Acta Scientific Paediatrics (ISSN: 2581-883X)

Volume 5 Issue 5 May 2022

Review Article

Comprehensive Clinical Approach to Nutritional Management in Preterm Infants: Review Article

Chakradhar Maddela*

Department of Neonatology, ESIC Medical College, Sanath Nagar, Telangana, India

***Corresponding Author:** Chakradhar Maddela, Department of Neonatology, ESIC Medical College, Sanath Nagar, Telangana, India.

DOI: 10.31080/ASPE.2022.05.0526

Received: April 06, 2022

Published: April 28, 2022

Abstract

Introduction: Nutrition is "the process of providing or obtaining the food necessary for the health and growth of cells or organisms" [1,2]. Preterm extremely low birth weight infants (ELBW) are born in mid trimester of pregnancy and experience sudden interruption of intrauterine nutrition at birth and delay in establishment of full enteral nutrition in postnatal life. Foetus multiplies in weight five times during last trimester and maximum accretion of nutrients occurs during same period of pregnancy [3] (Fenton 2013). These babies are prone to develop extra uterine growth restriction (EUGR) in early infancy, [4] Embleton 2001. Parenteral nutrition (PN) is a mandatory life saving and nutrition promoting intervention for preventing EUGR, tissue breakdown and achieving optimum nutrition, growth and development until full enteral feeds are established. Hence, assessment of nutritional needs, early aggressive parenteral nutrition and early trophic feeds within 24 of life [5], incremental increase in enteral feeds with extracted fresh human milk, full enteral feeds, breast milk fortification, preterm formula feeds and post discharge plan are crucial in the nutritional management of extremely low birth weight infants.

Methods: A Boolean literature search conducted in February 2022 through online databases - PubMed, Web of Science (WOS), Google Scholar, Cochrane library, Researchgate and manual search for scientific articles and texts with the title topic and keywords - preterm infants, nutrition, needs, requirements and management. The retrieved articles were screened with title and abstract for interested study research title. Retrieved 33 articles from PubMed, 10 from Cochrane library, 27 from WOS, 6 from Google scholar, 2 from researchgate and 12 from other sources. Articles were also searched through citations and references from collected study articles. Study restricted to articles written in English language. The following filters were used in retrieving study articles - free full text articles, Human, Newborn, Systematic reviews, meta-analysis, randomized control trials (RCTs), Clinical trials and Reviews. Animal studies were excluded. The retrieved articles were screened for the interested research title topic after going through the article title and abstract. A total of 32 study papers were analysed.

Results: The collected study papers were narrated with the subheadings - definition, nutritional needs of ELBW infant, TPN, enteral nutrition (minimal enteral nutrition, MEN and nutritional feeds), human milk fortifier, feeding intolerance, nutritional assessment, catch up growth and feeding advice at discharge.

Keywords: Preterm; Infant; Nutrition; Management; Requirements

Abbreviations

CNR: Calorie Nitrogen Ratio; DEBM: Donar Expressed Breast Milk; ELBW: Extremely Low Birth Weight; ECF: Extracellular Fluid; EMBM: Expressed Mother's Breast Milk; GIR: Glucose Infusion Rate; GRV: Gastric Residual Volume; HMF: Human Milk Fortifier; HC: Head Circumference; MEN: Minimal Enteral Nutrition; NEC: Necrotizing Enterocolitis; NICU: Neonatal Intensive Care Unit; NEPDF: Nutrient Enriched Post Discharge Formula; PN: Parenteral Nutrition; PTI: Preterm Term Infant; PPHN: Persistent Pulmonary Hypertension of Neonate; PENALD: Parenteral Nutrition Associated Liver Dysfunction; PMA: Postmenstrual Age; RCT: Randomized Control Trial; TPN: Total Parenteral Nutrition; WOS: Web of Science

Introduction

Nutritional needs of ELBW infants [6]

