

Echocardiography of the Right Ventricle in Infancy: Do Early Feeding Practices Make a Difference?

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Abstract

Background: The role of various feeding practices during infancy on the development of the cardiac structures, particularly the right side of the heart is not clearly defined.

Aim: To compare structures and functions of right side of the heart in exclusively breastfed and formula fed babies in the first year of life.

Methods: A cross-sectional study was conducted for 76 healthy infants age 6 to 24 months of life of whom 38 were exclusively breastfed (EBF) and 38 were formula fed (FF) in the first six months of life. The right ventricular functions and dimensions of the chamber were assessed by echocardiography. The measurements included % fractional shortening (%FS), right ventricular velocity time integral (RV-VTI), cardiac output (CO) and tricuspid annular plane systolic excursion (TAPSE), e prime and s prime.

Results: Mean values of %FAC for right side was significantly higher in EBF infants in ($51.33, \pm SD = 5.20$) than in FF infants (49.22 ± 3.75) at $P < 0.05$. There was a significant increase in mean RV VTI values in EBF infants (17.2 ± 2.73) than FF infants (15.9 ± 1.94) $P < 0.01$. We noticed significant increase (COP) in EBF infants (5.81 ± 1.01) than FF infants (5.26 ± 1.18). TAPSE was significantly higher in EBF infants (1.56 ± 0.18) than FF infants (1.46 ± 0.20) at $P < 0.05$. There was no significant difference was identified between male and female infants in both groups.

Conclusion: The findings suggest that early feeding patterns in infancy may influence functions and structures of right side of the heart in infancy. Exclusive breastfeeding supports higher performance and may explain their exhibit higher resilience to cardiac insults later in life.

Keywords: Echocardiography; Right Ventricle; Breastfeeding; Formula Feeding; Cardiac Function; Infancy

Introduction

The cardiovascular system has high growth and developmental rates in early life and suboptimal diet during this period such as infancy may permanently affect cardiovascular development [3]. So, the patterns of nutritional exposures during infancy have an essential role in the cardiovascular development and associated cardiovascular disease that may occur in adulthood [1,2].

Breastfeeding might have protective vascular effects.

Aim of the Study

The aim of this study is to compare cardiovascular structures and function of right chamber of the heart in exclusively breast-fed and formula-fed babies in the first year of life.

Materials and Methods

Study design and population

This is cross sectional case-control study that compromise cardiac functions and dimensions in exclusively breastfed (EBF) infants with infants who were not breastfed i.e. formula fed (FF). This study was carried out for 76 infants aged from 3 - 12 months, this was divided into two groups: Group (I): 38 EBF infants, Group (II): 38 FF infants. Inclusion criteria were included healthy full term babies from birth until age of one year of both male and female babies and exclusively breastfeeding or formula feeding from birth. Exclusion criteria were included major congenital anomalies, acute or chronic diseases, babies on medications or exposed to irradiation and congenital heart disease. The children were selected from the outpatient clinic of Benha university Hospital. Anthropometric measurements for weight, supine length and head circumference were done by standard methods. Body mass index (BMI) was used as an indicator of overweight or obesity and was calculated from weight in kg by length squared in meters [4]. General and systemic examination for heart and chest were done to exclude any abnormality.

Ethical approvals

The study was approved by Ethics Committee of Faculty of Benha University. Confidentiality was taken in consideration by using code number cod refer to name of the baby. Verbal informed consents were obtained from parents of all subjects of the study.

Echocardiography studies

Cardiac output (CO), heart rate (HR) and body surface area (BSA) were estimated by standard methods. Echocardiography measurements included right ventricular diameter (RVd mm), Right ventricular out tract diameter (RVOT mm), right ventricular velocity time integral (RV VTI/cm), Tricuspid annular plane excursion (TAPSE), Percent Fractional shortening (%FS) or %fractional area change (%FAC) were measured using methods recommended by the American Society of Echocardiography [5]. Right ventricular mass (RV mass) was computed using the formula derived by: $(4/5 \text{ Pi D1D2L})$ [6,7]. Two-D, M-mode, continuous pulsed and color Doppler echocardiography were performed with standard sweeps including subcostal, parasternal, apical and suprasternal views. Missing echocardiograms were mainly due to crying behaviour or unavailability of equipment or absence of Sonographer [7].

