Nutrition in preterm infants: A review of optimised oral and parenteral nutritional strategies

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ABSTRACT

Background: Nutrition is a cornerstone of a preterm infant's life, providing the essential nutrients required to support the body's fundamental functions ensures survival. However, meeting the nutritional needs of preterm neonates presents unique challenges, as their feeding requirements far exceed those of full-term infants. Despite advancements in feeding strategies, poor growth rates and neurocognitive disabilities remain prevalent in this population, largely due to feeding difficulties, increased respiratory workload, and immature gastrointestinal systems.

Objective: This review seeks to explore preterm nutrition and the availability of sufficient nutrients for the support, growth and weight gain of preterm infants in a manner comparable to a fetus of the same gestational age.

Method: This narrative review investigates the physiological effects of preterm birth on infant organ systems, the distinctive nutritional needs of preterm neonates, and the various factors influencing their nutritional status, such as mode of delivery, maternal corticosteroid use, breastfeeding practices. It also examines current nutritional strategies, including intravenous administration of dextrose, amino acids, and lipids for severely preterm infants.

Key Findings: Preterm infants face unique challenges such as underdeveloped organs, environmental challenges which do not exist in the third trimester in the uterus but exist in neonatal care units.

Conclusion: Breast milk is key for preterm nutrition. Its fortification especially for infants that are very preterm is recommended if the mother lacks of access to an ideal diet. Administration of micronutrients such as Iron, Zinc, Vitamin D, E, K, and A help prevent preterm morbidity and mortality. The administration of probiotics to preterm infants to improve GUT maturity and digestion is currently under consideration.

Keywords: Nutrition, preterm, infants, malnutrition, feeding

Nutrition chez les nourrissons prématurés: revue des stratégies nutritionnelles orales et parentérales optimisées

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RÉSUMÉ

Contexte: La nutrition est un pilier essentiel à la survie du nourrisson prématuré. Fournir les nutriments indispensables au maintien des fonctions vitales garantit sa survie. Cependant, répondre aux besoins nutritionnels des nouveau-nés prématurés pose des défis particuliers, car leurs besoins alimentaires dépassent largement ceux des nourrissons nés à terme. Malgré les progrès réalisés en matière de stratégies d'alimentation, les retards de croissance et les troubles neurocognitifs restent fréquents dans cette population, principalement en raison des difficultés d'alimentation, d'une charge respiratoire accrue et d'un système gastro-intestinal immature.

Objectif: Cette revue vise à explorer la nutrition des prématurés et la disponibilité de nutriments suffisants pour soutenir la croissance et la prise de poids, de manière comparable à un fœtus du même âge gestationnel.

Méthode: Cette revue narrative examine les effets physiologiques de la prématurité sur les systèmes organiques du nourrisson, les besoins nutritionnels spécifiques des nouveau-nés prématurés et les différents facteurs influençant leur état nutritionnel, tels que le mode d'accouchement, l'utilisation de corticostéroïdes par la mère et les pratiques d'allaitement. Elle examine également les stratégies nutritionnelles actuelles, notamment l'administration intraveineuse de dextrose, d'acides aminés et de lipides pour les nourrissons très prématurés.

Principaux résultats: Les nourrissons prématurés sont confrontés à des défis uniques, tels que le sous-développement de leurs organes et des facteurs environnementaux qui n'existent pas au cours du troisième trimestre de grossesse, mais qui sont présents dans les unités de soins néonatals.

Conclusion: Le lait maternel est essentiel à la nutrition des prématurés. Son enrichissement, notamment pour les grands prématurés, est recommandé si la mère n'a pas accès à une alimentation optimale. L'administration de micronutriments tels que le fer, le zinc et les vitamines D, E, K et A contribue à prévenir la morbidité et la mortalité liées à la prématurité. L'administration de probiotiques aux prématurés afin d'améliorer la maturation du microbiote intestinal et la digestion est actuellement à l'étude.

Mots-clés: Nutrition, prématurité, nourrissons, malnutrition, alimentation

INTRODUCTION

The burden of preterm birth (PTB) as a critical public health crisis. It has been identified as the leading cause of death in children under five years old worldwide.[1] Approximately 13.4 to 15 million babies are born preterm annually, representing about 1 in 10 births world-wide. Sub-Saharan Africa bears a disproportionately high burden of preterm birth.[2] This is characterized by significant neonatal mortality and long-term developmental challenges. African specific literature across sub-Saharan Africa report preterm births rates ranging from 3.4 % to 49.4 %.[3] However, complications from preterm births are the leading cause of neonatal death in this region. It is responsible for approximately 40% of all neonatal deaths. Unfortunately, Nigeria ranks as the third-highest contributor to preterm births globally.

