

## Original Research Article

# Safety of aggressive nutrition bundle- aggressive parenteral nutrition, standardized feeding policy, human milk fortification and probiotics in babies born less than 34 weeks of gestation: a prospective analytical cohort study

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## ABSTRACT

**Background:** Despite changes in nutritional interventions in neonatal intensive care units worldwide, significant proportion of preterm babies are growth restricted at discharge. Authors intended to look at the feasibility of aggressive nutrition bundle (aggressive parenteral nutrition, standardized feeding policy, fortification and probiotics) in preterm neonates.

**Methods:** This single centre prospective analytical cohort study, involving babies born before 34 weeks of gestation, was conducted in a tertiary hospital. Aggressive parenteral nutrition and enteral nutrition bundle intervention was started within 24 hours of birth. Clinical, laboratory and anthropometrical parameters were monitored longitudinally to ensure safety of this intervention.

**Results:** Mean gestational age and birth weight of the cohort (n=107) was 30.6 weeks (SD±2.6) and 1147 grams (SD±287) respectively. Out of 107 babies, 67.3% (n=72) have extra uterine growth retardation (EUGR) at discharge and was more in small for gestational age neonates (p=0.001). With this aggressive parenteral and enteral nutrition bundle intervention, medical necrotizing enterocolitis (NEC) developed in 7.4 % (n=8) babies while surgical NEC was seen in 1.9%. (n=2). Early onset and late-onset sepsis occurred in 1.8% and 5.4% of babies respectively while mild hyperammonemia, mild hypertriglyceridemia, raised creatinine and urea developed in 12.4%, 4.6%, 7.4% and 11.7% respectively. Hyperglycemia and hypoglycemia were present in 8.8% and 5.6% babies respectively.

**Conclusions:** Aggressive nutrition bundle (aggressive parenteral nutrition, standardized feeding policy, fortification and probiotics) can be safely employed in preterm babies. There is an urgent need to design a study to see the impact of this approach on incidence of EUGR in preterm babies.

**Keywords:** Aggressive nutrition bundle, Parenteral nutrition, Preterm babies, Safety

## INTRODUCTION

Malnutrition during critical stages of development in prematurely born infants is associated with long lasting negative effects on growth and neurodevelopment, at

least through school age and possibly also into adulthood. American academy of Pediatrics recommends that growth of postnatal preterm infants in both their anthropometric indices and body composition should be same as normal fetus for same gestational age.<sup>1</sup> Lower rates of weight

gain and head growth are associated significantly with incidence of cerebral palsy, mental developmental index < 70 and neurodevelopmental impairment at 18 month of age.<sup>2</sup> Poor head growth in postnatal preterm infants is associated with increased prevalence of motor and cognitive impairment at 3-8 years and loss of 4.1 IQ points in adults.<sup>2</sup> A recent study of preterm infants found a significant relationship between slow growth and the likelihood of cerebral palsy, Mental Developmental Index (MDI) score less than 70 and neurodevelopmental impairment.<sup>3</sup> A recent study of neurodevelopmental outcomes at 18 months in preterm infants demonstrated an increase of 8.2 MDI points for each 1g/kg/day protein and 4.6 MDI points for each 10kcal/kg/ day in the first week of life.<sup>4</sup> Efforts during the past two decades to develop standardized feeding guidelines have begun to show some success in reducing the incidence of extra uterine growth restriction (EUGR). Such guidelines provide intense nutritional support through a combination of early parenteral and enteral nutrition, with steady increment in the enteral feeding and fortification, has shown some improvement. Compared with historical controls, benefits of this approach has shown an earlier regaining of birth weight, an earlier achievement of full enteral nutrition, reduction in the duration of parenteral nutrition, and improved anthropometry at 36 weeks' post-menstrual age (PMA) or discharge.<sup>5</sup> Essentially all recent recommendations for feeding preterm infants have documented the need for increased energy and protein intake started as early as possible after birth.<sup>6,7</sup> Actual practice of aggressive or individually optimized nutrition of preterm infants, however, continues to lag behind such recommendations. The mean gestational age and birth weight of the cohort was 30.6 weeks (SD±2.6) and 1147 grams (SD±287) while 59.8% (n=64) of the enrolled population was small for gestational age (SGA). The mean duration of NICU stay was 28.3 days (SD±16.7). PN characteristics are shown in table 2 wherein median time to start PN was 13 hours (IQR, 4-18) while mean days of PN administration was 6.5 days (SD±2.6). Most of these studies have been carried out in developed countries and data from developing countries is lacking. It is well known that infant characteristics such as environment and genetic factors differ in our country in comparison to developed countries. Moreover, in the Indian setup, the proportion of small for gestational age babies is more when compared to appropriate for gestational age babies. Baseline characteristics of Indian new born babies being different from babies born to mothers in developed countries, this study was conducted to demonstrate feasibility of aggressive nutrition bundle (aggressive parenteral nutrition, standardized feeding policy, fortification and probiotics) intervention in Indian preterm neonates and the impact of this intervention on incidence of EUGR in our unit.

