Efficacy of early enteral feeding with supplemented mother's milk on postoperative outcomes of cardiac surgical infants: A randomized controlled trial

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ABSTRACT

Introduction : **Congenital heart disease (CHD)-associated malnutrition is a systemic consequence of CHD. Dietary recommendations to fulfill nutritional requirements are lacking. This randomized controlled trial (RCT) was conducted to determine the efficacy of early enteral feeding with supplemented expressed breast milk (suppl-EBM) versus expressed breast milk (EBM) in improving the weight of postoperative cardiac surgical infants.**

Objective : **The primary objective was the weight change between the EBM group and the suppl-EBM group at the 15th postoperative day (POD) or intensive care unit (ICU) discharge. The secondary objectives were to compare the ventilation duration (VD), length of ICU stay (LOICUS), length of hospital stay (LOHS), macronutrient consumption, adverse events, sepsis, and mortality between the two groups.**

Materials and Methods : **This study was a parallel-group, open-labeled, single-blinded, variable block size RCT conducted at a tertiary care teaching hospital in northern India. Full-term breastfed infants ≤6 months, weighing ≥2.5 kg at birth, and undergoing congenital cardiac repair were enrolled in this study. The infants were fed either EBM or supplemented EBM in control and intervention groups, respectively. Weight and length were measured at baseline and 15th POD or at ICU discharge. Biochemical parameters at baseline and every alternate day, sepsis parameters every third POD and VD, LOICUS, LOHS, macronutrient consumption, and adverse events were assessed daily.**

Results : **The mean weight, weight change percentage, and weight for age z score were significantly higher in the supplemented EBM group ($P < 0.05$). The macronutrient consumption was significantly higher in the intervention group ($P < 0.05$). No significant difference was found between the two groups for VD, LOICUS, and LOHS ($P > 0.05$). The sepsis was higher in the EBM group. However, the mortality rate did not differ between the two groups ($P > 0.05$).**

Conclusion : **Supplemented feeding may improve the weight of postoperative cardiac infants with no serious adverse events.**

Keywords : Congenital heart disease, pediatric cardiac surgery, postoperative nutritional care

Access this article online

Quick Response Code:

Website: https://journals.lww.com/aopc

DOI: 10.4103/apc.apc_160_24

How to cite this article: Singal A, Sahu MK, Kumar GT, Aeri BT, Manral M, Agarwala A, *et al.* Efficacy of early enteral feeding with supplemented mother's milk on postoperative outcomes of cardiac surgical infants: A randomized controlled trial. Ann Pediatr Card 2024;17:320-30.

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Submitted: 22-Aug-2024 **Revised:** 09-Oct-2024 **Accepted:** 01-Nov-2024 **Published:** 24-Dec-2024

INTRODUCTION

Congenital heart disease (CHD) constitutes a large proportion, about one-third of all congenital malformations.[1] In the past few decades, the accelerated birth prevalence of CHD has made it a common birth defect globally.[2] In India, it accounts for about 8.07/1000 live births. The survival rate has improved in the last decades, possibly due to technological advancements.[3] However, CHD-associated malnutrition remains a challenge.

Most infants with CHD are born with a normal weight. However, the incidence of malnutrition increases gradually with growing age due to inappropriate feeding and malfunctioning of the heart.[4] Infants with CHD are malnourished at the time of clinical presentation, before and after repair of the cardiac defect.[5-7] Malnutrition associated with CHD is influenced by several factors, such as increased energy expenditure, inadequate dietary intake, hypermetabolism, feeding difficulty, malabsorption, gastrointestinal malformations, feeding intolerance, frequent feeding interruptions, and failure to thrive.[8-10] Due to feeding-associated difficulties, ensuring adequate nutritional intake in postoperative cardiac surgical infants becomes a challenge.[11,12] Iatrogenic malnutrition results especially due to delayed initiation of nutritional support after cardiac surgery but also due to an inadequate supplementation of protein and energy.

Inadequate calorie consumption affects postoperative convalescence and clinical outcomes, including prolonged mechanical ventilation, increased length of intensive care unit stay (LOICUS), and length of hospital stay (LOHS).[13-18] These short-term complications have a more significant impact on their weight than their height.[19] Prolonged nutritional deficits lead to long-term complications, including growth failure,[20] delayed neurologic, social, and emotional development.[21-24]

Breast milk is the best food for infants due to its nutritional composition and maternal bonding.[25,26] Despite breast milk's numerous benefits, calorie intake may not be sufficient to balance postoperative catabolism and support the growth and convalescence of pediatric cardiac surgical patients.[27] Hence, fortification of breast milk is required to meet these infant's increased nutritional requirements.[28]

It is well documented that meeting the targeted energy goal in postoperative cardiac surgical infants is extremely difficult.[11,14,29] Therefore, a standardized feeding protocol or nutritional algorithm-based approach is required to overcome the feeding-associated complications.[30,31] It may improve compliance with nutritional therapy and adherence to the feeding regime. It may also reduce deviation from scheduled feeding, which may lead to improved weight for age growth trajectories.[32-34] Unfortunately, there is a lacuna of nutritional recommendations/guidelines for feeding cardiac surgical infants postoperatively. Moreover, individual institute-based feeding practices are being followed, which leads to diversified nutritional management. Therefore, this study has been conducted to evaluate the efficacy of supplemented mother's milk in postoperative cardiac surgical infants compared to the standard feeding and to propose a stepwise algorithm focusing on nutritional management in infants following congenital cardiac repair. The hypothesis for the present study was "early enteral feeding with supplemented expressed breast milk (suppl-EBM) in postoperative cardiac infants, which may bring changes in body weight, ventilation duration (VD), LOICUS, LOHS, macronutrients intake, adverse events, sepsis, and mortality rate in the intervention group as compared to the control group."