- **Energy requirements**: Nutritional reserves of ELBW infants are sufficient for only first couple of days and needs total calorie requirement of 110-135 kcal/kg/day in the initial days. However, calories of 100-120/kg/day are sufficient when given by parenteral route. These babies need 50kcal/kg/day for resting energy expenditure. The ELBW infants grow at 15-18gm/kg/day and require 67-83 kcal/kg/day apart from resting energy expenditure. Thus, approximately 24kcal/kg/day is required for energy accretion from proteins and 85-100kcal/kg/day from non-protein source.
- **Water and electrolyte requirements**: About 90% of body weight is water in ELBW and majority of this is in extra- cellular fluid (ECF) compartment. These babies, loss 12-15% of body weight during 1st two weeks of life in three stages [7] namely, transitional, diuretic and homeostatic phases.
- Most preterm infants require fluids at 60-80ml/kg/day (in humidified incubator) on day1 of life followed by increments of 10-20ml/kg/day until 150-180ml/kg/day is reached between 5-7 days of life.
- Sodium and potassium are usually not required in the 1st 2-3days of life and needs their provision in PN once diuretic phase starts from day3 onwards. Sodium is provided by 1-3mmol/kg/day and potassium 1-2mmol/kg/day. Urinary sodium level is a good indicator of sodium adequacy. Chloride requirements match with sodium and influenced by bicarbonate status.
- **Macronutrient requirements [8]:** Macronutrients are carbohydrates, fats and proteins. These are recommended in 60:30:10 ratio (carbohydrates 55-60%, Fats 25-30% and proteins 10-15%) for optimum utilisation by the body.
    - **Carbohydrates:** Glucose is the carbohydrate currency of blood. D-dextrose is the intravenous form of carbohydrate. One gram of glucose gives 3.4kcal (4kcal) of energy. Newborns require glucose at 4-12mg/kg/min. On an average, preterm babies need 6-8mg/kg/min of glucose to maintain plasma glucose levels at 2.5-8mmol/l. Brain is the main organ to utilize the majority of glucose supplied in these babies. Both hypo- and hyperglycemias are detrimental to body. After stable plasma glucose is achieved, the glucose infusion can be gradually increased by 0.5mg - 1mg/kg/min until 12-13mg/kg/min is achieved. Hyperglycaemia can be treated by lowering the glucose infusion rate, GIR (not less than < 4mg/kg/min), early addition of amino acids in PN and reducing the lipid content in PN.
    - **Proteins:** Early protein provision is essential to avoid tissue breakdown. One gram of protein gives 4kcal of energy. About 12% of total calories should be provided by proteins (amino acids). Lean body mass reflects the protein intake and monitored by blood urea estimation. To prevent negative nitrogen balance, 1.5gm/kg/day of protein is needed in early days. Each gram of protein intake should be accompanied by 18-25kcal of energy from non- protein source. The ELBW infants need 3.5-4gm/kg/day of proteins. Intravenous amino acids with glucose infusion stimulates insulin secretion, prevents hepatic glucose production and hyperglycaemia. Parenteral protein should be initiated within 24 hours of life at 2-2.5gm/kg/day and increased at increments of 0.5-1gm/kg/day until 3.5-4gm/kg /day is reached.
    - **Lipids:** These are high energy yielding (1gm = 9kcal) macronutrients. Early lipid infusion as 20% emulsion prevents essential fatty acid deficiency and provides long chain fatty acids. Twenty percent lipid emulsion gives rise to 2kcal/ml. Lipids should be started preferably on day1 of life with 2gm/kg/day as separate aqueous solution over 24 hours. Lipid intake is gradually increased at 0.5-1gm/kg/day until 3.5gm/kg/day is reached.

Micronutrient requirements [8]:

- **Calcium, phosphorous and magnesium:** These are required for neuromuscular function and bone matrix formation. Their homeostasis is a complex phenomenon and needs continuous supply of calcium, phosphate, magnesium, vitamin D, proteins, calories and parathyroid hormone secretion. Maximum accretion of calcium at 120-160mg/kg/day occurs during third trimester. In early postnatal life, calcium and phosphorus should be given in 1:1 molar ratio (1.5mmol/kg/day) and magnesium at 0.18-0.2mmol/kg/day by parenteral route along with vitamin D supplementation of 800-1000IU/day.
- **Copper**: In Utero copper accretion occurs at 30microgm/kg/day. Early milk rich in copper with gradual decrease in the mature milk. Recommended dose of copper is 150-200microgm/kg/day.
- **Zinc:** It is essential for enzyme, immune and cellular function. Zinc deficiency hampers linear growth, infection prone, mucocutaneous lesions and neuro-developmental delay. Recommended zinc intake is 2-2.25mg/kg/day with zinc-copper intake ratio of < 20:1.
- **Iron:** Iron is essential for neurological function. It is a component of myoglobin and haemoglobin. Iron is prooxidant (increased glutathione peroxidise) and invites infections when given in excess. Delayed cord clamping improves iron stores. Iron deficiency is associated with serum ferritin levels < 19microgm/L. Oral iron supplementation is recommended at 2 weeks of life in infants < 1500gm with 2-3mg/kg/day.