## METHODS

This single center prospective analytical cohort study was conducted in a neonatal intensive care unit of a tertiary

teaching hospital in western India by implementing aggressive nutrition bundle (aggressive parenteral nutrition, standardized feeding policy, fortification and probiotics). It was initiated on 1 January 2015 and prospectively done over a period of 16 months and completed on 30 April 2016. Purposive sampling technique was employed wherein 138 babies were enrolled.

### Inclusion criteria

- Preterm neonates less than 34 weeks at birth admitted to NICU and received only mother's milk, were included in this study.

### Exclusion criteria

- Babies with major congenital anomalies, not requiring intravenous fluids and refusal of consent from parents.

Primary outcome was to study the feasibility of aggressive nutrition bundle (aggressive parenteral nutrition, standardized feeding policy, human milk fortification and probiotics) while secondary outcomes were to study time to achieve enteral feed volume of 150 ml/kg/day, time to regain birth weight, length of hospital stay, incidence of late onset sepsis and incidence of EUGR.

The study was approved by Institutional review board and scientific committee and informed consent was obtained from parents.

### Intervention

Intervention included aggressive parenteral nutrition and enteral feeding bundle comprising standardized feeding policy, human milk fortification and probiotics supplementation.

All eligible neonates received parenteral nutrition starting with 2.5 grams/kg/day of amino acids (Aminoven 10%) and 2 grams/kg/day of lipids (SMOF lipid 20 %) within 24 hours of birth. Increments were done over 2 days to administer 3.5 grams/kg/day and 3 grams/kg/day of amino acids and lipids respectively (amino acids 3 grams/kg/day on day 2 and 3.5 grams/kg/day on day 3, lipids 2.5 grams/kg/day on day 2 and 3 grams/kg/day on day 3, subject to calorie nitrogen ratio target to be maintained around 150) and both were administered over 24 hours duration. PN was prepared under laminar flow with aseptic precautions and attached to babies daily at 12 noon. The feeding protocol was developed by consensus of faculty members on the basis of review of literature and other centres' feeding protocols. Enteral feeding was initiated and advanced as per standardized feeding regimen (SFR). Minimal enteral nutrition (20 ml/kg/day) with expressed own mother's milk (EBM) or pasteurized donor human milk (PDHM) (20 ml/kg/day)

was started as soon as possible depending on the clinical stability of the baby and increased by 20 ml/kg/day depending on tolerance. Human milk fortification (HMF) was started at enteral feeding volume of 150 ml/kg/day and administered as per manufacturer recommendation and was continued till baby reaches 2000 grams of weight. Probiotics were added along with trophic feeds. Enrolled neonates were supplemented with freshly reconstituted contents of allocated sachets every day and continued till corrected age of 34 weeks. Reconstitution of dry powder in the sachets was done using sterile water for injection or breast milk when available. Flushing of feeding tube with 0.5ml distil water was done after probiotic administration. Vitamin D, iron and multivitamin supplementation was provided to all the enrolled neonates as per standard practice. Clinically babies were monitored for complications like hemodynamic instability, feeding intolerance, intra ventricular haemorrhage, signs of sepsis, respiratory support, retinopathy of prematurity, necrotizing enterocolitis etc. Laboratory monitoring was done by obtaining serum ammonia, triglycerides, urea creatinine, sodium, potassium, ionic calcium, academia and bilirubin one day after attaining maximum dose of PN (i.e. on day 4).

Blood sugar was monitored in each shift and weight was recorded daily. PN was discontinued when enteral feed volume reached 120ml/kg/day. PN was stopped midway in case of hypoglycaemia (<50mg/dl), hyperglycaemia (>180mg/dl), hyperkalaemia (>5.5meq/l), hyperammonaemia (>200mcg%), hypertriglyceridemia (>200mg/dl), academia (pH<7.3) or kidney dysfunction (urea >100mg/dl and creatinine >1.5mg/dl). PN was restarted if abnormal values returned to normal when repeated after 48 hours.

