El-Asheer *et al.*
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Diastolic blood pressure and lipid profile in breastfed versus formula-fed infants as early indicators for CVD: a cross-sectional study

Osama M. El-Asheer[1*], Marwa A. Dahpy[2,3], Shazli R. Ahmed[1], Khalil A. Mohamed[4], Salah Eldin A. Amry[1] and Deiaaeldin M. Tamer[1]

Abstract

Background: Cardiovascular disease is one of the major causes of death in the world. Low-density lipoprotein cholesterol (LDL-C) is a major cause of cardiovascular disease. Longevity of breastfeeding and *exclusiveness* have both been proposed as possible moderators of the hazard of future CVD. Dyslipidemia, which includes high levels of triglycerides, low levels of high-density lipoprotein cholesterol (HDL-C), with higher levels of LDL-C, as well as hypertension, obesity, and insulin resistance, accelerates atherosclerotic progression and increases the danger of CVD. The consumption of infant formula has been linked to rapid growth, which raises fat accumulation in late infancy and programmed aberrant vascular biology linked to early CVD.

Objectives: This study aimed to compare the blood pressure and lipid profiles of breastfed and formula-fed infants in an effort to determine the cause of the differences.

Results: Both the breastfed and the formula-fed groups showed negligible differences in blood pressure, systolic blood pressure, and blood sugar. Regarding the lipid profile, breastfed newborns had significantly higher levels of Total cholesterol (P <0.001), Triglycerides (P 0.02), HDL-C (P <0.001), LDL-C (P 0.01) and Non-HDL (P <0.001). Newborns who were breastfed had greater levels of non-HDL cholesterol than infants who were fed formula.

Conclusion: Early infancy breastfeeding was linked to a higher lipid profile in breastfed infants, suggesting it may have long-term cardiovascular health benefits that should be supported. The molecular mechanism through which breastfeeding regulates lipid metabolism was revealed by further research.

Keywords: Breastfeeding, Lipid profile, Blood pressure, Infants, Diastolic blood pressure

Background

An important global source of illness and mortality is cardiovascular disease (CVD). It has been established that atherosclerosis develops over the course of a person's lifetime and starts early in life [1].

Risk factors might occur as early as childhood and persist into maturity, according to a number of studies in children and adolescents, demanding early recognition to design a main protective plan. Numerous epidemiological studies from various nations and races have demonstrated that nutrition significantly affects the likelihood of developing adult diseases, starting in fetal life and continuing through early human development. The so-called metabolic programming that occurs during intrauterine life is greatly influenced by nutrition. Hypertension, obesity, insulin resistance, and dyslipidemia all hasten the atherosclerotic process and raise the risk of CVD. Dyslipidemia is defined as having elevated levels of LDL-C, higher levels of TG, and low levels of HDL-C, with insulin resistance (IR). Numerous studies in children and

*Correspondence: asheer1970@gmail.com; asheer1970@aun.edu.eg
[1] Pediatric Department, Faculty of Medicine, Assiut University, Asyut, Egypt
Full list of author information is available at the end of the article

adolescents have revealed that risk factors can exist as early as childhood and persist into adulthood, necessitating early recognition to develop a primary protection strategy. Higher serum total cholesterol concentrations observed in breastfed than in formula-fed infants (< 12 months), because of higher cholesterol content in human milk than in infant formulae, suggest a possible epigenetic effect of breast milk on lifelong regulation of lipid metabolism by a "nutritional programming" consequent to early exposure to human milk high cholesterol content. This stimulus may modulate cholesterol metabolism by regulating hydroxymethylglutaril coenzyme A (HMG-CoA) reductase activity or by increasing LDL receptor activity resulting in lower serum total cholesterol levels in adults who were exclusively breastfed in infancy. Moreover, high concentrations of long-chain polyunsaturated fatty acids (LCPUFA) in breast milk are incorporated into the cell membranes of the vascular endothelium and increase endothelial nitric oxide synthesis providing a possible explanation of the role of human milk in reducing blood pressure in adults who were exclusively breastfed during infancy [2].