S. No.	Nutrients	Requirements per 100 KCAL
1.	Proteins	3.2 – 4.1 gm
2.	Carbohydrates / glucose	10.5 12 gm
3.	Fats	4.4 – 6.0 gm
4.	Linoleic acid	350 – 1400 gm
5.	Alpha Linoleic acid	50 mg
6.	Arachidonic acid	16 – 39 mg
7.	DHA	11 – 27 mg
8.	Vitamin A	1199 – 2464 IU
9.	Vitamin D	800 – 1000 IU
10.	Vitamin E	3.0 – 14.9 IU
11.	Vitamin K	4 – 25 mcg
12.	Vitamin B1	125 – 275 mcg
13.	Vitamin B2	180 – 365 mcg
14.	Vitamin B6	41 – 273 mcg
15.	Vitamin B12	00.8 – 0.7 mcg
16.	Folic acid	32 – 90 mcg
17.	Vitamin C	10 – 42 mg
18.	Pantothenic acid	800 – 1900 mcg
19.	Biotin	1.5 – 15 mcg
20.	Sodium	63 – 105 mg
21.	Potassium	60 – 120 mg
22.	Chloride	95 – 161 mg
23.	Iron	1.8 – 2.7 mg
24.	Zinc	1 – 1.8 mg
25.	Calcium	110 – 130 mg
26.	Phosphorus	55 – 80 mg
27.	Choline	7 – 50 mg
28.	Inositol	4 – 48 mg
29.	Manganese	6.3 – 25 mcg
30.	Copper	90 – 120 mcg
31.	Iodine	10 – 50 mcg
32.	Selenium	4.5 – 9 mcg
33.	Chromium	0.022 – 1.112 mcg
34.	Molybdenum	0.27 – 4.5 mcg
35.	Fluoride	1.4 – 55 mcg

Table 1: Nutritional requirements of ELBW infants (ESPGHAN European Society for Paediatric Gastroenterology, Hepatology and Nutrition): [8].

Total parenteral nutrition (TPN): "is provision of nutrition for metabolic requirements and growth through the parenteral route". TPN is an expensive, technically skilled procedure with associated merits and demerits. In preterm infants (PTI), it should be initiated early and continued until ¾ of nutritional needs are achieved by enteral feeds [9]. All TPN preparations should be carried in a sterile zone with utmost care. It needs well trained NICU nurses, appropriate laboratory back up and equipment like infusion pumps. Preterm infants lose 1% of body protein per day if they kept on only dextrose infusion after birth [10]. TPN is indicated in 1. PTI < 30 weeks GA 2. Birth weight < 1250 gm 3. No enteral feeds by day 5 irrespective of GA and weight and 4. Inability to tolerate enteral nutrition.

TPN Calculation for ELBW infants [11]