If PN was stopped for 24 hours after initiation, because of any reason, it was not counted as parenteral nutrition. Anthropometry including weight (daily), length (weekly) and head circumference (weekly) was recorded with the help of a digital weighing scale which was calibrated at regular intervals, infant meter and a non-stretchable elastic tape respectively.

### Statistical analysis

Data were entered in Microsoft Excel and analyzed using Stata Version 13.1 (Stata Corp, College Station, Texas, USA). Mean with standard deviation, median with interquartile range for linear variables, and proportions for categorical variables were calculated. Mann-Whitney test was used for non-parametric data.

The proportions were compared using chi square test or Fisher's exact test (for low expected cell counts). We calculated z scores for weight based on Fenton's growth chart for pre-term infants.<sup>8</sup> A p value of less than 0.05 was considered to be statistically significant.

## RESULTS

A total of 107 babies were enrolled and followed up for outcomes in this study. The baseline characteristics of enrolled babies are shown in (Table 1). The mean gestational age and birth weight of the cohort was 30.6 weeks (SD±2.6) and 1147 grams (SD±287) while 59.8% (n=64) of the enrolled population was small for gestational age (SGA). The mean duration of NICU stay was 28.3 days (SD±16.7). PN characteristics are shown in table 2 wherein median time to start PN was 13 hours (IQR, 4-18) while mean days of PN administration was 6.5 days (SD±2.6).

**Table 1: Baseline characteristics of neonates (N=107).**

Variable	N (%)
Assisted reproduction	23 (27%)
Multiple pregnancies	25 (23.4%)
Pregnancy induced hypertension	55 (51%)
Abnormal umbilical artery doppler	50 (46.7%)
Vaginal delivery	25 (23.4%)
Male gender	61 (57%)
Small for gestational age	64 (59.8%)
Birth weight (grams)*	1147 (±287)
Gestational age (weeks)*	30.6 (±2.6)
Stay in NICU (days)*	28.3 (±16.7)
Corrected gestational age at discharge (weeks)*	35.8 (±2.2)
Discharge weight (grams)*	1477.4 (±217)

Mean amino acid and fat intake was 3.2 grams/kg/day and 2.8 grams/kg/day respectively while mean calorie nitrogen ratio (CNR) was 137.7 (SD±24.7).

**Table 2: Parenteral nutrition (PN) characteristics.**

Nutritional intervention	Mean±SD
Age at PN started (in hours)*	13 (4-18)
Days of PN	6.5 (±2.0)
Fluid intake (ml/kg/day)	130.4 (±30.4)
Amino acid intake(grams/kg/day)	3.21 (±0.5)
Fat intake	2.84 (±0.5)
Calorie nitrogen ratio	137.7 (±24.7)
Non protein calories	82.6 (±26.0)
Carbohydrate calories	53.18 (±19.4)
Fat calories	29.4 (±8.47)

\*Median (IQR)

With this aggressive nutrition bundle, we found that 16.1% (n=17) neonates developed feeding intolerance while 7.4% (n=8) encountered necrotizing enterocolitis (NEC) and 5.6% (n=6) developed chronic lung disease (CLD).

Blood product component (packed red cell, fresh frozen plasma and platelet) transfusion was required in 18.6% (n=20) of the cohort during entire NICU stay. Median

duration of ventilation and antibiotics was 4 days (IQR, 2-11) and 5 days (IQR, 3-21) respectively (Table 3).

**Table 3: Complications encountered during study period (n=107).**

Parameter	N (%)
Feed intolerance	17 (16.1%)
Necrotizing Enterocolitis	8 (7.4%)
Fresh Frozen Plasma transfusion	4 (3.7%)
Platelet transfusion	4 (3.7%)
Packed Red Cell transfusion	12 (11.2%)
Chronic Lung Disease	13 (12.1%)
Days of ventilation*	5 (2-8)
Antibiotic days*	5 (3-21)

\*Median (IQR)

With this aggressive intervention, the incidence of EUGR at discharge in this cohort was 67.3% (n=72). The median time to reach full enteral feed volume of 150ml/kg/day and regain birth weight was 8 days (IQR, 6-15) and 10 days (IQR, 5-18) respectively.

