed a direct connection to increased left ventricular size and decreased fractional shortening after researchers controlled for the factors of gestational age birth weight sex and delivery method. The study found no statistical significance between ejection fraction and QTc interval after researchers adjusted for various factors. The study results should be understood as potential early cardiovascular adaptation because most findings stayed within expected neonatal limits and the study design followed observational methods. Researchers need to conduct longitudinal studies which must include necessary sample-size calculations and record complete participant movement and track neonatal iron biomarkers and indexed echocardiographic measurements and follow-up results to evaluate ongoing effects and clinical importance.

Limitations

The research contains multiple restrictions. The first restriction of the cross-sectional observational study design prevents the researchers from determining causal relationships and evaluating whether neonatal cardiac variations last beyond the first postnatal month. The second limitation arises because no sample size calculation was conducted before the study which resulted in identical group sizes of 75 neonates in each group thus creating selection bias; the study needs to provide details about its enrolment process and total number of births during the research tenure. The third requirement mandates that research groups need to show their participants' gestational age and birth weight differences while researchers conducted multivariable adjustment. The fourth limitation of the study exists because researchers did not assess neonatal iron biomarkers which prevents them from establishing direct links between neonatal iron levels and cardiac conditions. The research shows restricted generalizability because of its single-center design and moderate-sized participant group which lacks advanced echocardiographic methods like myocardial strain analysis.

Declarations

Conflict of interest:

All the authors state that there is no conflict of interest.

Funding:

No external funding was received for this study.

Contributor statement:

All authors contributed significantly to the study. Dinesh Venkatesan led the study design, data collection, laboratory work, echocardiographic data analysis, and initial drafting of the manuscript.

Sajeetha Kumari R supervised the research, validated the findings, and finalized the manuscript, while Tridip Mitra, Prem Mishra, Deeksha Punniyamoorthy, Ashok Chandrasekaran, Rajiv Janardhanan, Venkataraman P and Alfairose Jahangeerbasha provided clinical, methodological, analytical, and expert support throughout the study and contributed to manuscript review and approval.

Ethics Approval:

The current study was conducted in accordance with the principles of the Declaration of Helsinki (2013 revision) and the Indian Council of Medical Research (ICMR) National Ethical Guidelines for Biomedical and Health Research involving Human Participants. This study was approved by the Institutional Ethical Committee of SRM MCH & RC on July 19, 203 (Ethics Clearance Number: 8539/IEC/2023). Written informed consent was obtained from all participants before enrolment.

Trail Registry with date of Registration:

Not applicable

Clinical Trial No:

Not applicable

Data Availability Statement:

The data that support the findings of this study are available from the corresponding author upon reasonable request. Due to participant confidentiality, the raw data cannot be made publicly available.

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References

1. A. Debella, A. Eyeberu, T. Getachew, G. Atnafe, B. Geda, and M. Dheresa, “Perinatal outcomes in anemic pregnant women in public hospitals of eastern Ethiopia,” *Int. Health*, vol. 15, no. 3, pp. 274–280, May 2023, doi: 10.1093/inthealth/ihac021.
2. M. Malhotra, J. B. Sharma, S. Batra, S. Sharma, N. S. Murthy, and R. Arora, “Maternal and perinatal outcome in varying degrees of anemia,” *International Journal of Gynecology & Obstetrics*, vol. 79, no. 2, pp. 93–100, Nov. 2002, doi: 10.1016/S0020-7292(02)00225-4.
3. J. L. Finkelstein, A. V. Kurpad, B. Bose, T. Thomas, K. Srinivasan, and C. Duggan, “Anaemia and iron deficiency in pregnancy and adverse perinatal outcomes in Southern India,” *Eur. J. Clin. Nutr.*, vol. 74, no. 1, pp. 112–125, Jan. 2020, doi: 10.1038/s41430-019-0464-3.