- Total fluid calculation is based on bodyweight and gestational age in ml/kg/day.
    - Fluid and Electrolytes requirement for ELBW infants -During early transitional phase, fluid and electrolytes requirement are 90-110 ml/kg/day, Sodium (Na) 0-1mmol/kg/day, Potassium (Kmmol/kg/day) 0; during diuretic phase, fluids- 90-140ml/kg/D, Na-2-5mmol/kg/D, K-0-2 mmol/kg/D and during growing phase, fluids-140-190ml/kg/D, Na-3-5mmol/kg/D and K-2-3mmol/kg/D.
- **Lipid calculation:** Requirement is 1-3gm/kg/day. Lipids (20% lipid emulsion has less phospholipid, SMOF preferred over Intralipid) should be infused as separate infusion even via a peripheral vein (isotonic). Monitor triglycerides (< 300mg/dl) in conditions like sepsis, respiratory distress, persistent pulmonary hypertension of neonate (PPHN) and hyperbilirubinemia (restrict lipid infusion to 0.5 to 1gm/kg/day). Steps in lipid calculation - gm/kg/day, gm/day, conversion of gm/day to volume/day in ml, calculation in ml/kg/day and ml/hour (ml/kg/day divided by 24). Lipids are infused over 20-24hrs. Carnitine supplementation enhances lipid utilization.
- **Calculation of aqueous solution:** It contains dextrose, amino acids, vitamins and trace elements. It should be given as separate infusion.
- **Dextrose-amino acids calculation:** Deduce lipids volume and any additional fluids in ml from total fluids required per day.
- **Dextrose calculation:** Calculate GIR in mg/kg/min usually 6mg/kg/min with incremental increase by 1-2mg/kg/min to

reach final level of 12mg/kg/min. Further steps in calculation include - desired GIR in mg/kg/min x kg BW = mg dextrose/min, dextrose in mg/min divided by 1000 (1gm = 1000mg) = dextrose in gm/min, dextrose in gm/min x 1440(minutes/day) = gm/day, dextrose in gm/day divided by total fluids in ml/day x 100 = percentage of dextrose.

- **Calculation of amino acids as 10% Aminoven:** Determine total amino acids as gm/kg/day of protein based on postnatal age. Further steps in calculation include - gm of protein/kg/day x kg BW = gm/day, proteins gm/day divided by fluid in ml/day x 100 = percentage of amino acids.

Micronutrients calculation

Sodium requirement is 2-3meq/kg/day and needs 4 to 6 ml of 3% saline.

Potassium requirement is 1-2meq/kg/day. Potassium chloride (KCL-15%) 1ml = 2meq.

Calcium requirement is 2meq/kg/day. Calcium gluconate (10%) 1ml = 0.45meq. Approximately 4ml/kg/day of 10% calcium gluconate is needed.

Magnesium 0.3meq/kg/day is required. Magnesium sulphate (50%) 1ml = 4meq.

Trace elements added in the form of Neotrace (not easily available in India). Injection Celecel (Chromium, Copper, Manganese and Selenium) should be added in a dose of 0.1 - 0.2 ml/kg.

Vitamins - injection paediatric MVI 1ml/kg as aqueous solution should be used.

Aqueous solution containing dextrose, amino acids, micronutrients and vitamins is delivered through a burette containing bacterial filter and connected to Y connector (triple lumen) of peripheral, umbilical or central vein to which the lipid infusion is attached. Restrict proteins to 12% and PN osmolality to 850mosm when peripheral vein is selected.

Calorie nitrogen ratio calculation: CNR is equal to the sum of carbohydrate calories (8gm × 3.4) plus lipid calories (gm×9) multiplied by 6.25 ÷ amino acids in gm. Normal range is 100 to 200 calories/gm. Approximately 25 non-protein kilocalories/Kg are required for every 1gm protein/kg promote protein utilization.

TPN Complications [12]:

Sepsis - is more common with central lines.

- **Dextrose related:** hyperglycaemia > 125mg/dl and hypoglycaemia < 40mg/dl. Hyperglycemia should be treated when blood glucose is > 200mg/dl.
- **Lipid related:** Hyperlipidemia, PENALD (parenteral nutrition associated liver dysfunction). Fish oil-based lipid preparation may reverse PENALD (13) (Park HW).
- **Protein related:** Metabolic acidosis.
- **Fluid related:** Hypervolemia and hypovolemia.
- **Catheter related:** Infection and dislodgement.
- **Haematological complications:** Thrombocytopenia and eosinophillia.

Enteral nutrition

All ELBW infants are born in a nutritional emergency state with low micro and macro nutrient reserves and their high demand. Enteral feeds should be offered in hemodynamically stable preterm babies, initially with minimal enteral nutrition [14] (MEN). MEN is giving EBM of 12-24ml/kg/D as an alternative to enteral fasting. Early enteral feeds result in faster achievement of full enteral feeds [15].