**Table 4: Abnormal laboratory parameters observed during study period.**

Variable	N (%)
hs Patent ductus arteriosus	13 (12.1%)
Academia	7 (6.5%)
Hyponatremia	13 (12.1%)
Hypernatremia	5 (4.6%)
Hypokalaemia	4 (3.7%)
Hyperkalaemia	6 (5.6%)
Hyperammonaemia	8 (7.4%)
Hypertriglyceridemia	5 (4.6%)
Raised blood urea	11 (10.2%)
Raised blood creatinine	8 (7.4%)
Hyperglycaemia	9 (8.4%)
Hypoglycaemia	6 (5.6%)
Cholestatic jaundice	3 (2.8%)
Culture positive sepsis	14 (13.3%)
Intra ventricular haemorrhage	8 (7.4%)

Mean duration of hospital stay was 28.3 days ( $\pm 16.7$ ) in this study. Overall blood culture positive sepsis was present in 13.3% (n=14) while late-onset sepsis was present in 5.6% (n=6) of babies, followed by hyponatremia and elevated urea in 12.1% (n=13) and 10.2% (n=11) respectively.

**Table 5: Secondary outcomes.**

Parameters	Outcomes
Time to full enteral feeding* median (IQR)	8 days (6-15)
Time to regain birth weight, median (IQR)	10 days (5-18)
Length of hospital stay, mean ( $\pm$ SD)	28.3 ( $\pm 16.7$ )
Incidence of Late onset sepsis, n (%)	6 (5.6%)
Incidence of EUGR, n (%)	72 (67.3%)

\*150ml/kg/day

Hypoglycemia, hyperkalemia and acidemia was found in 5.6% (n=6), 5.6% (n=6) and 6.5% (n=7) respectively (Table 4 and 5).

## DISCUSSION

Safety of early amino acid administration is based on biochemical parameters such as acidemia, urea, ammonia and triglyceride concentrations and concentration of potentially neurotoxic amino acids; however, none of these parameters are specific to amino acid intolerance. Side effects observed with early and high dose amino acid infusion such as increased mean peak serum indirect bilirubin, lower base excess, lower concentrations of bicarbonates and increased blood urea nitrogen do not have short term clinical implications. Principal effects of earlier/higher rates of intravenous amino acid administration include increased weight gain, increased weight at discharge, and reduced growth restriction at term gestation. The optimum (safest and most efficacious) mixture of amino acids (both essential and non-essential) for very preterm infants has yet to be determined. There are likely to be different requirements at different stages of development, and unique metabolic conditions based on degree and types of illnesses, pathophysiology, and medical and surgical treatment. Subnormal plasma concentrations of selected essential amino acids can occur.<sup>9,10</sup> Although there has been a trend towards earlier and higher rates of infusion of intravenous lipids for preterm infants, with most now starting at least low-rate infusions (0.5–1.0 g/kg/day) on the first or second day after birth, there has been little study of the benefits or risks of this change in practice.<sup>11</sup> We have studied a cohort with changes in nutritional policy in our unit. Giving early TPN was potentially challenging task as it was prepared once daily at a specific time at our institute. If abnormal biochemical parameters were found after starting this intervention, the prepared PN unit was discarded. The incidence of such abnormal fluctuations was 7% in this study. Average amino acids and fat intake was 3.2 grams/kg/day and 2.8 grams/kg/day respectively in present study which was lower than the target maximum of 3.5 grams/kg/day and 3 grams/kg/day respectively because of discontinuing PN in view of deranged biochemical parameters after initiation. In contrast, The national institute of child health and human development (NICHD) neonatal research network reported an increase in weight, length, and head circumference at 36 weeks after this pattern of greater early versus lower late amino acid and protein supply.<sup>12</sup> The NICHD network study maintained a higher total protein and amino acid supply for a longer period, perhaps indicating that both early and sustained higher rates and plasma concentrations of protein and amino acids are necessary to produce greater gains in growth, at least of the brain.<sup>9</sup> The mean duration of NICU stay was 28.3 days ( $\pm 16.7$ ) in this study. In a similar Chinese study mean length of hospital stay was 26.4 days ( $\pm 12.9$ ) which was in agreement with present study.<sup>13</sup> A study by Shukla et al. showed that by adopting the new nutritional practice