4. C. Smith, F. Teng, E. Branch, S. Chu, and K. S. Joseph, “Maternal and Perinatal Morbidity and Mortality Associated With Anemia in Pregnancy,” *Obstetrics & Gynecology*, vol. 134, no. 6, pp. 1234–1244, Dec. 2019, doi: 10.1097/AOG.0000000000003557.
5. D. V. Yadav, T. Mitra, D. Punniyamoorthy, A. Murugesan, S. Kumari Raveendran, and R. Janardhanan, “Vitamins and Iron-Deficiency Gestational Anemia – A Review,” *J. Diet. Suppl.*, vol. 22, no. 6, pp. 887–906, Nov. 2025, doi: 10.1080/19390211.2025.2555013.
6. G. F. Gonzales and V. J. Suarez Moreno, “Niveles de hemoglobina para la determinación de la anemia: nueva guía de la Organización Mundial de la Salud y adecuación de la norma nacional,” *Rev. Peru. Med. Exp. Salud Publica*, pp. 102–4, Jun. 2024, doi: 10.17843/rpmesp.2024.412.13894.
7. M. K. Georgieff, “Iron deficiency in pregnancy,” *Am. J. Obstet. Gynecol.*, vol. 223, no. 4, pp. 516–524, Oct. 2020, doi: 10.1016/j.ajog.2020.03.006.
8. A. C. M. G. Figueiredo *et al.*, “Maternal Anemia and Low Birth Weight: A Systematic Review and Meta-Analysis,” *Nutrients*, vol. 10, no. 5, p. 601, May 2018, doi: 10.3390/nu10050601.
9. C. D. Holody *et al.*, “Perinatal iron deficiency alters the cardiac proteome and mitochondrial function in neonatal offspring,” *American Journal of Physiology-Heart and Circulatory Physiology*, vol. 328, no. 1, pp. H101–H112, Jan. 2025, doi: 10.1152/ajpheart.00412.2024.
10. E. I. Obeagu and G. U. Obeagu, “Hypoxia in Pregnancy: Implications for Fetal Development Article in International Journal of Current Research in Chemistry and Pharmaceutical Sciences,” 2024, doi: 10.22192/ijcrcps.
11. A. J. Patterson and L. Zhang, “Hypoxia and Fetal Heart Development,” *Curr. Mol. Med.*, vol. 10, no. 7, pp. 653–666, Sep. 2010, doi: 10.2174/156652410792630643.
12. D. V. Yadav, T. Mitra, D. Punniyamoorthy, A. Murugesan, S. Kumari Raveendran, and R. Janardhanan, “Vitamins and Iron-Deficiency Gestational Anemia – A Review,” *J. Diet. Suppl.*, vol. 22, no. 6, pp. 887–906, 2025, doi: 10.1080/19390211.2025.2555013.
13. D. Venkatesan *et al.*, “Impact of iron deficiency gestational anaemia on neonatal cardiac structure, function, and electrophysiology: a comparative cross-sectional study,” Feb. 2026, doi: 10.21203/RS.3.RS-8672612/V1.
14. M. Kluckow, I. Seri, and N. Evans, “Functional Echocardiography: An Emerging Clinical Tool for the Neonatologist,” *Journal of Pediatrics*, vol. 150, no. 2, pp. 125–130, Feb. 2007, doi: 10.1016/j.jpeds.2006.10.056.
15. Y. Singh, “Echocardiographic Evaluation of Hemodynamics in Neonates and Children,” *Front. Pediatr.*, vol. 5, Sep. 2017, doi: 10.3389/fped.2017.00201.
16. E. O. Ohuma *et al.*, “Association between maternal haemoglobin concentrations and maternal and neonatal outcomes: the prospective, observational, multinational, INTERBIO-21st fetal study,” *Lancet Haematol.*, vol. 10, no. 9, pp. e756–e766, Sep. 2023, doi: 10.1016/S2352-3026(23)00170-9.
17. M. F. Young, B. M. Oaks, S. Tandon, R. Martorell, K. G. Dewey, and A. S. Wendt, “Maternal hemoglobin concentrations across pregnancy and maternal and child health: a systematic review and meta-

analysis," *Ann. N. Y. Acad. Sci.*, vol. 1450, no. 1, pp. 47–68, Aug. 2019, doi: 10.1111/NYAS.14093;CSUBTYPE:STRING:SPECIAL;PAGE:STRING:ARTICLE/CHAPTER.

