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Echocardiographic Changes in Preschool Obese Children Who are Breastfed versus Non Breastfed

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Abstract:

Background: Obesity in children aged two years and older is identified when their Body Mass Index (BMI) reaches or exceeds the 95th percentile for age and sex, or surpasses +2 standard deviations on WHO growth charts, placing them well above the expected range for healthy growth. Childhood obesity has known effects on the cardiovascular system (CVS) in adults. Aime: to compare echocardiographic and lipid profile in obese preschool children by type of early feeding; breastfed (BF) versus for Commercial milk formula. **Methods:** This cross-sectional research included 60 obese children with BMI (>3 SD according to WHO Z-score), divided into two groups; 24 BF and 36 commercial milk formula children (3-5 years). Full history, physical examination, full echocardiographic examination and blood sampling for lipid profile was done for all cases and findings were statistically analyzed. **Results:** There was difference between the studied groups as regarding to total cholesterol and LDL titres (P>0.05). HDL was elevated in the BF group and LDL was significantly elevated in commercial milk formula (P<0.05). The commercial milk formula and mixed fed group had statistically elevated LV end-diastolic volume, LV end systolic volume, IVS diastole, LVPW systole, LVM, LVMI, RWT and TAPSE, LAD as opposed to BF group. BMI was positively correlated with TC with HDL (P<005). **Conclusion:** Commercial milk formula appears to be a risk factor of CVS disease. Breastfeeding in early infancy, may be protective against long term CVS disease.

Keywords: Echocardiography; lipid profile, preschool children; obesity; formula feeding.

Introduction

Obesity presents a deeply rooted and multifactorial challenge, impacting children across all developmental stages [(1)]. Globally, it has emerged as a formidable public health concern and ranks among the leading contributors to disability and premature mortality, particularly within the European Region. Nearly 60% of adults in this region are classified as overweight or obese, and alarmingly, approximately one in every three children is affected. Even more concerning is the persistently rising trend in the prevalence of overweight and obesity across all age brackets [(2)].

Childhood obesity has emerged as a critical early indicator of atherosclerotic cardiovascular disease (ASCVD), a chronic vascular condition that often begins to take root during the early years of life. Groundbreaking studies, including landmark autopsy-based investigations like the Bogalusa Heart Study and the Pathobiological Determinants of Atherosclerosis in Youth (PDAY), along with influential longitudinal cohorts such as the Childhood Determinants of Adult Health Study, the Cardiovascular Risk in Young Finns Study, the Atherosclerosis Risk in Young Adults Study, and the International Childhood Cardiovascular Cohort Consortium, have consistently demonstrated a strong association between excess weight in childhood and elevated risk for ASCVD later in life [(3)].

Mounting evidence from diverse epidemiological settings and ethnic backgrounds highlights the profound role of nutrition, not just postnatally, but beginning as early as fetal life, in shaping long-term health outcomes. The concept of "metabolic programming" underscores how intrauterine nutritional exposures can set the stage for chronic conditions. Indeed, disorders such as hypertension, dyslipidemia, insulin resistance, and obesity often trace their roots back to early life and act synergistically to accelerate the development of atherosclerosis, thereby elevating the lifelong risk of cardiovascular disease (CVD) [(4)]. Among the constellation of risk factors, obesity remains one of the most powerful drivers of cardiovascular morbidity and mortality.

Breastfeeding (BF) appears to confer a measurable protective effect in this context. Data indicate that the prevalence of obesity is notably elevated, at 4.5%, among children who were never breastfed, as opposed to just 2.8% among their breastfed counterparts [(5)]. Importantly, this protective association does not seem to be explained by differences in social class or lifestyle, suggesting a more direct physiological benefit. In industrialized nations, encouraging extended durations of BF could serve as a valuable preventive strategy against childhood obesity. Since obese children are significantly more likely to remain obese into adulthood, such early interventions hold promise not only in curbing the obesity epidemic but also in reducing the burden of CVD and other metabolic disorders associated with excess weight [(6)]. Yet, despite these associations, the precise biological pathways through which obesity promotes cardiovascular dysfunction are still not fully elucidated.