MATERIALS AND METHODS

The flow chart of the study is depicted in Figure 1.

Study design

The present study was a hospital-based, parallel-group, open-labeled, single-blinded, variable block-size randomized controlled trial (RCT). It was conducted at a tertiary care teaching hospital in northern India from January 1, 2019, to December 31, 2021, after obtaining ethical approval from the institutional ethical committees (Ref no-IHE 2019-2020/Admin 1162, and Ref no-IEC/NP-209/08.05.2015, RP-34/2015, OP-10/02.02.2018, OP-17/01.02.2019, OP-8/06.03.2020). This trial was registered with the Clinical Trial Registry, India (Ref no. CTRI/2018/02/012086).

Participants

Full-term infants (gestational age ≥37 weeks) diagnosed with acyanotic/cyanotic CHD, weighing ≥2.5 kg at birth, and aged ≤6 months at the time of surgery were included in the study. Those infants who were fed with exclusive breastfeeding or expressed breast milk (EBM) and underwent congenital cardiac repair with cardiopulmonary bypass (CPB) were enrolled in this RCT. The infants who underwent emergency operations, closed heart surgeries, syndromic children, those admitted with severe infection (sepsis) or on mechanical ventilation before surgery, fed with formula feed, and the parents refused to give consent were excluded from the study.

Objectives

The primary objective of the study is to determine the efficacy of suppl-EBM feeding to improve the weight of infants who underwent congenital cardiac repair compared to standard feeding, i.e. EBM feeding. The infants' weight was taken at baseline