18. J. Jung *et al.*, "Effects of hemoglobin levels during pregnancy on adverse maternal and infant outcomes: a systematic review and meta-analysis," *Ann. N. Y. Acad. Sci.*, vol. 1450, no. 1, pp. 69–82, Aug. 2019, doi: 10.1111/NYAS.14112;WGROUP:STRING:PUBLICATION.
19. Y. Chen *et al.*, "Maternal anaemia during early pregnancy and the risk of neonatal outcomes: a prospective cohort study in Central China," *BMJ Paediatr. Open*, vol. 8, no. 1, p. e001931, Jan. 2024, doi: 10.1136/BMJPO-2023-001931.
20. S. Kumari *et al.*, "Maternal and severe anaemia in delivering women is associated with risk of preterm and low birth weight: A cross sectional study from Jharkhand, India," *One Health*, vol. 8, p. 100098, Dec. 2019, doi: 10.1016/J.ONEHLT.2019.100098.
21. R. Jayalakshmi *et al.*, "The Effect of Maternal Haemoglobinopathies and Iron Deficiency Anaemia on Foetal Growth Restriction: A Systematic Review and Meta-Analysis," *Matern. Child Nutr.*, vol. 21, no. 3, p. e13787, Jul. 2025, doi: 10.1111/MCN.13787;ISSUE:ISSUE:DOI.
22. M. Stramba-Badiale *et al.*, "For neonatal ECG screening there is no reason to relinquish old Bazett's correction," *Eur. Heart J.*, vol. 39, no. 31, pp. 2888–2895, Aug. 2018, doi: 10.1093/EURHEARTJ/EHY284.
23. A. C. M. G. Figueiredo *et al.*, "Maternal anemia and birth weight: A prospective cohort study," *journals.plos.orgACMG Figueiredo, IS Gomes-Filho, JET Batista, GS Orrico, ECL Porto, RM Cruz PimentaPloS one, 2019•journals.plos.org*, vol. 14, no. 3, Mar. 2019, doi: 10.1371/JOURNAL.PONE.0212817.
24. M. T. Engidaw, T. Eyayu, and T. Tiruneh, "The effect of maternal anaemia on low birth weight among newborns in Northwest Ethiopia," *Scientific Reports 2022 12:1*, vol. 12, no. 1, pp. 15280-, Sep. 2022, doi: 10.1038/s41598-022-19726-z.
25. B. Alemu and D. Gashu, "Association of maternal anthropometry, hemoglobin and serum zinc concentration during pregnancy with birth weight," *Early Hum. Dev.*, vol. 142, p. 104949, Mar. 2020, doi: 10.1016/J.EARLHUMDEV.2019.104949.
26. T. Atakul and G. O. Reprod, "Comparison of Birth Weights of Pre-Delivery Anemic and Non-Anemic Routine Iron Supplemented Pregnant Women," *Gynecology Obstetrics & Reproductive Medicine*, vol. 26, no. 1, pp. 21–24, Mar. 2020, doi: 10.21613/GORM.2020.991.
27. B. Bhowmik *et al.*, "Maternal BMI and nutritional status in early pregnancy and its impact on neonatal outcomes at birth in Bangladesh," *BMC Pregnancy and Childbirth 2019 19:1*, vol. 19, no. 1, pp. 413-, Nov. 2019, doi: 10.1186/S12884-019-2571-5.
28. H. J. J. Mohamed *et al.*, "Maternal diet, nutritional status and infant birth weight in Malaysia: a scoping review," *SpringerHJJ Mohamed, SL Loy, AK Mitra, S Kaur, AN Teoh, SHA Rahman, MS AmarraBMC pregnancy and childbirth, 2022•Springer*, vol. 22, no. 1, Dec. 2022, doi: 10.1186/S12884-022-04616-Z.