When environmental factors interact with fetal DNA via epigenetic mechanisms, they modify an individual's physiology irreversibly over the course of their lifetime and have long-term consequences on the development of metabolic illnesses later in life [3].

Breastfeeding is regarded as an essential component of the World Health Organization's (WHO) "Global Action Plan for the prevention and control of non-communicable diseases 2013–2020" because both breastfeeding duration and exclusivity have been suggested as potential modifiers of the risk of later CVD [4].

Study outcome measure

In order to demonstrate the advantages of breastfeeding in reducing the burden of cardiovascular illnesses, we sought to evaluate the traditional and nontraditional lipid profiles and DBP as early indicators for CVD in breastfed versus formula-fed infants.

Methods

Study design and patients

This study is cross-sectional that was carried out at the outpatient nutrition clinic of the Assiut University Children Hospital, Assiut, Egypt, over a period of 12 months from January 2020.

Fifty infants apparently healthy aged 10–14 months attending the outpatient nutrition clinic were included in this study.

The exclusion criteria are infants with congenital malformations, family history of congenital dyslipidemia, infants with inborn error of metabolism, and infants with any chronic illness.

Data collection

All cases included in the research were subjected to the following:

Detailed history taking including age, sex, perinatal history, type of feeding in first 4 months "breast-feeding or formula-feeding," and socioeconomic status were determined.

Full clinical examination; general investigation: including all the vital signs: heart rate, blood pressure, respiratory rate, and body temperature. Systemic examination: chest, cardiac, abdominal, and neurological examination.

Measurements of the anthropometric parameters were done including weight and height. Chest circumference, mid-upper arm circumference (MUAC), and head circumference.

Investigations

Sample collection: 5 mL of blood was drawn on a plain tube for serum separation from each child after a full night fasting.

Serum lipid profile: including levels of total cholesterol (TC), triglyceride (TG), and high-density lipoprotein cholesterol (HDL-C) all were measured using colorimetric methods by kits supplied by Bio-Diagnostics Company (cat no.CH1220, TR2030, and CH1232, respectively). Low-density lipoprotein cholesterol (LDL-C) and VLDL serum concentrations were calculated using the Friedewald equation [5].

Non-traditional lipid profiles including non-HDL, TC/HDL, TG/HDL, and LDL/HDL were calculated.

Serum glucose levels were measured by the Randox enzymatic glucose kit (catalog no.GL364).

Results

Our findings demonstrate the general characteristics of the cases under study, such as the mean age of the breastfed group, which was 11.52 1.32 months, and the mean age of the formula-fed group, which was 11.64 1.55 months. Males made up the bulk of both categories. Ten (40%), 11 (44%), and 4 (16%) of the breastfed infants and 12 (48%), 9 (36%), and 4 (16%) of the formula-fed infants respectively had low, moderate, and high socioeconomic level. The average family size for those who were breastfed was 3.48, 0.91, and for those who were given formula, it was 3.32, 1.54. Measurements were collected of the anthropometric variables of height, weight, MUAC, and head circumference (Table 1).

Regarding clinical findings, both groups had insignificant differences as regards diastolic blood pressure (DBP) and systolic blood pressure (SBP). For laboratory

Table 1 Characteristics of studied cases among the enrolled groups

	Breastfed group (n = 25)	Formula-fed group (n = 25)	P-value
Age (months)	11.52 ± 1.32	11.64 ± 1.55	0.77
Sex			0.34
Male	17 (68%)	15 (60%)	
Female	8 (32%)	10 (40%)	
Socioeconomic status			0.28
Low	10 (40%)	12 (48%)	
Moderate	11 (44%)	9 (36%)	
High	4 (16%)	4 (16%)	
Family size (members)	3.48 ± 0.91	3.32 ± 1.54	0.65
Weight (kg)	9.54 ± 0.85	9.34 ± 1.59	0.98
Head circumference (cm)	44.56 ± 1.07	44.84 ± 1.36	0.42
MUAC (cm)	13.76 ± 0.87	13.88 ± 0.86	0.63
Length (cm)	72.32 ± 2.42	73.72 ± 4.17	0.15