Statistical analysis

The collected data were tabulated and analyzed using SPSS version 16 software (SPSS Inc, Chicago, ILL Company). Categorical data were presented as number and percentages, Chi square (χ^2) and Fisher’s exact test (FET) were used to analyze them. Quantitative data were tested for normality using Shapiro-Wilks test assuming normality at $P > 0.05$. Normally distributed variables were expressed as mean \pm standard deviation and analyzed by Student “t” test for 2 independent groups. Correlation studies were done using Pearson correlation for bivariate analysis. $P \leq 0.05$ was considered cut off of significance.

Results

There was no difference in BSA or heart rate between the breastfed and FF infants. However, COP was a significantly higher in breastfed infants (5.81 ± 1.01) than artificially fed infants (5.26 ± 1.18) with significant P value 0.036 as demonstrated in table 1, figure 1 and 2.

Variable	Breast fed (n = 38)			Artificially fed (n = 38)			F-ratio	P-value of significance
	Mean	\pm SD	Range	Mean	\pm SD	Range		
BSA	0.395	0.046	0.31 - 0.48	0.388	0.045	0.27 - 0.47	0.67	0.51 (NS)
HR (b/min)	119.3	7.49	100 - 132	120.5	7.79	100 - 140	0.67	0.51 (NS)
COP (l/min)	5.81	1.01	3.89 - 7.98	5.26	1.18	3.03	2.14	0.036 (S)

Table 1: Comparison of body surface area, heart rate and cardiac output in breastfed versus formula fed infants under-one year of age. BS: surface area, HR (b/min): heart rate beats per minute, COP l/m: cardiac output liters per minute, Cut off level of significance < 0.05, S: significant, NS: not significant.

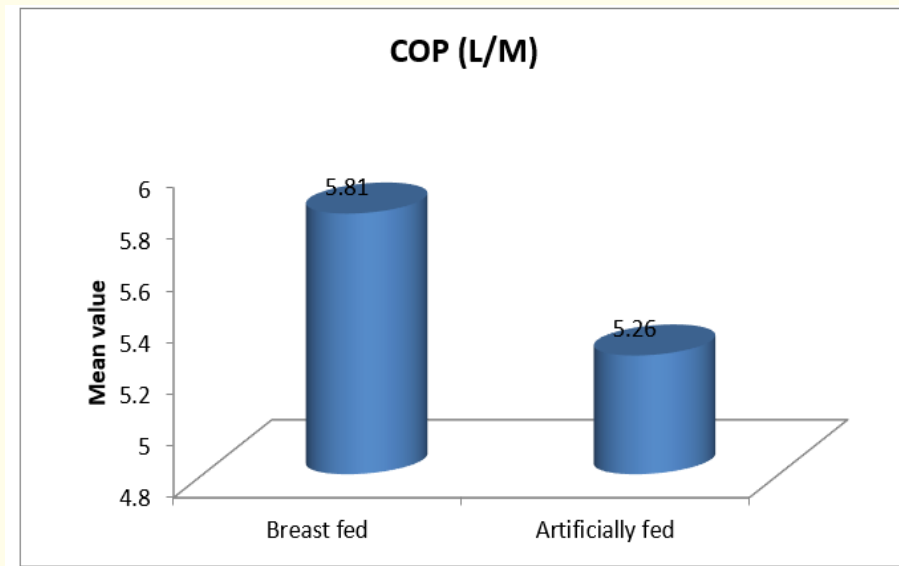


Figure 1: Bar chart showing COP among the studied groups.