Preterm babies can be defined as infants born alive on or before the 37th week of pregnancy.[4] Nutrition is very important for preterm infants. The diet made available to preterm infants is an intricate determining factor of infant survival. Nutrition in preterm infants could be ambiguous as their feeding needs are far higher than full-term infants.[5] Ideally, preterm infants should be in their last stage of growth as a fetus in the womb. At this last trimester stage, growth is four times faster than normal. Due to this exponential growth, intensive nutrition is necessary.[6] Obtaining physiological growth similar to that which occurs in the uterus is the primary goal when nourishing preterm infants. Despite the various feeding patterns and strategies, poor growth rates associated with neurocognitive disabilities have remained common among preterm infants.[7] Preterm infants in neonatal care units face challenges that do not exist in the third trimester in the uterus. Challenges such as the struggle to feed adequately, increased respiratory workload, and lack of maturity of the gastrointestinal tract. These challenges may lead to infant morbidity.[8] In particular, the lack of maturity of the gastrointestinal tract can lead to poor absorption of nutrients, causing malnutrition in the form of undernutrition (when there is a deficit in nutrients received by the body of an infant). Figure 1, shows the two major nutritional challenges in preterm infants.

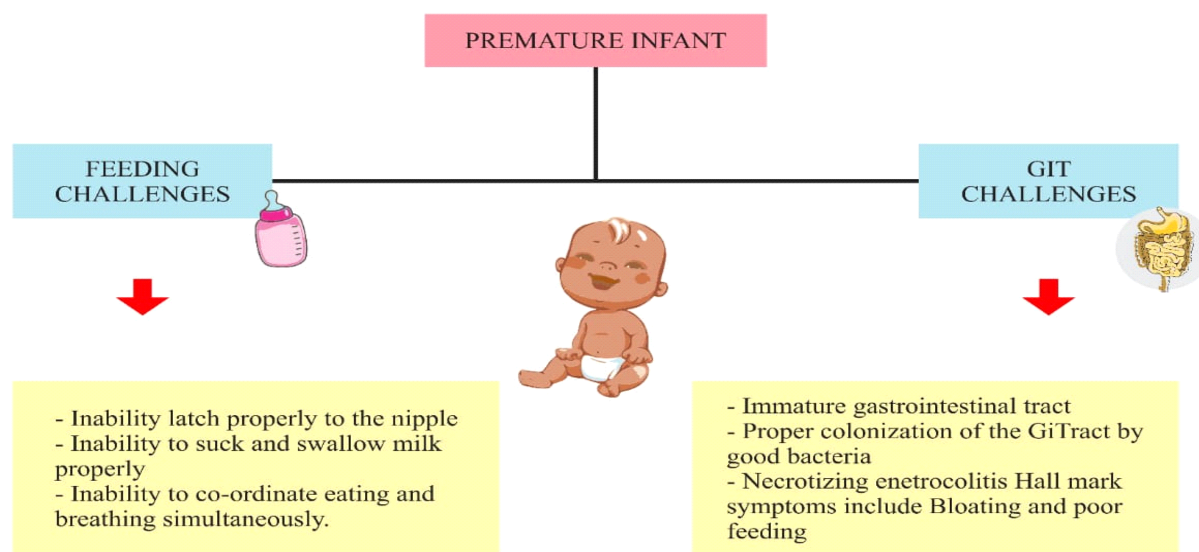

Figure 1. Illustration depicting the two major nutritional challenges in premature infants

It is important that the diet of a preterm infant be tailored to suit their gastrointestinal tract peculiarities.

The peculiarities include insufficient gastric storage and inability to digest properly.

The primary objective of this review is to identify key factors that affect nutrition of preterm infants and foster the provision and successful administration of nutrients sufficient to facilitate the growth rate and weight gain a normal fetus at the same gestational age would acquire.[9] This review addresses the determinants that shape the nutritional status of infants and how this, in turn, influences their chances of survival.[8, 9]

METHODOLOGY

Databases searched

The databases searched include PubMed, Scopus, Web of science, Cochrane Library, Embase, and Google scholar for comprehensive coverage for information regarding nutrition. Nutritional health data was sourced from the CDC and WHO.