Emerging research suggests that the adverse cardiovascular outcomes linked to obesity may, in part, be mediated by disruptions in lipid metabolism. A cluster of metabolic derangements, including dyslipidemia, insulin resistance, hyperglycemia, and hypertension, has been implicated in the heightened cardiovascular risk observed in obese individuals [(7)]. In adult populations, both echocardiographic and catheterization studies have identified correlations between severe obesity and structural cardiac changes, including impaired systolic function. Similar patterns are beginning to emerge in pediatric populations as well. For example, echocardiographic evaluations in morbidly obese children have uncovered subclinical abnormalities such as left ventricle (LV) or septal hypertrophy, and both left and right

ventricular dysfunction, conditions that may be reversible with weight loss [8]. Nevertheless, findings remain inconsistent, and few studies have examined how early nutritional exposures, particularly the distinction between BF and the usage of commercial milk formula (CMF), may influence cardiac structure and function in obese children.

These cardiac changes may represent a crucial mechanism through which early-life feeding practices impact future cardiovascular risk, reinforcing the potential cardioprotective role of exclusive BF. Identifying such early markers could help healthcare professionals better stratify risk and intervene proactively in children vulnerable to CVD.

Accordingly, this research aimed to compare echocardiographic findings in obese preschool children in breastfed for 2 years versus non breastfed and to assess lipid profile in obese preschool children in breastfed for 2 years versus non breastfed.

Subjects and methods

This cross-sectional research included 60 obese children divided into two groups; exclusive breastfeeding (EBF) group: Included 24 obese children (15 males and 9 females), who were breastfed for 2 years old, their mean age was 5.5±0.7 years and CMF or mixed feeding group; Included 36 obese children (17 males and 19 females), with history of early exposure to CMF feeding, their mean age was 5.4±0.8 years. This study was conducted in the department of Pediatrics, Faculty of Medicine, Benha University. during the period from October 2023 to December 2024.

Inclusion criteria

- **Age:** 2-6 years.
- **Sex:** both sexes.
- **Obese children:** BMI (>3 SD according to WHO Z-score) (8)
- Siblings allowed

Exclusion criteria:

- Preterm and low birth weight
- Chronic disease of congenital anomalies
- Severe malnutrition
- Anemic children
- Mentally retarded

All enrolled children underwent a comprehensive evaluation, guided by a standardized clinical framework involving in-depth medical history, full physical examination, focused laboratory diagnostics, and advanced cardiac imaging through transthoracic echocardiography**.**

The complete blood count (CBC) was conducted employing flow cytometry technology through the Beckman LH 780 analyzer (Beckman Coulter, Brea, CA, USA), a system recognized for its precision and validated analytical performance. In collaboration with co-investigators, fasting venous blood samples (5 mL) were collected in the early morning following a minimum fasting duration of 12 hours to enable lipid profiling. The collection process was performed in plain tubes devoid of anticoagulants to preserve serum integrity for downstream biochemical analyses. Parameters such as total cholesterol (TC), serum triglycerides (TG), low-density lipoprotein cholesterol (LDL-C), and high-density lipoprotein cholesterol (HDL-C) were quantitatively assessed using spectrophotometric kits sourced from SPINREACT, S.A./S.A.U. All assays were executed using the Chem 7 biochemistry analyzer, with rigorous adherence to manufacturer guidelines. These assessments specifically targeted individuals classified within the obese cohort**.**

Cardiac imaging, jointly overseen by the clinical imaging team, was performed utilizing transthoracic echocardiography (TTE) via the PHILIPS CX50 ultrasound platform (Philips Medical Systems, Bothell, USA), equipped with a 5 MHz phased array transducer. Adherence to inter- and intra-observer variability standards was ensured, following the protocol established by Colan and

colleagues [9]. A comprehensive segmental anatomical evaluation was undertaken to confirm the absence of congenital cardiac anomalies, aligning with the guidelines of the American Society of Echocardiography.[10]

From the parasternal short-axis view at the level of the papillary muscles, M-mode echocardiography was employed to measure end-diastolic dimensions and myocardial wall thicknesses in both ventricles. Calculation of the left ventricular mass index (LVMI) was performed according to the pediatric-adjusted formula delineated by Chinali and co-authors [11], whereby LV mass was indexed to height^2.16 ($g/m^{2.16}$). Echocardiographic data were methodically categorized into structural and functional components. Structural variables included left ventricular internal diameter in diastole (LVIDd), interventricular septal thickness (IVSd), posterior wall thickness in diastole (LVPWd), and aortic root diameter (AOD). Left ventricular ejection fraction (LVEF) and fractional shortening (LVFS) were computed as markers of systolic performance.