guidelines there was a significant improving trend towards reduced length of NICU stay.<sup>14</sup> In this study, 6.5% (n=7) and 4.7% (n=5) of babies died and left against medical advice respectively; 88% (n=95) babies were discharged home from hospital. Factors associated with mortality in present study were extreme low birth weight (< 1000 grams), prematurity (< 30 weeks of gestational age) and need of invasive ventilator support ( $p < 0.05$ ). In a study from north India, birth weight  $\leq 800$  grams, mechanical ventilation and hypotensive shock predicted mortality.<sup>15</sup> A Nigerian study found that babies with gestational age <32 weeks accounted for 34.2% mortalities.<sup>16</sup> Time to attain full feed volume of 150ml/kg/day was 8 days (IQR, 6-15) in present study while variations are seen worldwide. Brunnella et al, Wang et al, Milene et al, Luigi et al, have, in their studies, shown time to full feeds as 15, 17, 15.5 and 18 days respectively.<sup>17-19</sup> Earlier time to achieve full enteral feeds in present study may be because of strict adherence to SFR and different gestational age groups. Shukla et al, showed that by adopting the new nutritional practice guidelines there was a significant reducing trend in time to full feeds.<sup>14</sup> Graziano et al, has shown that upon implementation of enteral nutrition bundle mean duration of time to reach full feeds dropped from 21 to 18 days.<sup>20</sup> Lee et al, showed that implementation of a standardized feeding protocol for VLBW infants resulted in earlier successful enteral feeding without increased rates of major morbidities.<sup>21</sup> Median age of PN started was 13 hours (IQR, 4-18) in present study. Valentine et al, showed that early amino-acid (EAA) supplementation in preterm babies within 24 hours after birth than later had significantly greater weight gain and shorter duration of parenteral nutrition administration.<sup>22</sup> Most studies have found that positive protein balance in more aggressively fed preterm infants is safe and effective and not associated with hyperammonemia, uraemia, or metabolic acidosis.<sup>23,24</sup> Hyperkalemia often is reduced, and insulin secretion, known to be stimulated by such amino acids as leucine and arginine, is increased, producing higher plasma insulin concentrations, which are associated with a lower incidence of hyperglycemia and lower time-averaged glucose concentration.<sup>25-28</sup> A recent study prospectively randomized ventilator-dependent preterm infants into an early TPN group that received 3.5 g/kg/day amino acids and 3 g/kg/day 20 % intralipid, starting within 1 hours after birth, and a late TPN group that was started on a solution containing only glucose during the first 48 hours of life followed by 2 g/kg/day of amino acids and 0.5 g/kg/day of intralipid then increased by 0.5 g/kg/day to a maximum of 3.5 and 3 g/kg/ day, respectively. The early TPN group had significantly greater nitrogen retention throughout the seven-day study period than the late TPN group and significantly greater energy intake, plasma levels of cholesterol, triglycerides, and bilirubin (bicarbonate, blood urea nitrogen, creatinine, and pH were similar in both groups during the study period). Thus, aggressive intake of IV lipids (in this case, soybean oil) may be tolerated immediately after

birth by very preterm, VLBW infants without significantly increased metabolic risks.<sup>11</sup>

Carbohydrate calories mean were 53.18 kcal in present study. Nutrition can alter body composition was proved in study done by Kashyap et al, Greater rates of weight gain and nitrogen retention were observed at high-carbohydrate intake compared with high-fat intake at both gross energy intakes. Greater rates of energy storage and an increase in skin fold thickness were observed in group (high-energy high carbohydrate diet) despite higher rates of energy expenditure. These data support the hypothesis that at isocaloric intakes, carbohydrate is more effective than fat in enhancing growth and protein accretion in enterally fed low-birth-weight infants.<sup>29</sup> In present study acidemia was present in 6.5% (n=7) of enrolled babies. In a study on preterm infants receiving lower or higher dose of parenteral amino acids (1.5 or 3 g/kg/day) for short (5 hours), extended (24 hours), or prolonged (3-5 days) duration, acidosis was evident in all infants between day 2 and 5 after birth. Significantly lower early pH, higher blood urea nitrogen and greater weight loss was observed in infants with a large PDA and 65% of variance in acidosis was attributed to lower gestational age, weight loss, and PDA. This study clearly demonstrated that although low-birth-weight infants often develop metabolic acidosis in the first few days after birth, this occurs irrespective of dose and duration of parenteral amino acid administration. This may be due to renal immaturity resulting in higher bicarbonate loss by the renal tubules.<sup>30</sup> In present study overall incidence of NEC was 7.4 % (n=8) including 1.4% who developed surgical NEC which is comparable with NICHD data. As per NICHD data, incidence of NEC was 3% and 5% in ELBW and VLBW babies respectively. NEC depends upon various ante partum, intrapartum and postpartum factors giving rise to this difference. Also, definition of medical NEC and feed intolerance is overlapping, so it might be underreported.<sup>31</sup> In this study, increased blood urea was present in 10.2% (n=11) of neonates. Increased blood urea nitrogen levels should also be considered a sign that amino acids are effectively being oxidized, which releases ammonia, and that the liver is intact and healthy, enabling detoxification of the ammonia to urea via the hepatic urea enzyme cycle.<sup>23</sup> Careful management of parenteral fluids and co morbidities may reduce the incidence of uraemia and metabolic acidosis and promote protein accretion. Taken together, the results from these recent studies suggest caution in the use of high rates of amino acid infusion, particularly with solutions that are not optimized for very preterm infants, particularly those who are sick and physiologically unstable, and especially early after birth. Improvement of the metabolic and physiological condition of such infants is likely to be necessary before amino acid infusion at high rates would be safe and effective in promoting protein balance.<sup>32</sup> Hyperglycemia and hypoglycemia were present in 8.4% (n=9) and 5.6% (n=6) of the cohort in present study. Study by Diya et al, showed that hyperglycemia correlated with prolonged ventilator dependency and