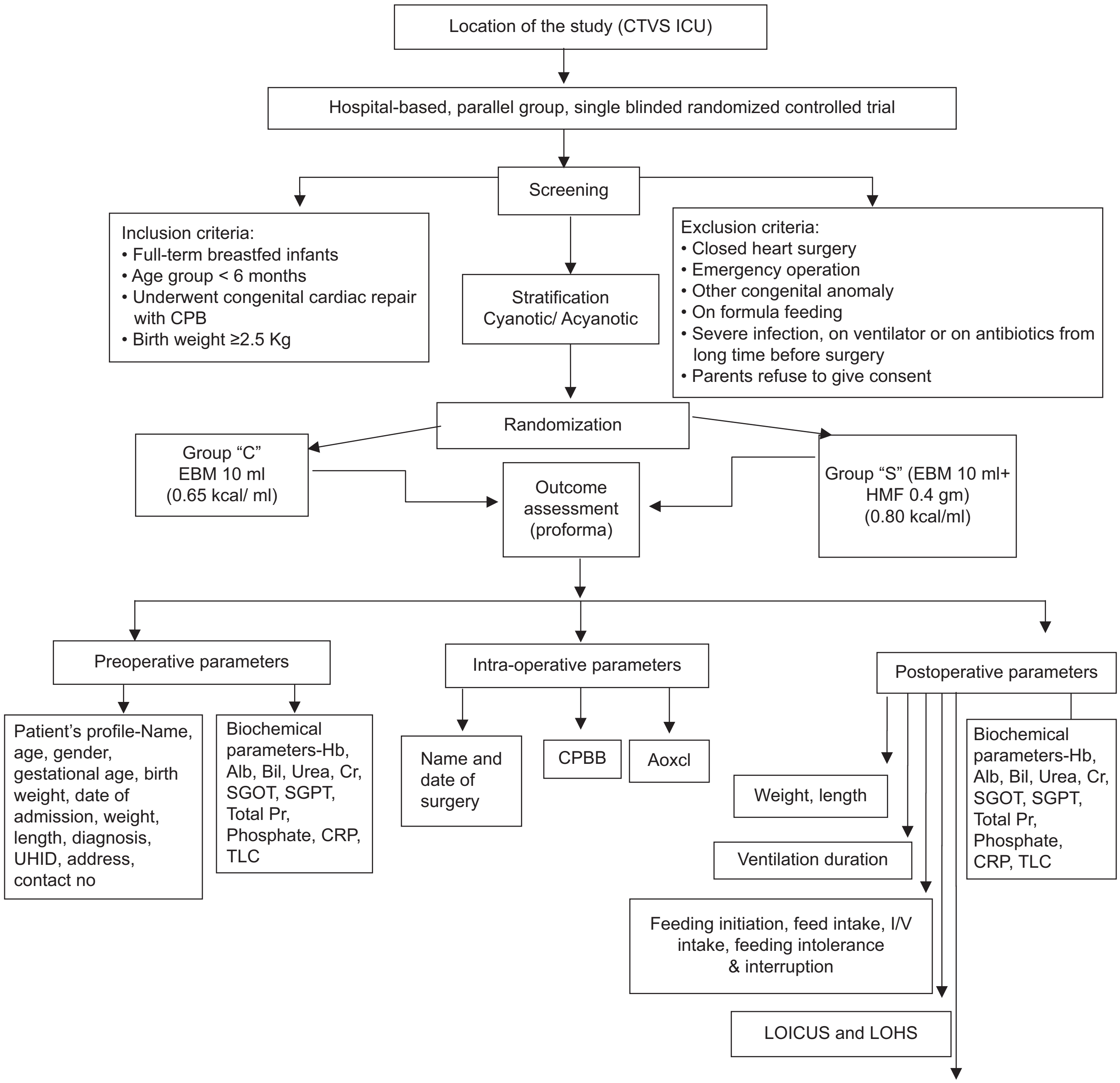

Figure 1: Flow chart of the study. Alb=Albumin, Aoxcl=Aortic cross-clamp, Bil=Bilirubin, CPB=Cardiopulmonary bypass, Cr=Creatinine, CRP=C-reactive protein, Hb= Haemoglobin, Kg= kilogram, LOICUS=Length of Intensive Care Unit Stay, LOHS=Length of hospital stay, SGOT=Serum glutamate oxaloacetate transaminase, SGPT=Serum glutamate pyruvic transaminase, Total Pr=Total protein, TLC=Total leukocyte count, Urea= Serum urea, HMF= Human milk fortifier

and at the 15th postoperative day (POD) or at ICU discharge (whichever is earlier).

Secondary objectives included comparing the mechanical VD, LOICUS, LOHS, infection, and mortality rate in EBM and suppl-EBM groups. The total energy, protein, fat, and carbohydrate intake per day during the intervention period (until 15th POD or ICU discharge) between EBM and suppl-EBM groups were also compared. The adverse events between the two groups (EBM and suppl-EBM) were noted.

Sample size

The mean difference in weight of 0.5 g was used to compare the nutritional and clinical outcomes of the infants fed with EBM and/or supplemented EBM (suppl-EBM).[29] The calculated sample size was 130 (65 in each arm), assuming a 5% significance level, 80% power, and 10% lost to follow-up.

Recruitment/enrollment

The patients were screened for eligibility, and those who met the inclusion criteria were enrolled in the study after obtaining parental consent. The subjects were stratified into two categories (cyanotic and acyanotic). Subjects from each category were randomized into control (EBM) and intervention (suppl-EBM) groups. A variable block size randomization method using a computer-generated randomization sequence was used. A staff member not involved in the trial generated this list. The assigned intervention was given per the sequence code revealed from the sealed opaque envelopes.

Intervention

The suppl-EBM group was fed with supplemented EBM, which contains EBM 10 ml + 0.4 g human milk fortifier (HMF), which provided 0.80 kcal/ml energy with 11.5% protein, 41.5% fat, and 44.6% carbohydrates. The EBM group was fed only EBM (EBM = 10 ml), which provided 0.65 kcal/ml energy with 7.3% protein, 47.7% fat, and 42.6% carbohydrates.

Implementation of feeding protocol

A nutritional algorithm was prepared for implementation of the feeding regime [Figure 2]:

a. Nasogastric/orogastric tube feeding was used to provide early enteral feeding. Patients were assessed for feeding initiation criteria, including hemodynamic stability, absence of mediastinal bleeding and low cardiac output, serum lactate < 4 mmol/L, and not on very high dose vasopressors. If the patient fulfilled the criteria, enteral feeding was started, preferably within 6 h of surgery
b. Both groups were fed from 0 to the 15th POD or until ICU discharge (whichever was earlier)
c. An initial test dose of 2–5 ml of EBM or suppl-EBM was given to the control or intervention groups, respectively. Feeding tolerance was assessed in both groups. Feeding was continued and advanced as per the feeding protocol. Total energy, protein, fat, and