29. D. González-Fernández, O. Muralidharan, P. A. Neves, and Z. A. Bhutta, “Associations of maternal nutritional status and supplementation with fetal, newborn, and infant outcomes in low-income and middle-income settings: An,” *mdpi.comD González-Fernández, O Muralidharan, PA Neves, ZA BhuttaNutrients, 2024•mdpi.com*, vol. 16, no. 21, Nov. 2024, doi: 10.3390/NU16213725.
30. R. A. de Assunção, A. W. Liao, M. de Lourdes Brizot, R. P. V. Francisco, and M. Zugaib, “Myocardial performance index in fetal anemia,” *Prenat. Diagn.*, vol. 35, no. 2, pp. 192–196, Feb. 2015, doi: 10.1002/PD.4526;ISSUE:ISSUE:DOI.
31. G. R. Polglase *et al.*, “Altered cardiovascular function at birth in growth-restricted preterm lambs,” *Pediatric Research 2016 80:4*, vol. 80, no. 4, pp. 538–546, May 2016, doi: 10.1038/pr.2016.104.
32. J. A. Leipälä, T. Boldt, U. Turpeinen, O. Vuolteenaho, and V. Fellman, “Cardiac Hypertrophy and Altered Hemodynamic Adaptation in Growth-Restricted Preterm Infants,” *Pediatric Research 2003 53:6*, vol. 53, no. 6, pp. 989–993, Jun. 2003, doi: 10.1203/01.pdr.0000061564.86797.78.
33. S. Fouzas *et al.*, “Neonatal cardiac dysfunction in intrauterine growth restriction,” *Pediatric Research 2014 75:5*, vol. 75, no. 5, pp. 651–657, Feb. 2014, doi: 10.1038/pr.2014.22.
34. A. Sehgal, T. Doctor, and S. Menahem, “Cardiac function and arterial indices in infants born small for gestational age: Analysis by speckle tracking,” *Acta Paediatrica, International Journal of Paediatrics*, vol. 103, no. 2, pp. e49–e54, Feb. 2014, doi: 10.1111/APA.12465;JOURNAL:JOURNAL:16512227;ISSUE:ISSUE:DOI.
35. A. Sehgal, R. Bhatia, and C. T. Roberts, “Cardiovascular response and sequelae after minimally invasive surfactant therapy in growth-restricted preterm infants,” *Journal of Perinatology 2020 40:8*, vol. 40, no. 8, pp. 1178–1184, May 2020, doi: 10.1038/s41372-020-0682-5.
36. E. Cotroneo *et al.*, “Iron homeostasis and pulmonary hypertension: Iron deficiency leads to pulmonary vascular remodeling in the rat,” *Circ. Res.*, vol. 116, no. 10, pp. 1680–1690, May 2015, doi: 10.1161/CIRCRESAHA.116.305265;WGROUP:STRING:PUBLICATION.
37. F. M. Severi *et al.*, “Uterine and fetal cerebral Doppler predict the outcome of third-trimester small-for-gestational age fetuses with normal umbilical artery Doppler,” *Ultrasound in Obstetrics and Gynecology*, vol. 19, no. 3, pp. 225–228, Mar. 2002, doi: 10.1046/J.1469-0705.2002.00652.X;WGROUP:STRING:PUBLICATION.
38. S. Savchev *et al.*, “Estimated weight centile as a predictor of perinatal outcome in small-for-gestational-age fetuses with normal umbilical, brain and uterine Doppler”.
39. N. Sommer, I. Strielkov, O. Pak, and N. Weissmann, “Oxygen sensing and signal transduction in hypoxic pulmonary vasoconstriction,” *European Respiratory Journal*, vol. 47, no. 1, pp. 288–303, Jan. 2016, doi: 10.1183/13993003.00945-2015.
40. F. Demir, S. Kayali, and D. G. Gokcebay, “Does Iron Deficiency Affect the Heart in Children?,” *J. Pediatr. Hematol. Oncol.*, vol. 44, no. 3, pp. 84–88, Apr. 2022, doi: 10.1097/MPH.0000000000002170.
41. R. E. Giesinger *et al.*, “Neurodevelopmental outcome following hypoxic ischaemic encephalopathy and therapeutic hypothermia is related to right ventricular performance at 24-hour postnatal age,”

Arch. Dis. Child. Fetal Neonatal Ed., vol. 107, no. 1, pp. 70–75, Jan. 2022, doi: 10.1136/archdischild-2020-321463.

42. E. Gadelrb, R. Ewaees, and H. A. Borayek, “The effect of iron deficiency anemia on myocardial function in pediatrics,” *Prog. Pediatr. Cardiol.*, vol. 72, p. 101698, Mar. 2024, doi: 10.1016/J.PPEDCARD.2023.101698.
43. S. S. Jonker *et al.*, “Cardiomyocyte enlargement, proliferation and maturation during chronic fetal anaemia in sheep,” *Exp. Physiol.*, vol. 95, no. 1, pp. 131–139, Jan. 2010, doi: 10.1113/EXPPHYSIOL.2009.049379;PAGE:STRING:ARTICLE/CHAPTER.
44. F. Telles *et al.*, “Changes in the Preterm Heart from Birth to Young Adulthood: A Meta-analysis,” *Pediatrics*, vol. 146, no. 2, Aug. 2020, doi: 10.1542/PEDS.2020-0146/77020.