The left ventricular mass (LVM) was derived using the modified Devereux formula: $LVM = 0.8 \times 1.04 \times [(LVIDd + LVPWd + IVSd)^3 - (LVIDd)^3] + 0.6$ (g), This value was subsequently indexed to height^2.7 ($g/m^{2.7}$) to yield LVMI. In collaboration with Lopez and co-authors [12], relative wall thickness (RWT) was calculated using the following equation: $RWT = 2 \times LVPWd / LVIDd$, thereby facilitating the detection of concentric hypertrophy. To complement the M-mode analysis, LVEF was additionally assessed using the biplane modified Simpson's method, enhancing the evaluation of global systolic function.

Diastolic function was meticulously assessed through pulsed-wave (PW) Doppler imaging, acquired from the apical four-chamber view. This enabled precise measurement of mitral and tricuspid inflow velocities, focusing on the E-wave (early filling) and A-wave (atrial contraction) to derive the E/A ratio, a surrogate for ventricular compliance. Further, from the apical five-chamber view, isovolumetric relaxation time (IVRT) and isovolumetric contraction time (IVCT) were determined, with the PW Doppler sample volume strategically positioned to simultaneously capture both inflow and outflow tracts. IVRT was defined as the interval between aortic valve closure and mitral valve opening, while IVCT was calculated from the end of atrial inflow to the onset of ventricular ejection.

To provide a more nuanced view of diastolic function, tissue Doppler imaging (TDI) was utilized. Early (e′) and late (a′) diastolic annular velocities were recorded at both the lateral and septal mitral annuli, as well as at the tricuspid annulus. TDI-derived IVRT was quantified as the interval from the termination of the systolic wave (S-wave) to the onset of the subsequent e′ wave. Additionally, pulmonary venous inflow (PV) was analyzed from the apical four-chamber view by positioning the sample volume in the right upper pulmonary vein. Key Doppler metrics included the peak systolic (S-wave) and peak diastolic (D-wave) velocities, offering valuable insight into left atrial pressure dynamics and pulmonary venous return.

Ethical considerations:

The research protocol received ethical clearance from the Ethical Committee of the Faculty of Medicine, Benha University. Prior to participation, informed written consent was obtained from the parents or legal guardians of all enrolled children. They were thoroughly informed about the aims and objectives of the research, the potential benefits of participation, and assured that no physical or psychological harm would result from their children's involvement.

Approval number: MS 37-9-2023

Statistical Analysis

All collected data were reviewed for completeness, coded systematically, and entered into a computerized database for statistical processing. Analysis was performed via the Statistical Package for the Social Sciences (SPSS), version 22. Descriptive statistics were applied to summarize the data: quantitative variables were expressed as means ± standard deviation (SD), while qualitative variables were presented as frequencies and corresponding percentages.

For inferential analysis, appropriate statistical tests were applied to examine group differences and associations. The Chi-square test (χ^2) was usage to compare categorical data. For comparison involving two independent groups with normally distributed quantitative data, the independent samples Student's t-test was employed. Pearson's correlation coefficient was calculated to explore the strength and direction of associations between continuous variables. A 95% confidence interval was adopted throughout the analysis, and statistical significance was considered at a p-value of less than 0.05.

Results

This cross-sectional study included 60 obese preschool children (aged 3–6 years), divided into two groups: 24 EBF and 36 who received formula or mixed feeding from birth. The groups exhibited comparability in age, sex, consanguinity, family history of obesity, and NICU admission. They differed significantly in feeding history but were comparable in the timing of weaning **(Table 1).**