- Search terms include:
  - o Preterm: "Preterm infant," "preterm newborn," "very low birth weight," "VLBW," "extremely preterm".
  - o Parenteral nutrition: "Parenteral nutrition," "intravenous nutrition," "amino acids," "lipids," "IV lipids," "early nutrition," "central venous access".
  - o Oral nutrition: "Enteral nutrition," "enteral feeding," "human milk," "mother's own milk," "donor human milk," "fortification," "HMF," "trophic feeding," "minimal enteral feeding".
  - o Strategies: "Optimized," "guidelines," "management," "early aggressive," "standardization".

Manual searching

Reference lists of retrieved relevant systematic reviews, narrative reviews, and meta-analyses were searched to identify additional studies.

Literature identification

Articles will be selected based on pre-defined inclusion and exclusion criteria to ensure relevance to optimized strategies.

Inclusion criteria:

- o Randomized Controlled Trials (RCTs), systematic reviews, meta-analyses, and observational studies focusing on preterm infants (<37 weeks gestation).
- o Studies published in English.
- o Studies focusing on optimized nutritional strategies (e.g., early parenteral amino acids >3g/kg/day, early enteral feeding, fortified human milk).
- o Guidelines from established organizations (e.g., ESPGHAN, ESPEN, ASPEN).

Exclusion Criteria:

- o Studies where full text is unavailable.
- o Studies focused solely on resource-limited settings without addressing optimized high-resource strategies.

Time frame of literature

Scientific and health literature from time period between 2010 - 2026, fit the inclusion criteria.

Synthesis of Literature

The gathered literature was synthesized narratively, focusing on comparing current practices and identifying "optimized" strategies (those leading to improved growth, less necrotizing enterocolitis (NEC), or better neurodevelopmental outcomes).

PRETERM BIRTHS

Infants that are born before this gestational age are more likely to die during the first four weeks of life (neonatal period) or the first year of life (infancy year). Globally an average of 15 million preterm infants is born yearly. Most of the preterm births occur in sub-Saharan Africa and Asia, one out of every ten infants are born premature.[10] Complications that arise as a result of preterm delivery in infants is the number one reason for deaths occurring in children under the age of five. Preterm births predispose infants to pulmonary, neurocognitive and ophthalmologic morbidity.[11] There is a glaring disparity between survival rates of preterm infants in high-, middle- and low-income countries. Inability to provide adequate medical care, necessary warmth and address breathing difficulties in preterm infants are major challenges faced in low-income countries. In middle income countries there is improper and below adequate use of technologies designed to aid nutrition and intensive care of preterm infants. About 95 % of preterm infant in high income countries survive after being born.[12] Survival rates for preterm infants in low-income countries are significantly lower than in high-income settings, with approximately 50 % of babies born preterm dying in these regions, largely due to lack of access to specialized care.[12]

Premature births can be divided into three subcategories according to the gestational period of birth. These are:

- Extremely preterm
- Very preterm
- Moderate to late preterm

Extremely preterm

These are births that occur before 28 weeks of gestation. Infants born extremely preterm weigh less than 1 g. Intensive care is necessary because vital organs required to function and keep the infant alive are not fully developed. Breathing difficulties are also experienced and chances of infant survival are very low.[13]

Very preterm

These are infants born between 28 to 32 weeks of gestation. Infants born under these circumstances usually weigh between 1000 - 1500 g. Infants born as moderate to late preterm also experience difficulties in feeding: inability to latch to the mother's breast and sub-optimal sucking and swallowing coordination. There is also elevated risk of hyperbilirubinemia due to bilirubin encephalopathy. Hypoglycemia and hypothermia may also be experienced.[14]

Moderate to late preterm

These are preterm births that happen between 32 to 37 weeks of pregnancy. In this case, one out of every five preterm infants are more likely not to survive. There is difficulty in breathing, feeding and digestion. Infants born very preterm are likely to suffer from neurodevelopmental challenges such as hearing impairment, cerebral palsy, and vision impairment.[15]

3.1 Effects of preterm birth on infants

The level of severity of preterm birth depends on the complications that arise because of infant prematurity and the effect of these complications on the possibility of infant survival.