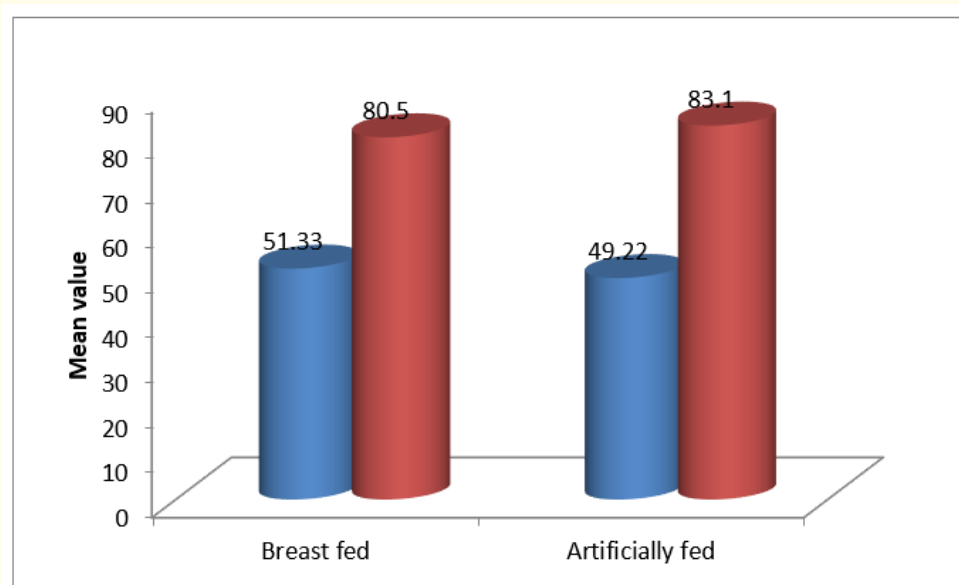


Figure 2: Bar chart showing FAC% among the studied groups.

Table 2 and figure 3 show that there was significant increase in percent fractional shortening (FS %) in EBF infants (51.33 ± 5.20) than FF infants (49.22 ± 3.75) with significant P value 0.05. RV VTI in EBF infants (17.2 ± 2.73) than FF infants (15.9 ± 1.94) with significant P value 0.022. Tricuspid annular plane systolic excursion (TAPSE) in breastfed infants (1.56 ± 0.18) than FF infants (1.46 ± 0.20) with significant P value 0.041.

Variable	Breast fed (n = 38)			Artificially fed (n = 38)			F- ratio	P-value level of significance
	Mean	± SD	Range	Mean	± SD	Range		
RTV.Mass	5.13	1.02	0.45 - 6.05	5.15	0.71	3.7 - 6.8	0.10	0.91 (NS)
%FAS	51.33	5.20	43.5 - 63.6	49.22	3.75	43 - 60	2.007	0.049 (S)
E cm/s	80.5	10.64	60 - 96.5	83.1	9.26	67 - 97	1.1	0.27 (NS)
E/A	1.30	0.15	1.1 - 2.0	1.31	0.17	1.1 - 2.1	0.43	0.67 (NS)
TAPSE/cm	1.56	0.18	1.1 - 2.0	1.46	0.20	1.1 - 2.0	2.08	0.041 (S)
RVOTmm	1.29	0.085	1 - 1.4	1.28	0.099	1 - 1.5	0.43	0.67 (NS)
RV VTI/cm	17.2	2.73	13.3 - 27.0	15.9	1.94	12.1 - 20.0	2.34	0.022 (S)
RV d/cm	1.31	0.11	1.1 - 1.7	1.27	0.09	1.1 - 1.5	1.24	0.21 (NS)

Table 2: Comparison of echocardiographic right ventricular dimensions and functions in breastfed versus artificially fed infants under-one year of age.