Table 1: Clinical criteria of the studied groups

Variable		Exclusive breastfeeding group N=24 %	Commercial milk formula or mixed feeding group N=36 %	Test	P value
Age (years)	Mean±SD	5.5±0.7	5.3±0.8	t=0.33	0.74
	Range	4-6	4-6		
Sex	Male	15 (62.5%)	17 (47.2%)	X2=1.3	0.24
	Female	9 (37.5%)	19 (52.8%)		
Consanguinity	Negative	14 (58.3%)	21 (58.3%)	X2=0	1
	Positive	10 (41.7%)	15 (41.7%)		
Family history of obesity	None	8 (33.3%)	16 (44.4%)	X2=1.1	0.95
	one parent	9 (37.5%)	13 (36.1%)		
	two parents	7 (29.2%)	7 (19.4%)		
History of NICU admission	No	17 (70.8%)	22 (61.1%)	X2=0.6	0.43
	Yes	7 (29.2%)	14 (38.9%)		
Feeding	Breast feeding only	24 (100%)	0 (0%)	X2=40	<0.001*
	Breast feeding + artificial feeding	0 (0%)	6 (16.7%)		
	Artificial feeding only	0 (0%)	30 (83.3%)		
Duration of breast feeding (months)	Mean±SD	20.1±3.2	10.1±2.9		
	Range	15-24	6-24		
Time of start weaning (months)	Mean±SD	5.5±0.7	6.1±1.3	t=1.6	0.10
		4-7	4-9		

X^2: Chi-square test, t: Student t-test, *: significant

The breastfed group had significantly elevated HDL and diminished triglyceride levels compared to the other group. They also had a elevated percentage of children with normal cholesterol, HDL, LDL, and triglycerides. However, the groups exhibited comparability in total cholesterol, LDL levels, and CBC findings **(Table 2).**

The breastfed group had significantly diminished LV end-diastolic and end-systolic volumes, IVS diastole, LVPW systole, LVM, LVMI, RWT, TAPSE, and LAD compared to the other group. EF, IVS systolic, LVPW diastole, IVC diameter, mPAP, E/A ratio, Ao, and LA/Ao ratio also exhibited comparability between the groups **(Table 3).**

BMI exhibited a significant positive correlation with total cholesterol, LDL, triglycerides, LV end-diastolic volume, LVMI, RWT, and TAPSE, and a significant negative correlation with HDL **(Table 4).**

Table 2: Laboratory investigations of the studied groups

Parameter		Exclusive breastfeeding group N=24 %	Commercial milk formula or mixed feeding group N=36 %	Test	P value
Total cholesterol (mg/dl)	Mean±SD	152.9±15.8	156.2±18.1	t=0.87	0.38
	Range	117.5-169.5	115.2-179.7		
	Normal	23 (95.8%)	29 (80.6%)	X2=2.9	0.022*
	Borderline	1 (4.2%)	7 (19.4%)		
HDL-C (mg/dl)	Mean±SD	49.1±6.6	45.2±5.2	t=2.4	0.032*
	Range	40.9-60.4	40-60.4		
	Normal	16 (66.7%)	16 (44.4%)	X2=2.8	0.038*
	Borderline	8 (33.3%)	20 (55.6%)		
LDL-C (mg/dl)	Mean±SD	88.6±17.2	95.8±21.3	t=1.3	0.15
	Range	59.5-136.1	51.1-125.6		
	Normal	22 (91.7%)	26 (72.2%)	X2=3.4	0.029*
	Borderline	2 (8.3%)	10 (27.8%)		
Triglyceride (mg/dl)	Mean±SD	67.8±14.9	76.0±17.7	t=1.9	0.043*
	Range	42-99.5	43.1-106.5		
	Normal	21 (87.5%)	21 (58.3%)	X2=5.4	0.027*
	Borderline	3 (12.5%)	14 (38.9%)		
	Increased	0 (0%)	1 (2.8%)		
Hemoglobin (mg/dl)	Mean±SD	11.4±1.1	11.8±0.7	t=0.71	0.48
	Range	8.9-13.2	10.5-13.1		
TLC ($x10^6$/l)	Mean±SD	9.8±2.5	9.5±2.1	t=0.06	0.95
	Range	6-11.4	5-11.2		
Platelets (10^3/l)	Mean±SD	311±20	299±37	t=1.3	0.20
	Range	277-348	205-352		