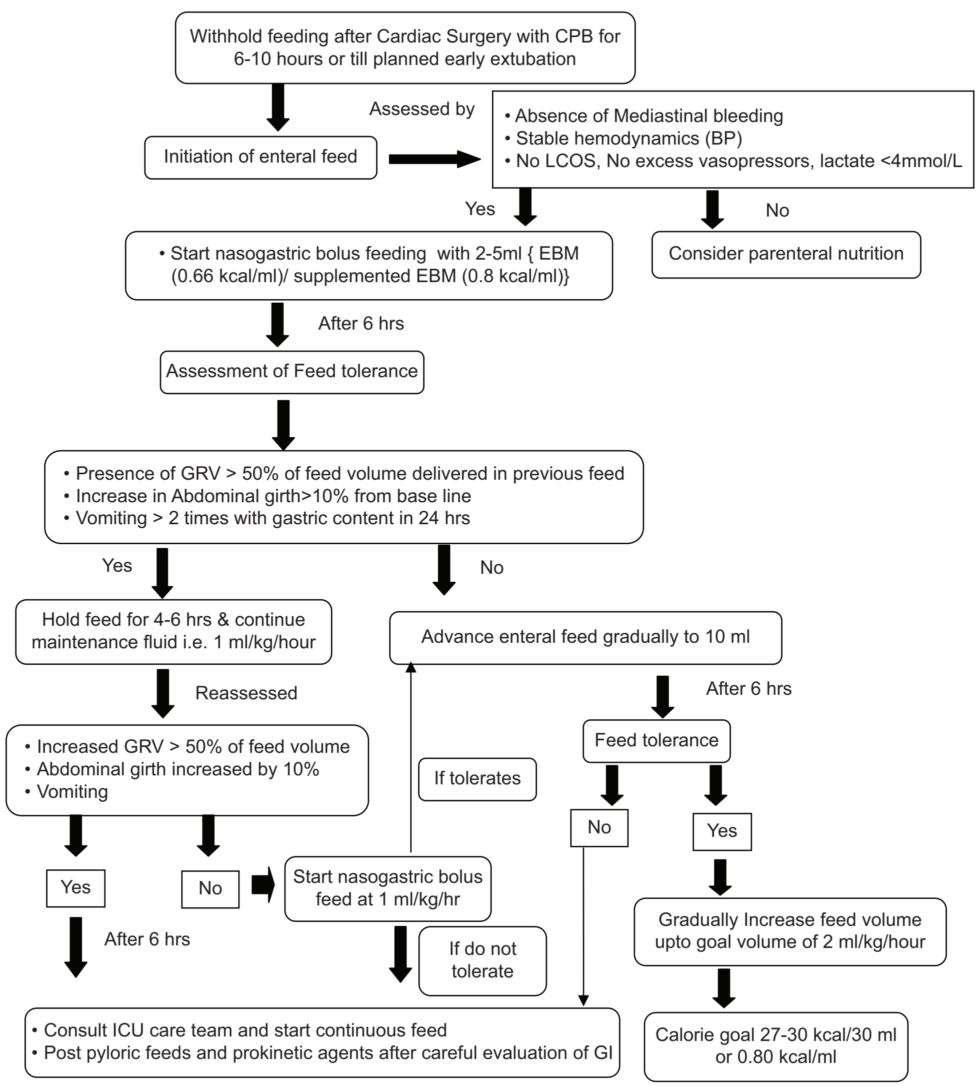

Figure 2: Algorithm for postoperative nutrition. BP=Blood pressure, GRV=Gastric residual volume, CPB=Cardiopulmonary bypass, LCOS=Low cardiac output syndrome

carbohydrate intakes were calculated daily using identical software (Profound Tech Solution, India)

d. Gastric residual volume (GRV), diarrhea, vomiting, and abdominal distension were used to assess the feeding tolerance in patients after 6 h of feeding. Feeding intolerance was defined as the presence of GRV more than 50% of the previous feed volume, diarrhea with watery/loose stool > 6 times, abdominal girth increase > 10% of the baseline, and vomiting more than 2 times with gastric content[35]
e. If the patient tolerated the feeding, it was continued with a volume of 5–10 ml/2nd hourly. In case of intolerance, feeding was withheld for 4–6 h, and maintenance fluid (1 ml/kg/h) was given
f. The patient was reassessed after 6 h. If symptoms resolved, bolus feeding was given at 1 ml/kg/h. If the patient tolerated the given feed volume, it was advanced to 10 ml, and concentration was increased for the supplemented group only to meet the target of 0.8 kcal/ml. If intolerance persisted, it was withheld for 4-6 h and reassessed again. If symptoms persisted, they were discussed with the team, and continuous feed was given at 1 ml/kg/h
g. If feeding was withheld due to any medical or surgical procedure or any feed interruption for intolerance, feeding was started with the same composition and volume after stabilization
h. There were no guidelines for dietary recommendations for infants following congenital cardiac surgery. Therefore, the dietary recommendations available for normal healthy infants, i.e., 94 kcal/kg body weight (estimated average requirement 2020), were utilized for these infants.

Outcome measures

Weight and length were measured at baseline and 15th POD or at ICU discharge, whichever was earlier. Biochemical parameters were measured at baseline and every alternate day postoperatively. Infection-related parameters were assessed in all postcardiotomy children at every third POD (from 0 to 15th POD or until ICU discharge). Mechanical VD, length of ICU and hospital stay, mortality, adverse events, and feeding interruption were assessed daily and recorded as and when events occurred. Macronutrient consumption was calculated and recorded every day.

Statistical analysis

Intention to treat analysis was performed to compare outcome measures between two groups (EBM and suppl-EBM). Variables were checked for normal distribution, and mean or median values were used as appropriate. The data were summarized by mean ± standard deviation for normally distributed quantitative variables, median with interquartile range for variables with skewed distribution, and frequency with percentages for categorical variables. Subgroup analysis was performed among cyanotic and acyanotic infants between EBM and suppl-EBM groups.

An unpaired *t*-test/Wilcoxon rank-sum test was used to compare the quantitative characteristics of the two groups. Fisher's exact test and Chi-square test were performed to compare categorical variables. $P<0.05$ was considered statistically significant.

RESULTS

The schematic diagram of the conduct of the study is depicted in Figure 3. A total of 385 patients were screened for eligibility, and those who met the inclusion criteria and their parents gave consent were enrolled in the study. A total of 116 subjects were enrolled in the present study and stratified into two categories (cyanotic = 78; and acyanotic = 38). Subjects from both categories were randomized into two groups: 60 infants in the control group received EBM, and 56 infants in the intervention group received suppl-EBM. Among the EBM group, seven infants died, three had insufficient mother's milk, and two were lost to follow-up due to the COVID-19 lockdown. Among the suppl-EBM group, two infants died, and four infants had insufficient mother's milk during the intervention period.

In the present study, mean body weight (primary objective), length, and weight for age *Z* score of the infants at baseline were similar between the two groups (EBM and suppl-EBM) ($P > 0.05$) [Table 1]. Mean weight, weight change percentage, and weight for age *Z* score were significantly higher in the intervention group than in the control group ($P < 0.05$) at the 15th POD or ICU discharge [Table 2]. The most common surgery performed was total anomalous pulmonary venous connection repair in cyanotic infants and ventricular septal defect closure in the acyanotic group [Table 3].