RTV: Right Ventricular; FAS: Percent Fractional Area Shortening; RVOT: Right Ventricular Out Tract Diameter; RV VIT: Right Ventricular Velocity Time Integral; TAPSE: Tricuspid Annular Plane Excursion. Cut off level of significance < 0.05, S: significant, NS: Not Significant.

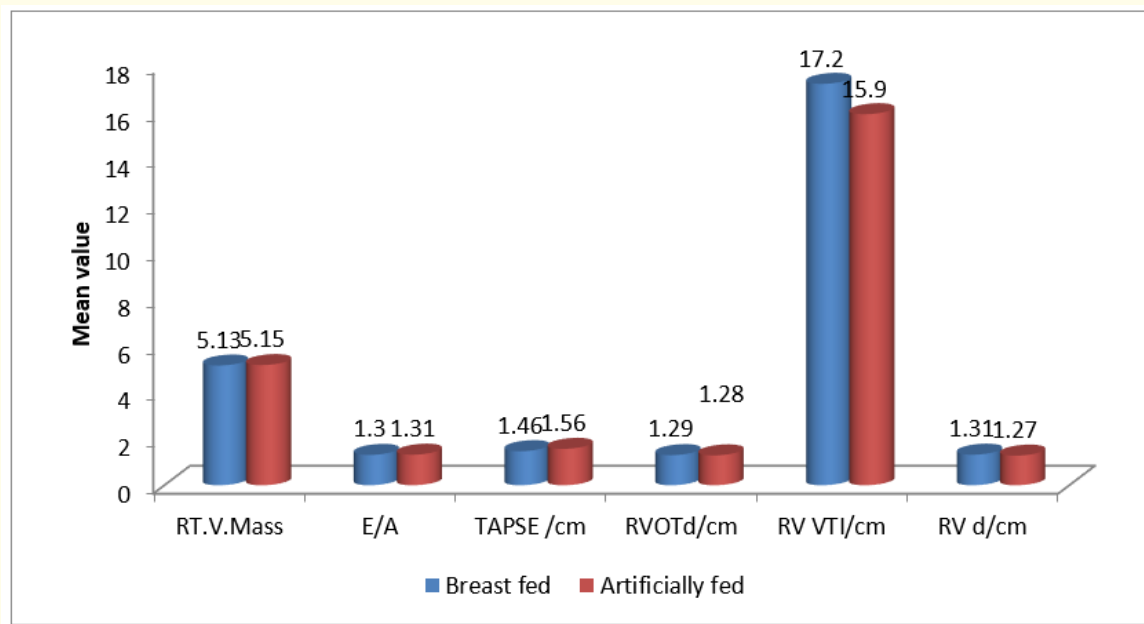


Figure 3: Illustration of right ventricular mass (RTV.Mass), E/A ratio, Tricuspid annular plane excursion (TAPSE), right ventricular outflow tract diameter (RVOT) and right ventricular velocity time integral (RV VTI) and right ventricular diameter (RV d) in breastfed and artificially fed infants.

Table 3 demonstrates there was no significant difference in all parameters measures in between males and females in both breastfed and formula fed infants under one year of age P > 0.05.

Table 4 presents correlations between body surface area (BSA) and the studied Echo parameters for the right ventricle in breastfed and artificially fed under one-year of age. There were highly significant correlations in breast fed and FF fed with BSA and %FAC (r0.6 at