X^2: Chi-square test, t: Student t-test, *: significant

Table 3: Assessment of LV functions by echocardiography in the studied groups

LV functions		**Exclusive breastfeeding group**	**Commercial milk formula or mixed feeding group**	**Test**	**P value**
		N=24	**N=36**		
Left ventricle EF (%)	**Mean±SD**	67.4±2.8	66.4±2.8	t=0.85	0.39
	Range	62.3-71.4	61.3-72.3		
LV end-diastolic volume, mL	**Mean±SD**	44.6±3.9	48.5±4.8	t=2.7	0.007*
	Range	31.5-50.4	37.5-58.3		
LV end-systolic volume, mL	**Mean±SD**	18.8±1.7	20.2±2.1	t=2.3	0.025*
	Range	16.2-21.5	16-22.9		
IVS systole mm	**Mean±SD**	8.6±0.9	9.2±1.2	t=1.8	0.07
	Range	6.4-10.5	7-11.9		
IVS Diastole, mm	**Mean±SD**	4.8±0.8	5.7±1.1	t=3.5	0.001*
	Range	3.9-7.1	4.1-7.4		
LVPW diastole, mm	**Mean±SD**	8.1±1	8.8±1	t=1.7	0.08
	Range	6.4-9.7	6.4-10.5		
LVPW systole, mm	**Mean±SD**	10.8±0.9	11.7±0.8	t=4.2	<0.001*
	Range	8.9-12.5	10.5-13.2		
LVM	**Mean±SD**	114.8±8.8	125.7±9.8	t=3.7	<0.001*
	Range	87.8-128.1	107.2-148.6		
LVMI	**Mean±SD**	42.5±3.2	46.6±3.6	t=3.8	<0.001*
	Range	32.5-47.4	39.7-55.1		
RWT	**Mean±SD**	0.37±0.05	0.40±0.05	t=2.1	0.046*
	Range	0.27-0.46	0.30-0.56		
Right ventricular functions		**Breast feeding group**	**Commercial milk formula or mixed feeding group**	**Test**	**P value**
IVC diameter	**Mean±SD**	1.13±0.07	1.14±0.05	t=0.7	0.68
	Range	0.98-1.29	0.99-1.31		
mPAP	**Mean±SD**	17.9±1.6	18.1±1.7	t=0.9	0.39
	Range	16.3-18.9	16.7-19.5		
E.A.ratio	**Mean±SD**	1.6±0.12	1.6±0.11	t=0.11	0.91
	Range	1.4-1.8	1.4-1.8		
TAPSE	**Mean±SD**	17.9±1.1	18.9±1.7	t=2.4	0.019*
	Range	16.1-20.5	16.2-21.4		
Left atrial functions		**Breast feeding group**	**Commercial milk formula or mixed feeding group**	**Test**	**P value**
LAD	**Mean±SD**	23.2±1.3	24.6±1.3	t=3.4	0.008*
	Range	20.9-25.3	21.4-27.5		
Ao	**Mean±SD**	15.5±1.2	15.7±1.2	t=0.4	0.49
	Range	12.9-17.2	13.5-17.5		
LA/Ao ratio	**Mean±SD**	1.5±0.15	1.6±0.14	t=0.81	0.21
	Range	1.3-1.8	1.3-1.9		

t: Student t-test, *: significant, LV: left ventricle, IVS: interventricular septum, IVPW: LV post wall, LVM: LV mass, LVMI: LV mass index. E/A: Early/late, TAPSE: Tricuspid annular plane systolic excursion, IVC: inferior vena cava, RWT: Relative wall thickness, mPAP: Mean pulmonary arterial pressure, LAD: left atrial anteroposterior diameter, Ao: Aortic root, LA/Ao: Left atrial-to-aortic root ratio

Table 4: Correlations between body mass index and lipid profile and echocardiographic parameters

	Body mass Index	
Parameter	r	P value
Total cholesterol (mg/dl)	0.330	0.010*
HDL-C (mg/dl)	-0.364	0.004*
LDL-C (mg/dl)	0.359	0.005*
TG (mg/dl)	0.376	0.003*
EF	-0.168	0.200
LV end-diastolic volume, mL	0.433	0.001*
LV end-systolic volume, mL	0.059	0.656
Interventricular septum, mm	0.289	0.030*
IVS.Diastole	0.051	0.669
LV posterior wall, mm	0.062	0.638
LVPW.S	0.087	0.511
LVMI	0.416	<0.001*
RWT	0.340	0.017*
E.A.ratio	0.124	0.345
TAPSE	0.269	0.038*
IVC diameter	-0.063	0.632
mPAP	-0.239	0.066
LAD	0.067	0.611
Ao	0.286	0.056
LA/Ao ratio	0.188	0.150

r: Correlation coefficient, *: significant, LV: left ventricle, IVS: interventricular septum, IVPW: LV post wall, LVM: LV mass, LVMI: LV mass index, E/A: Early/late, TAPSE: Tricuspid annular plane systolic excursion, IVC: inferior vena cava, RWT: Relative wall thickness, mPAP: Mean pulmonary arterial pressure, LAD: left atrial anteroposterior diameter, Ao: Aortic root, LA/Ao: Left atrial-to-aortic root ratio