The analysis of secondary objectives showed that there was no significant difference between the two groups for VD, LOICUS, and LOHS ($P > 0.05$) [Table 4]. However, the macronutrient consumption, including energy, protein, and carbohydrates, was higher at several time

Table 1: Baseline characteristics of the subjects in expressed breast milk and supplemented expressed breast milk groups, (mean±standard deviation), median (range) or *n* (%)

Variables	EBM (*n*=60)	Supplemented EBM (*n*=56)	*P*
Male	52 (86.6)	41 (73.2)	0.069
Female	8 (13.3)	15 (26.7)	
Age (days)	90.5 (13–180)	78 (10–180)	0.217
Weight (kg)	3.6±0.9	3.5±0.9	0.923
Length (cm)	55.7±5.6	55.6±4.7	0.944
WAZ	−4.0±1.5	−3.5±1.5	0.084

EBM: Expressed breast milk, WAZ: Weight for age *Z*-score

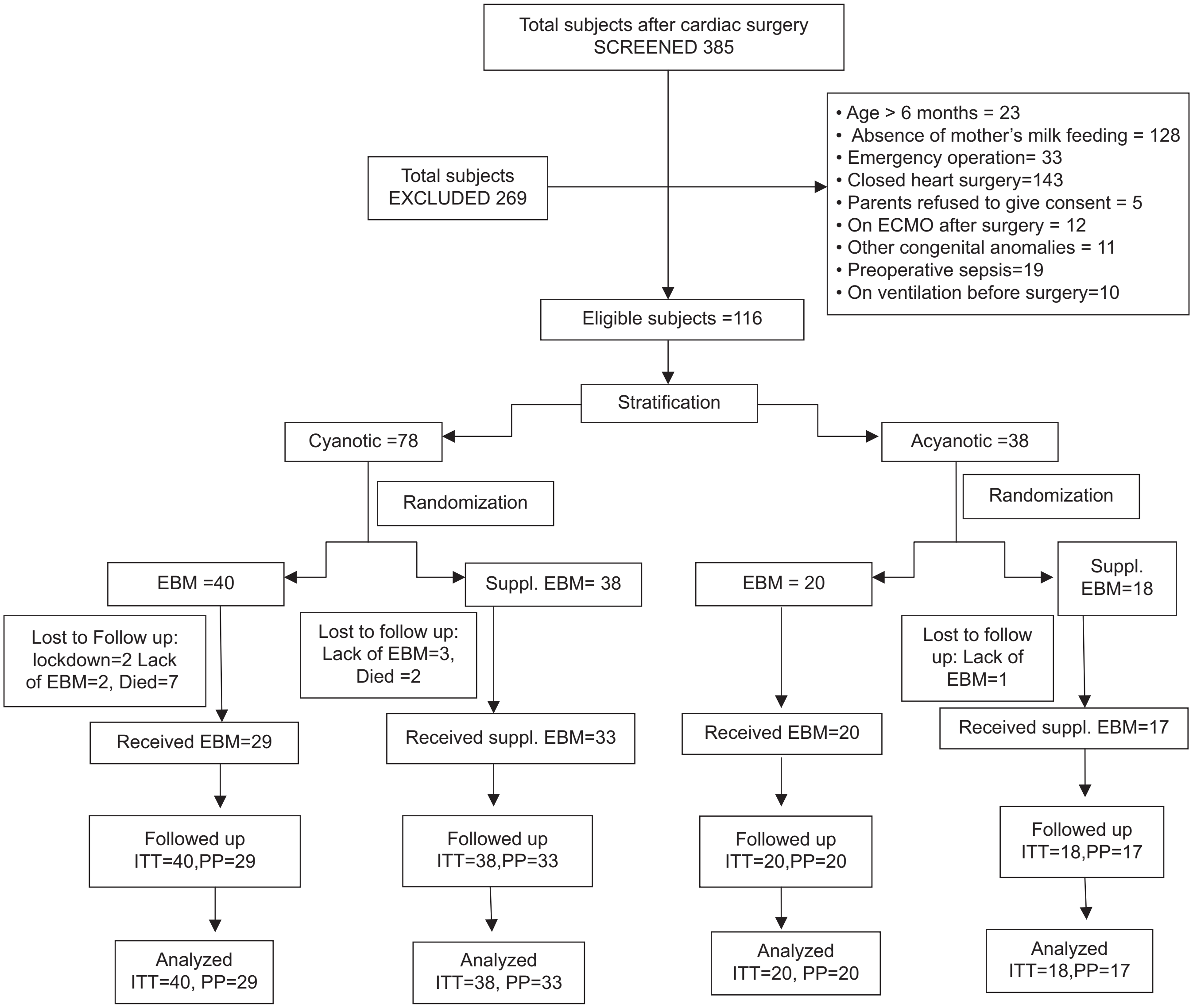

Figure 3: Schematic diagram of the conduct of the study . EBM= Expressed breast milk; ECMO= Extracorporeal membrane oxygenation; ITT= Intention to treat, PP=Per protocol

Table 2: Postoperative anthropometric measurements in expressed breast milk and supplemented expressed breast milk groups (mean±standard deviation)

Parameters	EBM (*n*=60)	Supplemented EBM (*n*=56)	*P*
Weight (kg)	3.4±0.9	3.8±1.0	0.015*
Weight change (%)	−7 (−28.8–60.7)	6.5 (−19.3–55.1)	0.000*
Length (cm)	56.0±5.5	55.9±4.8	0.891
WAZ	−4.4±1.6	−3.1±1.6	0.000*

*Difference is significant at *P*<0.05. WAZ: Weight for age *Z* score, EBM: Expressed breast milk

points in suppl-EBM group when compared to the EBM group ($P < 0.05$) [Table 5]. However, no major adverse events occurred with the infants in both groups during the study period [Table 6]. The sepsis rate was significantly higher in the EBM group than the suppl-EBM group ($P < 0.05$). However, the mortality rate did not differ between the two groups ($P > 0.05$) [Table 7].