Men: should be started on day1 with expressed mother's breast milk (EMBM - best choice) or donor expressed breast milk (DEBM - 2nd choice) with 1ml initially 6-8hrly for 3days followed by 12-24ml/kg/day as 2hrly feeds for the next 3days (along with parenteral nutrition). Feeds should be given as intermittent bolus feeds through orogastric tube, [16] Stocks 1980/[17] Hawes J 2004. Breast milk is ideal for MEN, and it protects from sepsis and NEC, [18] Lucas A 1990. Breast milk with prebiotics and probiotics exerts favourable effects on gut [19]. Johnson MJ suggested screening tool for nutritional risk for preterm infants in NICU as low, intermediate and high-risk strategy [20]. Both EMBM and DEBM should be given in full strength. EMBM has several advantages - preterm breast milk contains more protein, fat, energy and sodium, provide secretory IgA and antibodies, neutrophils, pre-pro and postbiotics, intestinal growth factors, healthy gut colonization, vitamin A, Zinc, better long-term neuro developmental outcome [21] lower sepsis and better survival rate in early infancy [22].

The advantages of MEN include the following [23] 1) Low feeding intolerance 2) Gut maturation 3) Early attainment of full enteral feeds 4) Stimulates gut motility 5) Less phototherapy 6) Early weight gain and discharge 7) Better bone mineralisation.

Nutritional feeds

Nutritional feeds in EPTI should be started on day 5 or 6 with 12-24ml/kg/day. Thus, 1ml of EMBM every 2hrly should be introduced and advanced with 1ml per feed every 24hr until full enteral feeds of 150-180ml/kg/day is reached. Monitoring and judicious vigilance is needed during the transition from PN to full attainment of enteral nutrition (milk intake of > 100ml/kg/D).

Rate of advancement of nutritional feeds

A multicentre RCT trial (Speed of increasing Milk Feeds Trial,

SIFT trial) [24] was conducted for judging the better feeding policy between slow (18ml/kg/day) and fast (30ml/kg/day) feeding increments for PTI. This study showed no associated increased risk for NEC in fast feeding group. Sisk PM 2008 [25] showed guidelines for incremental increase in feeds based on GA as follows

GA IN WEEKS	Initial Nutritional Feeds ml/kg/day	Advancement of feeds ml/kg/day
28 (trophic feeds initially)	12 - 15	15
29	12 - 15	15
30	12 - 18	18
31	12 - 25	25
32	18 - 25	35

Table 2

Human milk fortification

Human milk composition is variable, dynamic and lowered protein content for EPTI [26] (Ballard 2013). Fortification is aimed to improve micro and macronutrient composition of breast milk with preserved advantages (P/E ratio 3.6gm/120kcal) of EDBM. Extreme low birth weight babies who fed on exclusively breast milk attain lower mean weight for age at 2kg, (Lucas 1984). Powdered human milk fortifier (Lactodex HMF in India) should be added (1 sachet in 25ml of breast milk and administer immediately or within 20minutes of reconstitution to avoid increasing osmolality by maltodextrins) when baby receives > 100-150ml/kg/day of EMBM.

Feeding intolerance

Common in EPTI due to disordered peristalsis, immature gut, poor gastric emptying and dysadaptation to enteral feeds especially formula feeds.

Common features of feeding intolerance are - abdominal distension, large gastric residual volumes (GRV - > 2 - 3 ml/kg or > 50% of previous feeding volume), new visible intestinal loops, abdominal skin discolouration, hemodynamic instability, hypo-hyperglycaemia and positive stool test for blood. It may be an early warning sign of NEC.

Withheld the feeds if GRV is more than > 30-50% on two occasions with non-reassuring clinical status for 24hrs and reintroduce if clinical condition is reassuring.

Nutritional assessment and monitoring

Usually based on changes in body weight and fluctuations in energy intake. Both static assessment - a balance between intake and output and dynamic assessment - growth velocity over time is significant for all EPTI. MJ Johnson 2014 advised ABCDE approach for nutritional assessment in neonates [27] - A. Anthropometry, B. Biochemistry, C. Clinical, D. Dietary and E. Evaluation.