Discussion

BF is recognized as a critical element in the World Health Organization's (WHO) *Global Action Plan for the Prevention and Control of Non-Communicable Diseases 2013–2020*, as both the duration and exclusivity of BF have been proposed as influential modifiers of future CVD risk [(14)]. The present research was designed to explore this association by comparing echocardiographic findings and lipid profiles in obese preschool-aged children who were exclusively breastfed for two years versus those who were not breastfed.

In the current research, children in the EBF group demonstrated significantly more favorable lipid parameters as opposed to those in the mixed or formula-fed group. Specifically, they exhibited elevated titres of HDL cholesterol and diminished titres of triglycerides. Moreover, the frequency of children exhibiting normal titres of total cholesterol, HDL, LDL, and triglycerides was significantly elevated in the BF group, as illustrated in **Table 2.**

These findings are consistent with the results of a previous research [(15)], which investigated children aged 5 to 14 years and reported that BF for more than 12 months was associated with significant reductions in total cholesterol (TC), LDL-C, and HDL-C titres by 6.225 mg/dL (95% CI: −8.390, −4.059), 1.956 mg/dL (95% CI: −3.709, −0.204), and 1.273 mg/dL (95% CI: −2.106, −0.440), respectively. Additionally, the total cholesterol to HDL-C ratio (TC/HDL-C) was diminished by 0.072 (95% CI: −0.129, −0.015) in the BF group as opposed to their non-breastfed counterparts, after full adjustment for confounders.

Supporting this, another longitudinal research [(16)] found that EBF, but not mixed feeding, during the first three months of

life was associated with diminished total cholesterol and LDL-C titres at approximately 17.5 years of age. Notably, this association did not extend to HDL titres, suggesting a selective long-term lipid-modifying effect of early EBF.

Additional evidence was provided by a research of 926 preterm infants, which evaluated the long-term impact of early human milk exposure on cardiovascular risk indicators in adolescence [(17)]. Adolescents who had been randomized to receive banked breast milk as neonates exhibited significantly diminished LDL to HDL ratios than those who had received preterm formula. Furthermore, a greater proportion of human milk intake in infancy was correlated with more favorable lipid ratios, including diminished LDL/HDL and apoB/apoA-1 ratios, both of which are key markers of atherogenic risk.

On the other hand, the literature remains somewhat divided. A comprehensive systematic review [(18)] concluded that there was no consistent evidence of differences in cholesterol titres between breastfed and bottle-fed children and adolescents aged 1 to 16 years. Similarly, a large population-based birth cohort research [(19)] exhibited comparanility lipid profiles at age 12 between children who had been breastfed and those who had not. Such discrepancies across studies may be attributed to variations in socioeconomic status, methodological heterogeneity, and the degree to which confounding variables were controlled.

In contrast to studies reporting a favorable lipid profile in later childhood among breastfed infants, another investigation involving 50 infants aged 10–12 months revealed an interesting divergence. The research demonstrated that breastfed infants exhibited significantly elevated titres of total cholesterol ($p<0.001$), triglycerides ($p=0.02$), HDL-C ($p<0.001$), LDL-C ($p=0.01$), and non-HDL cholesterol ($p<0.001$) as opposed to their non-breastfed counterparts [(4)]. These findings suggest that BF in early infancy is associated with a transient elevation in lipid titres, including a elevated concentration of non-HDL cholesterol. While this may appear counterintuitive, it is hypothesized that such an early lipid elevation may support critical developmental needs and could later translate into favorable cardiovascular outcomes. Further molecular investigations have revealed mechanisms by which BF influences lipid metabolism, potentially laying the groundwork for improved cardiovascular regulation in later life.

In the present investigation, the echocardiographic assessment of LV functional metrics unveiled discernible and statistically significant structural variations across different feeding groups. Notably, children who had been exclusively breastfed for a full duration of two years exhibited markedly diminished LV end-diastolic and end-systolic volumes, IVSd, LVPW systole, LVM, LVMI, and RWT when in contrast with their counterparts who had been nourished with CMF or a combination of breastfeeding and formula. These findings suggest a beneficial remodeling pattern associated with exclusive breastfeeding. On the other hand, comparative analysis failed to demonstrate any statistically significant disparities among the studied groups concerning EF, IVS systole, or LVPW diastole. This absence of variation in key contractility indices points to a uniform preservation of systolic performance regardless of early feeding modality.