increased hospital length of stay in premature septic infants. Avoidance of excessive nutrient delivery and tight glycemic control during periods of acute metabolic stress may improve outcome in this patient population.<sup>33</sup> The incidence of EUGR depends on definition used for defining EUGR, and growth charts used to compare and calculate. Study by Shukla et al, showed that by adopting the new nutritional practice guidelines there was a significant reduction in extra uterine growth retardation and improving trend in discharge weight, HC and length percentile.<sup>14</sup> Incidence of EUGR, depending on weight at discharge, was 67.3% (n=72) in present study. This incidence, although high, is lower than the incidence found by some researchers worldwide. A north Indian study showed that the incidence of EUGR was 64.8% at discharge and 76.8% at term.<sup>34</sup> Dusick et al, showed that in 2003 NICHD data, 97% very low birth weight babies were EUGR at discharge and 40 % of these were having weight less than 10<sup>th</sup> centile at 18 months of age.<sup>35</sup> In a study from Western Australia and Korea, the incidence of EUGR in babies born < 28 weeks was 50% (5-40) and 67% respectively while studies from China has shown an incidence of 78.9% and 60% in VLBW babies.<sup>13,36,37</sup> It should be noted that the use of different intrauterine growth curves by these investigators contributed to the variability in the incidence of EUGR. Study by Graziano et al, showed that upon implementation of enteral nutritional bundle the percent of infants who were discharged with a weight above the 10<sup>th</sup> percentile increased from 65 to 81%.<sup>20</sup> In present study, babies born SGA were significantly EUGR at discharge than born AGA (p=0.0001). This was in agreement with previous studies which demonstrated that SGA status at birth was significantly associated with EUGR at discharge.<sup>5,38</sup> Early enteral feeding is advantageous because it improves the functional adaptation of the gastrointestinal tract by stimulating hormone secretion and gastrointestinal motility. It also decreases the need of total parenteral nutrition and its associated complications. Despite this, early enteral feeding is often delayed in high risk infants because it has been thought to be associated with an increased risk of NEC. In this study, median time to full enteral feeding was 8 days (IQR, 6-15). Various studies have shown that after implementation of enteral nutritional bundle, the time to full feeds has reduced significantly.<sup>13,20</sup> A meta-analysis of five RCTs conducted on preterm infants did not find any extra risk of NEC in infants randomized to early feeding.<sup>38</sup> Late-onset sepsis was present in 5.6% (n=6) babies in our cohort which was comparable to other studies while incidence of CLD and IVH was 12.1% (n=13) and 7.4% (n=8) which was in agreement to NICHD network data.<sup>31, 39</sup>

## CONCLUSION

Aggressive nutrition bundle (aggressive parenteral nutrition, standardized feeding policy, fortification and probiotics) was safely tolerated by Indian preterm babies including SGA neonates in this study. With this aggressive nutrition bundle, the incidence of EUGR in

our cohort was relatively less at discharge than some of the previous studies. Similarly, time to full enteral feeds, time to regain birth weight and associated complications were comparable to other studies. Nutritional interventions alone have not helped in reducing EUGR. Region specific extra uterine growth charts may help in getting the true incidence of EUGR.

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