Anthropometric assessment

Should include daily recordings of weight, input - output charts and constant supervision. Weight is the most commonly recorded measurement in NICU and comprises baby's lean mass, fat and extracellular fluid. Daily weight recording can be plotted on Fenton growth chart. Weekly recordings should include head circumference (HC > 0.9cm/week) and length (> 1cm/week) and mark on growth charts (NICHD growth observation curve). HC is the surrogate measure of brain growth.

Biochemical assessment (laboratory)

Should include daily recording of blood glucose - initially 6-12hrly, urinary glucose, serum electrolytes (initially), weekly recording of serum electrolytes (3-4times/week followed by weekly), blood urea [< 2mmol/l = inadequate protein intake, 3times/week later weekly], serum albumin(< 1.6mmol/l = protein deficiency), Liver function tests, hematocrit, haemoglobin, reticulocyte count, triglycerides (4hrs after increase in dose, later weekly < 200mg/dl), bone markers (alkaline phosphatase > 900IU/L and phosphate < 1.8mmol/l or < 4mg/dl = metabolic bone disease).

Clinical assessment

Should be carried daily for hydration status, general health and for signs suggestive of any disease status.

Dietary assessment

Should include daily calculation of macro-micronutrients for both enteral and parenteral nutrition.

Evaluation

Should be done daily and weekly for adequacy of nutrients, hydration and growth.

ELBW babies who grow at > 18gm/kg/day in weight, > 0.9cm/wk in HC and > 1cm/wk in length had better neuro developmental outcome [28] (Ehrenkranz 2006).

Catch up growth and feeding advice at discharge

Catch up growth is an increased growth rate on nutritional provision after a transient period of growth lag secondary to nutritional inadequacy or illness. It may be associated with increased insulin resistance and cardiovascular risk at later age [28].

PTI with adequate weight for post menstrual age (PMA) should be kept on breastfeeding with periodic growth monitoring [31]. Babies with inadequate weight for PMA at discharge should receive fortified human breast milk or nutrient enriched post discharge formula (introduce NEPDF 22/30 - when 2-2.5kg wt) until 52weeks of PMA to provide better P: E ratio at 3gm/100kcal [30]. Nutrient enriched preterm formula (NEPTF 24/30) fed infants got better cognitive outcomes [32] in male babies (Lucas 1998) at 7-8years age. The preterm formula NEPTF 24/30 milk is intended for babies < 2kg weight or < 35wks GA.

Conclusion

Preterm infants especially ELBW and VLBW are at risk of developing EUGR and NEC. Early aggressive parenteral nutrition along with early enteral nutrition preferably with breast milk (MEN followed by nutritional feeds) is essential and mandatory for achieving optimum growth, prevention of NEC and better longterm outcomes. Breast milk either from own mother or donor mother is the choice of milk for preterm infants. Providing correct protein energy ratio is essential for enhanced protein utilization and attaining optimum growth. Once full nutritional feeds are achieved, fortification of breast milk and or introduction of nutrition enriched post discharge formula from nicu discharge along with supplementation of long chain PUFA (52 weeks PMA) is recommended.

Conflict of Interest

There are no conflict of interest for this study.

Sponsors

There are no sponsors for this study.

Bibliography

1. Sanjay Patole., *et al.* "Nutrition for the Preterm Neonate - A clinical perspective". Springer (2014).

2. Dorland Medical Dictionary (definitions)

3. Fenton TR., *et al.* "Validating the weight gain of preterm infants between the reference growth curve of the foetus and term infant". *BMC Pediatrics* 13 (2013): 92.

4. Embleton NE., *et al.* "Postnatal Malnutrition and Growth Retardation: An evitable consequence of Current Recommendation in Preterm Infants?" *Pediatrics* 107.2 (2001): 270-273.

5. Karen Simmer., *et al.* "Aggressive Nutrition for Preterm Infants - Benefits and Risks, Science Direct". *Early Human Development* 83 (2007): 631-634.

6. "The Provision of Parenteral Nutrition within Neonatal Services - A Framework of Practice". *British Association of Perinatal Medicine (BAPM)* (2016).

7. John M Lorenz., *et al.* "Practical Neonatology (Polin RA and Yoder MC), Chapter 3, 5th Edition".

8. C Agostoni., *et al.* "Enteral Nutrient Supply for Preterm Infants: Commentary from ESPGAN Committee on Nutrition". *JPGN* 11 (2010).