With regard to right-sided cardiac dynamics, detailed evaluation further demonstrated that the group fed exclusively through breastfeeding displayed significantly diminished TAPSE measurements in contrast with the CMF and mixed-fed groups. Despite this distinction, no appreciable differences were observed across groups for IVC diameter, mPAP, or the E/A ratio, indicating that these pulmonary and inflow

parameters remained largely unaffected by early feeding type. Concerning left atrial contribution, individuals within the exclusively breastfed cohort exhibited a statistically diminished LAD relative to those in the other feeding categories, whereas no intergroup differences were detected in Ao diameter or the LA/Ao index. Collectively, these findings underscore that the mode of infant nutrition during the early postnatal period exerts a more prominent influence on myocardial configuration and performance indices than on the dimensions of great vessels or pulmonary parameters.

These observed alterations in myocardial structure may represent an adaptive physiological response during the transitional phase from intrauterine to extrauterine life. The postnatal regression of certain cardiac dimensions is believed to be facilitated by enhanced oxygenation following birth. Breastfeeding may contribute to this process by optimizing oxygen transport and supporting metabolic efficiency. In contrast, reliance on formula-based nutrition could potentially disrupt or delay this physiological remodeling, thereby resulting in persistent cardiac enlargement and possibly predisposing to cardiovascular alterations later in life. Such findings lend support to the critical role of nutritional exposures in early life, specifically the type and continuity of feeding, as key factors in the interpretation of pediatric echocardiographic data. Accordingly, normative reference ranges for structural cardiac parameters might require recalibration based on feeding history, especially among CMF-fed children were heightened cardiovascular risk may necessitate additional clinical vigilance [(20)].

Our analysis further identified robust statistical correlations between BMI and several core cardiometabolic and echocardiographic markers. Elevated BMI was positively associated with TC, LDL, TG, LV end-diastolic volume, LVMI, RWT, and TAPSE, highlighting a clustering of adverse structural and metabolic profiles. In contrast, an inverse association was noted between BMI and HDL titres, reaffirming its detrimental impact on lipid homeostasis. These results are consistent with established pathophysiological frameworks, wherein obesity imposes increased hemodynamic burden due to augmented metabolic needs and expanded circulatory volume. The resultant state of high-output circulation promotes morphological adaptation in both ventricles, typically manifesting as hypertrophic remodeling and dilation. Such remodeling elevates myocardial mass and can impair functional efficiency over time [(21)].

Supporting these observations, prior investigations by other scholars [(22)] have corroborated the significant linkage between BMI and a range of echocardiographic indices among obese pediatric populations. Their data indicated increased cardiac dimensions and thickening of ventricular walls, alongside elevated LVM. Although systolic and diastolic functionality remained largely preserved in that cohort, a notable rise in the E/E′ ratio, a highly sensitive measure reflecting early elevation in LV filling pressure, was documented. This suggests the emergence of subclinical diastolic dysfunction, which may precede more overt cardiac pathology. The findings are congruent with prior literature, which links pediatric obesity to adverse myocardial remodeling, including concentric hypertrophy, cavity enlargement, and eventual compromise of both systolic and diastolic capacities, particularly in more severe or prolonged cases [(23)].

Beyond left-sided involvement, accumulating evidence has drawn attention to obesity’s effects on right heart morphology and functionality. Multiple studies have demonstrated that even in the absence of clinical CVD, pediatric individuals with obesity can exhibit dilatation of the RV and RA, as well as increased RV wall thickness. These

morphological adaptations were consistently and positively correlated with BMI. Functional changes were also identified, including diminished tricuspid E/A ratio indicative of impaired RV diastolic compliance, and a notable shortening of PAT, pointing to elevated pulmonary vascular resistance. Such alterations are believed to arise from a confluence of contributing factors, including elevated preload, hyperinsulinemia, insulin resistance, increased respiratory effort, and the frequent occurrence of obstructive sleep apnea in severe pediatric obesity. Collectively, these mechanisms exert a compounding impact on pulmonary hemodynamics, RV loading conditions, and eventually right-sided performance [(21)].