Data expressed frequency (percentage) and mean (SD). P value was significant if < 0.05

Continuous data were compared by The Student t-test while nominal data were compared by the chi-square test

MUAC mid-upper arm circumference

findings, the results showed that the breastfed group had significantly higher total cholesterol (170.76 ± 49.15 vs. 122.92 ± 21.62 (mg/dl); $P < 0.001$), triglycerides (176.16 ± 75.97 vs. 134.80 ± 41.54 (mg/dl); $P = 0.02$), HDL-C (46 ± 12.14 vs. 35.57 ± 9.42 (mg/dl); $P < 0.001$), and LDL-C (86.36 ± 42.67 vs. 61.30 ± 18.94 (mg/dl); $P = 0.01$) and insignificant differences as regards blood glucose (Table 2).

Non-traditional lipid profiles, such as TC/HDL, TG/HDL, and LDL/HDL, were evaluated among the cases under study; they revealed no discernible differences between the two groups. Infants who were breastfed had non-HDL levels that were considerably higher than infants who were fed formula (125.16 43.58 vs. 86.98 22.54 (mg/dl); P 0.001) (Table 2).

The age of introducing supplemental foods had a significant negative link with serum triglyceride ($r = -0.54$, P 0.001) in the breastfed group, but not with other parameters, according to the correlation analysis (Table 3) (Fig. 1).

Levels of non-HDL had insignificant correlations with systolic and diastolic blood pressure ($P > 0.05$).

Comparing normal and abnormal levels of total cholesterol and LDL-C in each group showed insignificant differences as regards systolic and diastolic blood pressure with exception of significantly higher SBP among breastfed infant with normal LDL in comparison with those with high LDL (86.83 ± 6.60 vs. 79.57 ± 6.80 (mg/dl); $P = 0.02$) (Table 3).

Discussion

Infanthood is seen as a crucial time for a child's growth and development. According to a previously published study, infants that acquire weight quickly during infancy are more susceptible to ailments later in life [6, 7]. In this study, blood pressure and lipid profiles of breastfed versus formula-fed newborns were compared as a potential early CVD biomarker.

When it came to economic status, where low to moderate state was usually present in the study, we did not find any significant differences between the two groups of newborns in the current study. Apart from the availability of infant formula, it is well-recognized that several cultural, social, economic, and psychological factors influence nursing habits [8, 9]. According to

Table 2 Blood pressure, blood glucose and serum lipid profile, and non-traditional lipid profile among the enrolled group

	Breastfed group (n = 25)	Formula-fed group (n = 25)	P value
DBP (mmHg)	54 ± 3.43	54.40 ± 4.16	0.71
SBP (mmHg)	84.80 ±7.32	87.80 ± 7.08	0.14
Blood glucose (mg/dl)	108.92 ± 11.13	108.12 ± 13.43	0.82
Total cholesterol (mg/dl)	170.76 ± 49.15	122.92 ± 21.62	**< 0.001**
Triglycerides (mg/dl)	176.16 ± 75.97	134.80 ± 41.54	**0.02**
HDL-C (mg/dl)	46 ± 12.14	35.57 ± 9.42	**< 0.001**
LDL-C (mg/dl)	86.36 ± 42.67	61.30 ± 18.94	**0.01**
TC/HDL	3.82 ± 0.99	3.63 ± 0.96	0.49
TG/HDL	4.17 ± 2.48	3.99 ± 1.53	0.76
LDL/HDL	2.08 ± 1.11	1.87 ± 0.77	0.42
Non-HDL (mg/dl)	125.16 ± 43.58	86.98 ± 22.54	**< 0.001**

Data expressed mean (SD). Student t-test was used, and the P value was significant if < 0.05

HDL high-density lipoprotein, *LDL* low-density lipoprotein, *TC* total cholesterol, *TG* triglycerides