Variable	Males (n = 19)		Females (n = 19)		F-ratio	P-value level of significance*
	Mean	± SD	Mean	± SD		
Formula fed						
RTV.Mass	5.24	0.68	5.06	0.74	0.79	0.43
FAC%	52.06	5.46	50.18	4.71	1.06	0.29
E cm/s	80.76	10.62	80.20	11.05	0.15	0.88
E/A	1.31	0.13	1.31	0.20	0.103	0.92
TAPSE /cm	1.52	0.18	1.59	0.18	1.08	0.28
RVOTd/cm	1.29	0.11	1.27	0.08	0.47	0.64
RV VTI/cm	18.09	3.12	16.42	2.01	1.95	0.059
RV d/cm	1.29	0.10	1.25	0.08	1.31	0.19
Breastfed						
RTV.Mass	5.38	0.58	4.74	1.40	1.92	0.064
FAC%	52.06	5.46	50.18	4.71	1.06	0.29
E cm/s	80.76	10.62	80.20	11.05	0.15	0.88
E/A	1.31	0.13	1.31	0.20	0.103	0.92
TAPSE /cm	1.50	0.20	1.40	0.18	1.43	0.16
RVOTd/cm	1.30	0.07	1.27	0.10	0.95	0.34
RV VTI/cm	16.04	2.19	15.83	1.54	0.31	0.75
RV d/cm	1.29	0.10	1.32	0.13	0.77	0.44

Table 3: Echo parameters according to sex among breastfed and artificially fed infants under one year of age.

RTV: Right Ventricular; FAS: Percent Fractional Area Shortening; RVOT: Right Ventricular Out Tract Diameter; RV VIT: Right Ventricular Velocity Time Integral; TAPSE: Tricuspid Annular Plane Excursion. *Cut off level of significance < 0.05, S: significant, NS: Not Significant.

P0.001 and r0.5 at P = 0.002 respectively), TAPSE (r0.5 at P = 0.002 and r0.5 at P = 0.002 respectively) and RVOT ((r0.5 at P = 0.001 and r0.6 at P = 0.001 respectively) but not with RV mass, E cms E/A ratio in both breastfed and formula fed infants under one year of age P > 0.05.

BSA with	Breast fed (n = 38)		Artificially fed (n = 38)	
	r	P	r	P
RTV.Mass	0.233	0.17	0.233	0.17
FAC%	0.592	<0.001 (HS)	0.483	0.002 (S)
E cm/s	0.219	0.199	0.062	0.71
E/A	-0.165	0.33	0.306	0.061
TAPSE /cm	0.501	0.002 (S)	0.516	=0.001 (HS)
RVOTd/cm	0.539	=0.001 (HS)	0.645	<0.001 (HS)
RV VTI/cm	0.771	<0.001 (HS)	0.204	0.22
RV d/cm	0.167	0.33	0.312	0.056

Table 4: Correlation between Body surface area (BSA) and the studied Echo parameters for the right ventricle in breastfed and artificially fed under one-year of age.

RTV: Right Ventricular; FAS: Percent Fractional Area Shortening; RVOT: Right Ventricular Out Tract Diameter; RV VIT: Right Ventricular Velocity Time Integral; TAPSE: Tricuspid Annular Plane Excursion. Cut off level of significance < 0.05, S: significant, NS: Not Significant.

Table 5 presents correlations between body mass index (BMI) and the studied Echo parameters for the right ventricle in breastfed and artificially fed under one-year of age. There were significant correlations in FF fed with BMI and RV mass (r0.4 at P = 0.015), %FAC (r0.4 at P0.03), and RVOT (r0.4 at P = 0.01) but not with other parameters under study P > 0.05. BMI correlated with RV VTI in breastfed (r0.4 at P+0.03) but not with other parameters under study P > 0.05.

BMI with	Breast fed (n = 38)		Artificially fed (n = 38)	
	r*	P	r	P
RTV.Mass	0.08	0.61	0.393	0.015 (S)
FAC%	0.326	0.053	0.358	0.027 (S)
E cm/s	0.064	0.71	0.306	0.062
E/A	-0.115	0.50	0.184	0.26
TAPSE /cm	0.238	0.16	0.232	0.16
RVOTd/cm	0.157	0.36	0.401	0.013 (S)
RV VTI/cm	0.357	0.032 (S)	0.110	0.51
RV d/cm	0.033	0.84	0.064	0.70

Table 5: Correlation between Body mass index (BMI) and the studied Echo parameters for the right ventricle in breastfed and artificially fed under one-year of age.