9. Miller M., *et al.* "From parenteral to enteral nutrition: a nutrition-based approach for evaluating postnatal growth failure in preterm infants". *Journal of Parenteral and Enteral Nutrition* 38 (2014): 489-497.

10. Denne SC and Poindexter BB. "Evidence supporting early nutritional support with parenteral amino acid infusion". *Seminars in Perinatology* 31 (2007): 56-60.

11. Sudha Chaudari., *et al.* "Total Parenteral Nutrition in Neonates". *Indian Pediatrics* 43.17 (2006).

12. Velaphi., *et al.* "Review Article: Nutritional Requirements and Parenteral Nutrition in Preterm Infants". *Journal of Clinical Nutrition* 24.3 (2011).

13. Park HW., *et al.* "Parental Fish Oil Containing Lipid Emulsions May Reverse Parental Nutrition - Associated Cholestasis in Neonates: A Systematic Review and Meta-Analysis". *Journal of Nutrition* 145.2 (2012): 277-283.

14. Arslanoglu S., *et al.* "Donar Human Milk for Preterm Infants: Current Evidence and Research Directions". *JPGN* 57.4 (2013).

15. Leaf A., *et al.* "Early or Delayed Enteral Feeding for Preterm Growth - Restricted Infants: A Randomized Trial". *Pediatrics* 129.5 (2012): e1260-1268.

16. Stocks J., *et al.* "Effect of Nasogastric tubes on nasal resistance during infancy". *ADC* 55 (1980): 17-21.

17. Hawes J., *et al.* "Nasal versus oral route for placing tubes in preterm or low birth weight infants". *CDSR* (2004).

18. Lucas A and Cole T. "Breast milk and neonatal necrotizing enterocolitis". *Lancet* 336.8730 (1990): 1519-1523.

19. Jape GA., *et al.* "Probiotics for preterm infants - time to end all controversies". *Microbial Biotechnology* 12.2 (2019): 249-253.

20. Johnson MJ., *et al.* "Developing a new screening tool for nutritional risk in neonatal intensive care". *Acta Paediatrica* 104.2 (2015): e90-93.

21. Horta BL., *et al.* "Breast feeding and Intelligence: a systemic review and Metaanlysis". *Acta Paediatrica* 104 (2014): 14-19.

22. Lucas A., *et al.* "Breast milk and subsequent intelligence quotient in children born preterm". *Lancet* 339.8788 (1992): 261-264.

23. Lucas A and Hudson G. "Preterm Milk as a source of protein for low-birth-weight infants". *ADC* 59.9 (1984): 831-836.

24. Doring J., *et al.* "Controlled Trial of Two Incremental Milk-Feeding Rates in Preterm Infants". *The New England Journal of Medicine* 381 (2019): 1434-1443.

25. Sisk PM., *et al.* "Human Milk Consumption and full enteral feeding among infants who weigh < 1250gm". *Pediatrics* 121.6 (2008): e1528-1533.

26. Ballard O., *et al.* "Human milk composition: Nutrients and bioactive factors". *Paediatric Clinics of North America* 60.1 (2013): 49-79.

27. MJ Johnson., *et al.* "How to use: Nutritional assessment in neonates". *ADC Education and Practice* 100 (2015): 147-154.

28. Ehrenkranz RA., *et al*. "Growth in the neonatal intensive care unit influences neurodevelopmental and growth outcomes of extremely low birth weight infants". *Pediatrics* 117.4 (2006): 1253-1261.

29. Singhal., *et al.* "Feeding Preterm Infant Today for Later Metabolic and Cardiovascular Outcomes". *JOP* 162.3 (2013).

30. Anna Conred., *et al.* "Post discharge nutrition for the preterm infant". *JNN* 19 (2013): 217-222.

31. Bai-Horng Su., *et al.* "Optimizing Nutrition in Preterm Infant, Science Direct". *Pediatrics and Neonatology* 55 (2014): 5-13.

32. Lucas A., *et al.* "Randomized trial of early diet in preterm babies and later intelligence quotient". *BMJ* 317 (1998).