Table 3 Cholesterol and LDL-C levels in relation to blood pressure and in each separate group

	Breastfed group		P	Formula-fed group		P
	Normal level ($n = 21$)	High level ($n = 4$)		Normal level ($n = 25$)	High level ($n = 0$)	
Cholesterol level and blood pressure						
Diastolic blood pressure (mmHg)	53.71 ± 3.49	55.50 ± 3.10	0.35	54.40 ± 4.16	–	
Systolic blood pressure (mmHg)	85.47 ± 7.09	81.25 ± 8.53	0.30	87.80 ± 7.08	–	
LDL-C level and blood pressure						
Diastolic blood pressure (mmHg)	54.11 ± 3.47	53.71 ± 3.59	0.80	54.40 ± 4.16	–	
Systolic blood pressure (mmHg)	86.83 ± 6.60	79.57 ± 6.80	**0.02**	87.80 ± 7.08	–	

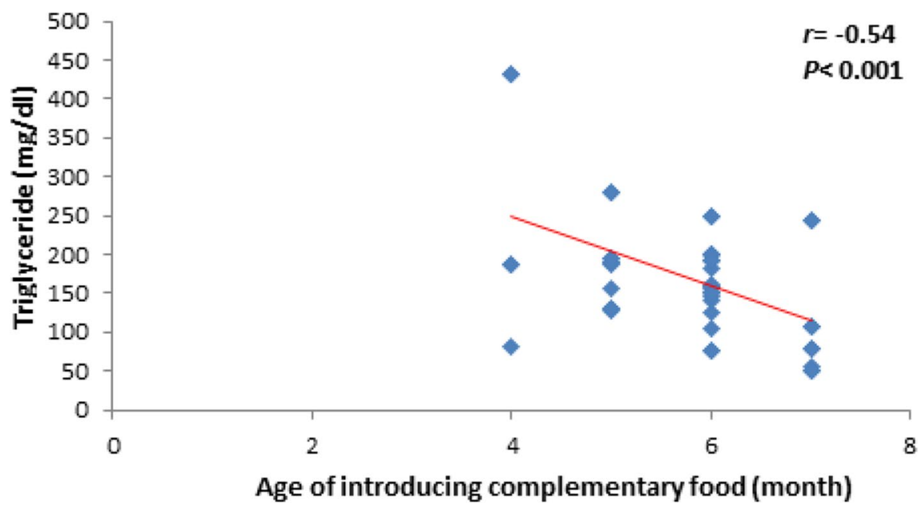

Fig. 1 Correlation between age of introducing complementary food and triglyceride in the breastfed group

the results of the current study, the BF group had significantly higher levels of triglycerides, HDL-C, LDL-C, and cholesterol (P 0.001, $P = 0.02$, P 0.001, and P 0.001, respectively).

In line with our findings of the present investigation, Harit et al. [10] showed that the feeding schedule influences the lipid profile in human newborns. They discovered that babies who were breastfed had considerably greater total and LDL-C. This study, however, did not support the current finding that the group of people who exclusively breastfed had significantly lower levels of HDL-C.

The similar results, which showed higher levels of LDL-C and HDL-C in the BF group, as well as the alterations between the absolute values of total cholesterol, HDL-C, LDL-C, and triglyceride in our study as compared to other studies, may be attributable to variations in a variety of factors, including methodology, blood sample type (either venous/capillary), time since the last feeding, feed preparation (dilution), and genetic makeup [11].

Another explanation for the higher total cholesterol and LDL-C levels in BF infants in our study is that breast milk contains much more cholesterol than cow's milk, which suggests that the greater intake of dietary cholesterol may be to blame.

Another argument is that human milk contains more cofactor apo E II or has higher lipase activity, which may promote both external and endogenous lipolysis for TG and raise serum fatty acid levels [10].