*r: Pearson Correlation; P: p-value level of significance (two paired significance), cut off P < 0.05 (S).

Discussion

In this cross-sectional study among healthy children in first 24 months of life of both sex, we found that FAC % values in EBF infants were significantly higher than FF infants although both were within the normal range. Percent FS (FAC) has been suggested to be a reliable echocardiographic marker of RV function [8]. To our knowledge, differences in %FS or shortening has not been extensively studied in relation to early feeding practices in EBF versus FF infants. Normal values range from 43 ± 18%, and a value < 35% is indicative of RV systolic dysfunction [9]. Several recent studies have successfully utilized RV FS% by echocardiography to monitor RV function in both neonates and children with congenital heart disease, pulmonary hypertension, and sickle cell anemia [10-12].

In children, there is controversy about the reliability of RV FS as a marker of RV EF and its use in the assessment of RV systolic function. Some studies suggested that the RV FS % was decreased in children who developed pulmonary arterial hypertension as compared to a control cohort [13]. There were studies that suggested that a lower RV FS was independently associated with transplantation in infants with hypoplastic left heart syndrome [14].

The significant increase cardiac output (COP) in EBF infants in our study as compared to FF infants suggests that the increase in the %FS could have been the underlying cause. This reflects a more active cardiovascular system in the EBF infants to meet their needs of growth and development, particularly for the rapidly growing structures of the brain. Our study found a mild decrease in the HR of EBF infants compared to the FF infants but without significant differences. This probably reflects a tolerance mechanism that enables them to increase their reserve under stressful situations.

We found that there was a significant increase in mean right ventricular velocity time integral (RV VTI) values in EBF infants. There were studies that suggested evaluating VTI in relation to HR because of strong negative correlations between VTI and heart rate (HR) [15-17]. In accordance with this, there was another study that showed a negative correlation, particularly in children < 7 years of age [18]. This relationship is likely caused by a predominantly frequency-based regulation of CO and becomes less obvious in larger ventricles that are also able to vary their systolic volume using the Frank-Starling mechanism [19]. The product of VTI and HR (VTI × HR), also called MD, compensates for the fact that VTI values at low HRs will result in comparable CO with those of low VTI values at high HRs [18].

In our study we found a statistically significant increase mean tricuspid annular plane systolic excursion (TAPSE) values in EBF infants compared to FF infants. TAPSE is a good indicator of RV function and indicates a superiority of RV function in infants who are EBF. Also,

there was a positive correlation between TAPSE and age in both EBF infants ($r=0.45$, $p = 0.006$) and FF infants ($r=0.6$, $p = < 0.001$), and a positive correlation between TAPSE and BSA in both EBF infants ($r=0.5$, $p = 0.002$) and FF infants ($r=0.5$, $p = 0.001$), there was no significant difference was identified between male and female infants in both groups. To our knowledge, we found no studies that reported differences in RV TAPSE in relation to EBF versus FF but irrespective to feeding there was a study that suggested evaluating mean TAPSE values in relation to age group, height, weight, body mass index, and body surface. Body surface area showed a strong positive correlation with TAPSE values [20]. There was another study that had showed TAPSE values with a positive correlation with increasing age and surface area, with no significant differences between sexes [21]. Another study evaluated TAPSE values in relation to gestational age, infant's age, weight, sex and showed that body weight and weeks of gestation were strongly positively correlated with TAPSE values with no significant differences between sexes [22]. Similarly, TAPSE values were found to be correlated to body surface area (BSA) with no significant differences in TAPSE values between males and females [23].

It is still possible that more detailed functional cardiovascular measurements, such as endothelial dysfunction, arterial stiffness, right or left ventricular diastolic filling patterns might be influenced by breastfeeding [24].