DISCUSSION

The present study shows that early enteral feeding with supplemented mother's milk is feasible and safe using a feeding protocol in postcardiac surgical infants. It also highlights that supplementation of mother's milk significantly improves their weight compared to standard feeding. The studies done in China showed similar findings in weight improvement with postoperative nutrition intervention. A retrospective analysis has shown a significant difference in weight with 30 days of nutritional intervention between the two groups.[36] Further studies conducted on infants below 6 months reported that postoperative nutritional intervention

Table 3: Surgeries performed for cardiac defects

Name of the surgery	*n* (%)
Cyanotic	
TAPVC	21 (26.9)
ASO	21 (26.9)
ASO + VSD	11 (14.1)
ASO + VSD + PDA	6 (7.6)
ASO + ASD	5 (6.4)
Truncus arteriosus repair	4 (5.1)
TAPVC + ASD	3 (3.8)
TAPVC + VSD	2 (2.5)
ASO + PDA	2 (2.5)
ASO + ASD + PDA	2 (2.5)
TAPVC + PDA + ASD	2 (2.5)
ASO + VSD + ASD + PDA	1 (1.2)
DORV	1 (1.2)
Acyanotic	
VSD	17 (44.7)
VSD + PDA	7 (18.4)
ALCAPA	4 (10.5)
ASD + MVR	2 (5.2)
AVSD	2 (5.2)
AVSD + PDA	1 (2.6)
VSD + ASD	1 (2.6)
Complete AVSD	1 (1.2)

Values are expressed as *n* (%). ASD: Atrial septal defect, ASO: Arterial switch operation, ALCAPA: Anomalous left coronary artery from the pulmonary artery, VSD: Ventricular septal defect, AVSD: Atrio VSD, DORV: Double outlet right ventricle, PDA: Patent ductus artriosus, MVR: Mitral valve replacement, TAPVC: Total anomalous pulmonary venous return

Table 4: Mechanical ventilation duration, length of intensive care unit and hospital stay, median (range) in expressed breast milk and supplemented expressed breast milk groups

Variables	EBM (*n*=60)	Supplemented EBM (*n*=56)	*P*
Ventilation duration (h)	72.8 (5–384)	74.6 (5.1–264)	0.493
LOICUS (days)	7.5 (2–15)	7 (1–15)	0.900
LOHS (days)	13 (2–174)	13 (5–48)	0.660

LOICUS: Length of intensive care unit stay, LOHS: Length of hospital stays, EBM: Expressed breast milk

for 7–10 days improves the weight significantly in the intervention group.[29,37,38] However, the study conducted by Cui *et al.* reported no significant change in weight with 5 days of nutritional intervention.[11] A recent meta-analysis showed that the standard mean difference (Standard mean difference (SMD) =4.99 g/day, $P < 0.001$) of weight among infants following congenital cardiac repair was significantly higher in the intervention group compared to the control group.[28] In the present study, we did not find any change in the length of the babies in the study population. None of the other studies reported a change in length similar to our study.[18,39] Overall, there are scarce research data on the effect of nutritional intervention on postoperative outcomes (weight and length) of cardiac surgical infants. Until today, evidence of well-designed, well-powered, RCTs investigating the clinical significance of an early initiated nutrition therapy in high-risk cardiac patients after surgery remains sparse.

Table 5: Postoperative macronutrient consumption in expressed breast milk and supplemented expressed breast milk groups, mean±standard deviation, median (range)