It is currently unknown whether the physiological hypercholesterolemic condition experienced by exclusively BF infants throughout early infancy has any benefits for neurodevelopment. Infants who are exclusively breastfed may experience increased serum cholesterol levels during this period because infants need more cholesterol for rapid brain development, which is mostly given by docosahexaenoic acid and linolenic acid in breast milk. Additionally, due to priming, children who are exposed to high dietary cholesterol early in life are better able to handle high dietary cholesterol loads later in life [10].

Infants with higher cholesterol levels may be better prepared to produce less cholesterol later in life. Despite greater concentrations of plasma lipids later in life that are thought to be atherogenic, studies have revealed that breastfed babies had a decreased chance of evolving coronary heart disease and associated risk factors [10, 12].

In the first 3 months of life, nursing exclusively is linked to a lipid profile that is less atherogenic. Breastfeeding may be significant in preventing cardiovascular disease because it shifts the whole population's distribution of cholesterol toward a lower level, despite its minimal effect on LDL-C.

Hiu et al. were unable to show if prolonged breastfeeding results in a longer exposure to a high-cholesterol diet during infancy, which had a negative impact on cardiovascular health through other mechanisms in their study [13].

Long-chain polyunsaturated fatty acids may help control blood pressure since they are crucial structural elements of tissue membrane systems, such as the vascular endothelium [14]. Interestingly, neither SBP nor DBP significantly differed between BF or formula-fed infants in the current study.

Neonatal metabolic characteristics are impacted by feeding practices. Healthy-term breastfed infants up to 1 week of age had considerably lower blood glucose levels than formula-fed infants, which may be related to the lower energy content of breast milk during the early postnatal days. However, compared to newborns who are fed formula, their ketone body concentrations are higher. During hypoglycemia, the neonatal brain is better able to utilize ketone bodies as fuel, saving glucose and preserving neurological function [15, 16].

According to our findings, there were no statistically significant connections between blood glucose levels and the other lipid profile characteristics ($P > 0.05$). Additionally, it was found that, apart from the negative significant association with serum triglyceride ($r = -0.39$, P 0.001), the age of introduction of complementary food had an insignificant correlation with various parameters ($P > 0.05$).

Except for slightly greater non-HDL among the BF group, the current study's findings regarding non-traditional lipid profiles showed that both groups had minimal differences in terms of heart disease risk. According to Timby et al., who reported similar results to the current study, both groups of babies had LDL-C/HDL-C ratios that were insignificantly different, with significantly greater non-HDL levels among the breastfed group [17].

Conclusion

Breastfeeding in the first few months of life should be encouraged as it is linked to a higher lipid profile, indicating that it may have long-term advantages for cardiovascular health. However, additional research is still needed to fully understand the long-term implications of these findings, including the biological mechanisms by which breastfeeding affects lipid metabolism, the health benefits of exclusive breastfeeding in comparison with formula feeding, and the best age to start introducing formula milk for those who have the option.

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Authors' contributions
The authors read and approved the final manuscript. O.M.E. and SE. A. A. designed the study; evaluated the patients; and collected, analyzed, and interpreted the data. K.A.M., SH.A., and M.A.D contributed to the conception and design of the study, literature search, and manuscript review. M.A.D. contributed to the biochemical laboratory assessment, interpretation of the data analysis, manuscript writing, and review. D.M.T. shares in writing, revision, and publication. All authors helped in revising and approving the manuscript.

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Availability of data and materials
All data generated or analyzed during this study are included in this published article and its additional file.

Declarations

Ethics approval and consent to participate
The study was approved by the ethics committee of the Faculty of Medicine, Assiut University (IRB no: 17100591). Written informed consents were taken from parents with an explanation of the benefits of the study, risks expected, and suggested treatment for each case**.**

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

Author details
[1]Pediatric Department, Faculty of Medicine, Assiut University, Asyut, Egypt. [2]Medical Biochemistry and Molecular Biology department, Faculty of Medicine, Assiut University, Asyut, Egypt. [3]Medical Biochemistry and Molecular Biology Department, Armed Force's College of Medicine, Cairo, Egypt. [4]Pediatric Department, Faulty of Medicine, Cairo University, Cairo, Egypt.

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