The current study showed that the TAPSE and RV-VTI were significantly high in EBF infants. This indicates the RV functions were more developed and optimal in the EBF especially that FAC% was also high in the EBF infants. The finding of higher RV FS% in EBF result in higher blood flow to the lungs, enhancing oxygenation of blood returning from the body structures, this also indicates the RV function is more superior in the EBF than in the FF. This can be explained by the fact that breastfeeding is an active process whereas FF is passive and does not require more effort by the infant [25].

There were significant correlations between BMI and RV mass and FAC among FF and RV VTI in breastfed. The significance of these findings are difficult to interpret, but since BMI is an indicator of overweight or increased size of the child, it is thereby expected that RV mass and %FAC would be increased with increased size of child. Among breastfed the correlation with RV VTI may be an adaptive change to overcoming pulmonary tissue resistance caused by overweight. A study conducted to assess oxygen saturations in breastfed and formula fed, showed that breastfed had higher oxygen saturations and thereby better oxygenation of their tissues and organs particularly to the rapidly growing brain [26]. A study of left ventricular echo parameters in infants less than two years of age showed that left ventricular mass was higher in overweight and obese children while %FAC was higher in obese but not overweight as compared to normal children of the same age. The research team concluded that such findings indicate that ventricular mass adapts to needs of lean body mass, which can be assumed to interpret the findings in our study [27]. Since increases in ventricular mass correlate with high blood pressure and in the case of the RV with pulmonary hypertension, hence this can be taken as a flag sign for children with increased risk of pulmonary hypertension and can explain the increased risk of FF infants to develop respiratory disease.

The values were significant even after adjusting infant sex, gestational age adjusted standard deviation (SD) scores for age and anthropometric study, maternal age, parity, maternal cardiovascular risk factors, family history for cardiovascular diseases, pregnancy complications, and paternal smoking status. The European study on echocardiographic data [28] of over 2,000 healthy children reported no significant differences in echocardiographic values for the left ventricle between the sexes. Previous studies have studied cardiovascular structures in relation to age, height, weight and BSA [29]. The strength of this study is the availability of detailed information about the duration and exclusivity of breastfeeding. This enabled us to investigate the influence of EBF in first 6 months of life on the cardiac functions using FF infants as a control group. However, we found no studies that reported differences in cardiac dimensions related to EBF versus FF infants. Hence, to our knowledge this is the first study that reports such findings. But, there was a study that suggested early nutrition may already influence cardiovascular structures and functional development from early childhood onward [30]. Various other studies have shown a significant association between breastfeeding in infancy and biomarkers that predict later development of cardiovascular disease [31]. The current study supports these previous studies and show that RV functional and dimensional differences between EBF and FF could be a pointer to increased susceptibility to cardiac disease. It appears that breastfeeding increases tolerance to stresses that may compromise the right side of the heart as pulmonary disease or hepatic or right sided cardiac anomaly in infants and children. It thereby supports child survival and optimizing child growth and development and resilience to later stresses in life.

Limitations of the Study

A potential limitation of the study is that the associations between breastfeeding and Right cardiac structures may depend on additional dietary patterns. In the analysis, we did not adjust for other components of infant diet. Another limitation was that because of the

young age at examination and the limited time available at the visits, we were not able to get a higher percentage of successful cardiovascular measurements as left side of the heart.

Conclusion

Results from this cross-sectional study suggest that early developmental changes in the right side of the heart can be influenced feeding patterns in infancy. These changes are not influenced by sex, but by BSA and BMI. Encouraging mothers to breastfeed exclusively in the first six months of life can influence optimal development of cardiac functions in early life and decrease the risk of cardiovascular disease in later adulthood life. Restricting formula feeding in early life to rare medical conditions is beneficial to both mother and child. However, these children who are exposed to formula need to be followed up for cardiac functions in later life, especially if obese. Optimal early feeding practices need to be supported by healthy life styles in later years such as healthy diet, physical exercise, avoidance of exposure to smoking and non-stressful life. Further research is required to replicate these findings and to investigate whether, and to what extent, these changes contribute to an increased risk of cardiovascular disease in later life.

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