Days	Energy (kcal/day)			Carbohydrate (g/day)			Fat (g/day)			Protein (g/day)		
	EBM (*n*=60)	Supplemented EBM (*n*=56)	*P*	EBM (*n*=60)	Supplemented EBM (*n*=56)	*P*	EBM (*n*=60)	Supplemented EBM (*n*=56)	*P*	EBM (*n*=60)	Supplemented EBM (*n*=56)	*P*
0	26.3 (0–85.6)	31.7 (0–87.3)	0.419	2.8 (0–9.1)	3.5 (0–9.8)	0.247	1.4 (0–4.5)	1.4 (0–4)	0.991	0.4 (0–1.56)	0.9 (0–2.5)	0.001*
1	60.9 (0–171.3)	79.3 (15.8–190.5)	0.117	6.4 (0–18.2)	8.9 (1.7–21.5)	0.055*	3.2 (0–9.1)	3.6 (0.7–8.7)	0.825	1.1 (0–3.1)	2.2 (0.4–5.4)	0.000*
2	62.6 (0–202.2)	94.9 (7.9–190.5)	0.001*	6.6 (0–29.4)	10.7 (0.8–21.5)	0.000*	3.1 (0–8.4)	4.3 (0.3–8.7)	0.043	1.1 (0–2.8)	2.7 (0.2–5.9)	0.000*
3	72.4 (0–207.5)	79.3 (0–198.4)	0.434	7.7 (0–22.5)	8.9 (0–22.4)	0.237	3.8 (0–11)	3.6 (0–9.1)	0.644	1.3 (0–5.3)	2.2 (0–5.7)	0.000*
4	70.8 (0–210.8)	95.2 (0–206.3)	0.019*	7.5 (0–22.4)	10.7 (0–23.2)	0.005*	3.7 (0–11.2)	4.3 (0–9.5)	0.139	1.2 (0–4)	2.7 (0–5.9)	0.000*
5	79 (0–263.8)	95.2 (15.8–198.4)	0.081	8.4 (0–28)	10.9 (1.7–22.4)	0.026*	4.2 (0–14)	4.3 (0.7–9.1)	0.630	1.4 (0–4.8)	2.7 (0.4–5.7)	0.000*
6	79 (6.5–263.5)	115 (15.8–214.9)	0.002*	8.4 (0.7–28)	12.9 (1.7–24.1)	0.000*	4.2 (0.3–14)	5.3 (0.7–10)	0.090	1.4 (0.1–4.8)	3.1 (0.4–6)	0.000*
7	79 (0–263.6)	125 (35.7–214.9)	0.001*	8.4 (0–28)	14.1 (4–24.1)	0.000*	4.2 (0–14)	5.7 (1.6–10)	0.050*	1.4 (0–4.8)	3.4 (1–6)	0.000*
8	84 (6.5–263.6)	117 (31.7–214.9)	0.002*	8.9 (0.7–28)	13.2 (3.5–24.1)	0.000*	4.4 (0.3–14)	5.7 (1.4–10)	0.050*	1.5 (0.1–4.8)	3.1 (0.9–6)	0.000*
9	84 (13.1–263.6)	127 (0–214 0.9)	0.002*	8.9 (1.4–28)	14.3 (0–24.1)	0.000*	4.4 (0.7–14)	5.8 (0–10)	0.096	1.5 (0.2–4.8)	3.3 (0–6)	0.000*
10	92.2 (13.1–263.6)	127 (7.9–214.9)	0.003*	9.8 (1.4–28)	14.3 (0.8–24.1)	0.000*	4.9 (0.7–14)	5.8 (0.3–10)	0.132	1.6 (02–4.8)	3.6 (0.2–6)	0.000*
11	100±48.7	123.5±45.5	0.008*	10.7±5.3	13.9±5.1	0.001*	5.2±2.5	5.7±2.1	0.259	2±1	3.4±1.2	0.000*
12	101.3±47.3	124.9±45.1	0.007*	11±5.2	14.1±5.1	0.001*	5.2±2.4	5.7±2.1	0.221	2±1	3.5±1.3	0.000*
13	102±48.5	125.3±43.6	0.008*	11±5.93	14.1±4.9	0.001*	5.2±2.5	5.8±2.2	0.239	2±1	3.5±1.2	0.000*
14	103.1±48.4	124.5±43.6	0.014*	11.1±5.3	14.1±5	0.002*	5.3±2.5	5.7±2	0.355	2±1	3.5±1.2	0.000*
15	103.1±48.1	126.3±43.8	0.008*	11.1±5.2	14.3±5	0.001*	5.3±2.5	5.8±2	0.260	2±1	3.5±1.2	0.000*

*Difference is significant at $P<0.05$, Values are represented as *n* (%). EBM: Expressed breast milk

Table 6: Adverse events in expressed breast milk and supplemented expressed breast milk groups

Days	Diarrhea			Aspiration			Abdominal distension		
	EBM (*n*=60)	Supplemented EBM (*n*=56)	*P*	EBM (*n*=60)	Supplemented EBM (*n*=56)	*P*	EBM (*n*=60)	Supplemented EBM (*n*=56)	*P*
0	0	0	0	7 (11.6)	9 (16.0)	0.594	0	2 (3.5)	0.231
1	0	2 (3.5)	0.231	7 (11.6)	4 (7.1)	0.531	3 (5)	2 (3.5)	1.000
2	5 (8.3)	6 (10.7)	0.757	6 (10)	6 (10.7)	1.000	5 (8.3)	4 (7.1)	1.000
3	9 (15)	11 (19.6)	0.625	8 (13.3)	4 (7.1)	0.365	6 (10)	4 (7.1)	0.744
4	7 (11.6)	11 (19.6)	0.307	10 (16.6)	6 (10.7)	0.425	5 (8.3)	6 (10.7)	0.757
5	10 (16.6)	11 (19.6)	0.810	7 (11.6)	8 (14.2)	0.784	3 (5)	5 (8.9)	0.480
6	10 (16.6)	12 (21.4)	0.637	11 (18.3)	5 (8.9)	0.182	5 (8.3)	6 (10.7)	0.757
7	9 (15)	13 (23.2)	0.344	7 (11.6)	3 (5.3)	0.325	7 (11.6)	4 (7.1)	0.531
8	8 (13.3)	9 (16.0)	0.795	9 (15)	1 (1.7)	0.017	6 (10)	3 (5.3)	0.493
9	9 (15)	8 (14.2)	1.000	7 (11.6)	3 (5.3)	0.325	5 (8.3)	2 (3.5)	0.718
10	10 (16.6)	7 (12.5)	0.605	6 (10)	3 (5.3)	0.493	7 (11.6)	2 (3.5)	0.165
11	9 (15)	6 (10.7)	0.585	7 (11.6)	1 (1.7)	0.062	4 (6.6)	3 (5.3)	1.000
12	11 (18.3)	6 (10.7)	0.299	7 (11.6)	1 (1.7)	0.062	4 (6.6)	3 (5.3)	1.000
13	10 (16.6)	7 (12.5)	0.605	6 (10)	1 (1.7)	0.115	3 (5)	3 (5.3)	1.000
14	11 (18.3)	6 (10.7)	0.299	6 (10)	1 (1.7)	0.115	4 (6.6)	3 (5.3)	1.000
15	10 (16.6)	6 (10.7)	0.425	7 (11.6)	1 (1.7)	0.062	4 (6.6)	3 (5.3)	1.000