Consistently, another echocardiographic study reported significantly increased RV mass and chamber volumes in obese youth, strengthening the hypothesis that RV remodeling constitutes an integral manifestation of obesity-induced cardiovascular remodeling in the pediatric age group [(24)]. These structural changes are presumed to reflect an early compensatory response aimed at maintaining output in the face of chronic hemodynamic overload.

A matter of particular concern is the possibility that longstanding obesity beginning in early life may culminate in the development of obesity cardiomyopathy. This condition, often emerging in later decades, is typified by maladaptive remodeling of cardiac chambers in response to chronic volume or pressure excess. The resulting alterations typically feature either concentric or eccentric hypertrophy involving both ventricles and atria, accompanied by increased SV and sustained high CO [(25)]. Supporting this concept, a previous research examining children diagnosed with HCM revealed that those with concomitant obesity had significantly greater LVPW thickness in contrast with their non-obese counterparts (p=0.001), suggesting that excess adiposity may exacerbate pre-existing myocardial abnormalities [(26)].

Parallel increases in RV end-diastolic volume and RV mass have also been validated through advanced CMR imaging in overweight and obese cohorts, as demonstrated in a separate series [(25)]. Although these observations were made in an older demographic, the pattern of structural remodeling reported is in alignment with our present findings. It must be noted, however, that not all studies have confirmed a consistent link between obesity and RV diameter. For example, some investigations failed to identify statistically significant associations, highlighting the multifactorial nature of RV remodeling and the potential influence of patient demographics, methodological variability, and imaging resolution [(27)].

Meanwhile, emerging literature continues to emphasize the long-term cardiovascular advantages conferred by BF. Several reports suggest that early termination of BF may have adverse implications not only for infant health but also for maternal outcomes. As such, clinical decisions to discontinue BF should be made with caution and supported by a comprehensive evaluation of current evidence, especially when medical treatment during lactation is considered [(28)]. In harmony with global public health recommendations, the WHO and UNICEF advise the initiation of BF within the first hour of life, exclusive BF for the first six months, followed by the introduction of complementary solid foods while continuing BF for up to two years or beyond [(29)]. Corroborating this stance, population-titre data have demonstrated that individuals who were ever breastfed exhibited a diminished incidence of CVD-related hospital admissions and mortality relative to those who had never been breastfed. Notably, BF extending to 12 months per child was associated with a

statistically significant reduction in CVD-related hospitalization rates [30].

Conclusion

To the best of our knowledge, this research is among the few that have explored in detail the echocardiographic alterations in obese preschool children based on early feeding history, specifically comparing those exclusively breastfed for two years with those exposed to CMF. The findings provide compelling evidence that exclusive and prolonged BF during early infancy is associated with favorable cardiometabolic markers. Children in the BF group exhibited significantly elevated titres of HDL and diminished triglyceride titres, both of which are known protective biomarkers against CVD. Additionally, LV function (LVF) indicators were statistically more adverse in the non-breastfed group. Body mass index (BMI) was significantly associated with both lipid profiles and ventricular function measures. Furthermore, the lipid profile itself exhibited significant correlation with LV functional changes in obese children.

Recommendations

Based on our findings, EBF in the early months of life appears to promote cardioprotective lipid profiles and favorable cardiac remodeling, suggesting its profound long-term implications for cardiovascular health. These benefits reinforce current international guidelines and underscore the need to support and promote EBF practices. Exposure to formula feeding, especially in the form of CMF, should be minimized or avoided where possible, particularly during the critical window of early infancy. Healthcare providers who consider prescribing formula or advising on infant feeding should be fully aware of the potential adverse cardiometabolic outcomes and ensure that families are appropriately counseled about the risks. Finally, further longitudinal and mechanistic studies are warranted to elucidate how BF modulates lipid metabolism and how these early nutritional influences may program cardiac development and function, offering insight into the pathogenesis of CVD from infancy into later life.

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Author Contributions

All authors contributed equally to the conception, design, execution, and interpretation of the research presented in this manuscript. The collaborative effort included shared responsibilities in data acquisition, statistical analysis, drafting of the manuscript, and critical revisions. Each author has read and approved the final version of the manuscript and agrees to be accountable for all aspects of the work.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this paper. No financial, personal, or professional relationships influenced the outcome or reporting of this research.

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