Values are expressed as *n* (%)

Table 7: Sepsis and death in expressed breast milk and supplemented expressed breast milk groups

	EBM (60), *n* (%)	Supplemented EBM (56), *n* (%)	*P*
Sepsis (culture positive)	7 (11.6)	0	0.008*
Death	7 (11.7)	2 (3.6)	0.103

*p<0.05 is considered as significant, EBM: Expressed breast milk

Literature has shown that in the immediate postoperative period, the body weight of cardiac surgical infants increases due to systemic inflammation and third-space fluid retention.[17,40,41] However, it depends on many factors, such as age, type and complexity of cardiac defect, preoperative nutritional status, CPB duration, and aortic cross-clamp time.[4] This excess third-spaced fluid is usually removed by diuresis within 96 h as systemic inflammation settles. Therefore, the intervention duration was kept at 15 days for the present study. The babies' weight was measured when they were separated from the mechanical ventilation and invasive devices.

The present study showed that infants in the suppl-EBM group did not have major differences in biochemical blood parameters compared to those in the EBM group. Most of the values were within the reference range in the supplemented group, indicating that the planned intervention did not affect the infant's biochemistry. Therefore, it is safe to give high-calorie feed to infants following congenital cardiac repair in the ICU.

Albumin and C-reactive protein (CRP) are important markers used to assess the nutritional and inflammatory status of postoperative pediatric cardiac surgical patients.[42] Decreased CRP levels after surgery may indicate the shift from catabolism to anabolism.[43] The CRP levels were not significantly different between the two groups. However, the decreasing trend of CRP in the intervention group indicated a shift from catabolism to anabolism. Zhang *et al.*, in their study, reported similar findings.[12]

The feeding intolerance and interruption episodes were managed according to our ICU protocols. The possible explanations for feeding intolerance among the infants in this study could be poor cardiac function with gut hypoperfusion, systemic inflammation, bowel edema, high-dose inotropes and vasopressors, and sepsis. Similar findings were described in some of the previous studies.[11,12]

The nasogastric feed was started with the lowest volume and gradually escalated. During feeding intolerance, the feed was withheld for 4–6 h and then started with the same nutrient composition and volume after stabilization. Feeding interruptions also occurred during medical procedures like weaning from mechanical ventilation and extubation, sternum closure, and investigative procedures like bronchoscopies and tracheostomies.

The present study indicated that energy and protein consumption was significantly higher in the intervention group than in the control group. This was one very important finding from our study, which indicated the feasibility of improving macronutrient intake in these small babies in the immediate postoperative period by enteral route. Enriching the mother's milk with HMF helps augment the high requirement of calories and protein during this high catabolic postoperative period (as energy demand increases and restricted volume comes to force), and the infants counter the systemic inflammation better with good recovery.

Another important message from this study is that it is feasible to start enteral feeding early after surgery, within 6–8 h; soon, the intensive care team will be sure about the required conditions to start enteral feeding in these postoperative infants [Figure 2]. Furthermore, utilizing the gut early helps prevent gut translocation of bacteria and sepsis, as evident from our study. In consonance with the present study, other studies have shown a significant increase in daily energy and protein intake within 5–10 days of nutritional intervention with supplemented breast milk feeding.[11,29,37] Zhang *et al.* documented that the daily energy intake did not differ significantly between the two groups with 5 days of nutrition intervention. However, the protein intake was significantly higher in the intervention group.[12] The findings of the present study were similar to the results of a meta-analysis, which showed that the energy and protein intake in the intervention group was significantly higher than in the control group.[28]

Our study found that mechanical VD, LOICUS, and LOHS did not differ significantly between the two groups, similar to the results of the other studies.[11,12,29] A recent meta-analysis indicated that the SMD of MV duration, LOICUS, and LOHS was not significantly different between the control and intervention groups. However, two other studies (both RCTs) contradicted their report that VD significantly differed between the two groups.[38,44] In contrast to the present study, other studies have reported that the incidence of sepsis was higher in the intervention group but not statistically significant between the two groups.[11,29]

Limitations of the study

One major limitation of our study was that the calculated sample size could not be met due to the COVID-19 pandemic. As we had planned enteral feeding with EBM for both groups, the primary issue was insufficient mother's milk production in those babies who stayed for a more extended period in the ICU. Inflammatory markers would have been included in this study to better interpret the intervention's effect.

CONCLUSIONS

We concluded that postoperative cardiac surgical infants could safely have enteral feeding early within 6–8 h. Fortification of mother's milk with HMF, keeping it iso-osmolar, is possible. Feeding infants with supplemented EBM helped improve macronutrition compared to feeding infants with EBM only. The infants in the intervention group had shown increased weight, but their length remained the same in both groups. The macronutrient consumption was significantly higher in the supplemented EBM group. Adequate energy supplementation/consumption is the primary focus to reduce the short and long-term consequences like prolonged inflammation, edema, MV, infection, and sepsis, which would decrease the morbidity and mortality in postoperative babies. Supplemented mother's milk helped augment the extra required calories, protein, and other nutrients, which supported the postoperative convalescence of these babies.

Ethics clearance

Obtained from Institute Ethics Committee of AIIMS, New Delhi and Institute of Home Economics, New Delhi, India.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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