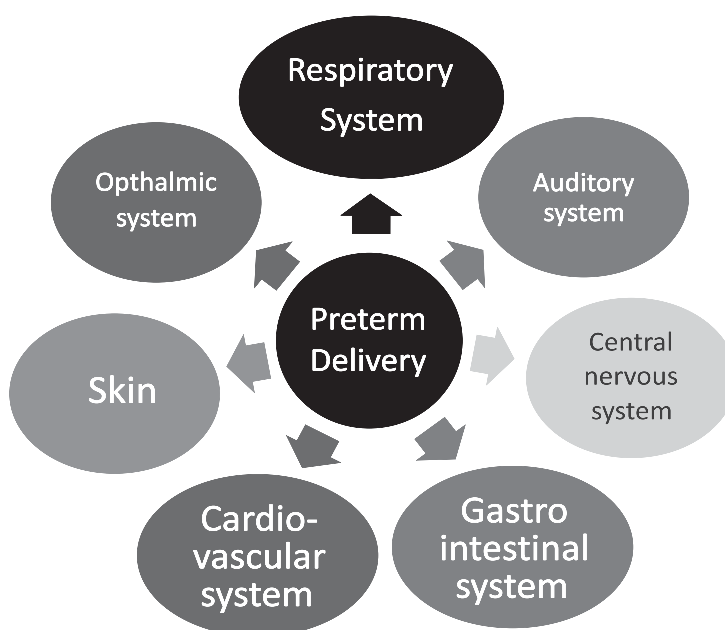

Figure 2 Flow chart of the various conditions that can arise in an infant from preterm delivery.

Preterm birth complications arise primarily from the immature status of the infant's organ systems. These organs are not fully developed and may most likely be lacking in the ability to support life outside the uterus. These organs make up systems that put up a fight for infancy survival. These include the central nervous system, ophthalmic system, auditory system, respiratory system, skin, gastrointestinal system and the cardiovascular system.[10] Figure 2, is a schematic diagram showing the body systems of an infant affected by preterm birth.

3.1.1 Central nervous system

For a developing fetus during pregnancy, the central nervous system starts as a neural groove. It then transforms into a neural tube which ends up as the brain and the spinal cord which continues to develop as the pregnancy progresses. Preterm birth is likely to have an adverse effect on the advancement of the central nervous system. Fetal activity, sensory input, and response are vital determinants of central nervous system maturity. Neurons develop and axons grow and get in touch with dendrites to give synapses. This process occurs from the 6th month of pregnancy to the child's third birthday. Research has shown that in the long term, preterm-born children have lower cerebral volumes at ages 7-15. Also, parts of their brain such as the cerebellum, grey matter, basal ganglia, and cortical white matter are lower in volume.[16]

3.1.2 Ophthalmic system

The development of the ophthalmic system commences six weeks after conception. It starts as an ophthalmic vesicle which then develops structurally into well-formed eyeballs. The retina located at the posterior portion of the eye is a vital organ for sight. However, it is vascularized at the latter stages of gestation. Preterm infants are likely to experience retinopathy due to organ prematurity. A disorder that is potentially blinding. This is when the blood vessels of the eyes are underdeveloped and hence unable to perform their required function after preterm birth.[6]

3.1.3 Auditory system

The ear in fully developed by the end of the 5th month of pregnancy. However, infants born as preterm are more likely to have hearing loss compared to full term babies. Hearing impairment can hinder speech development. Persistent pulmonary hypertension and cytomegalovirus infection both predispose preterm infants to hearing impairment.[17]

3.1.4 Respiratory system

The primary role of the respiratory system is the exchange of gas, via inhalation of oxygen and exhalation of carbon dioxide. Above 50 % of preterm infants born prior to the 27 th week of pregnancy have respiratory distress syndrome. Amongst preterm infants the earlier the week of delivery the higher the chances of developing respiratory distress syndrome. This condition is caused by a deficit in the surfactant production that aids gaseous exchange. It is also characterized by the lack of structural maturity of the lungs placing the infant on ventilation is a common approach to addressing this syndrome. In severe cases, apnea occurs due to respiratory immaturity, hence the absence of breathing. In this case the infant is placed permanently on a ventilator. Hypoxia and bradycardia are also respiratory conditions that have a high level of occurrence in preterm infants. Another respiratory challenge common with preterm infants is bronchopulmonary dysplasia. This can be described as the detection of deterioration of the lungs of a preterm infant.[6]

3.1.5 Skin

The skin serves as a barrier between the infant and the external environment. The skin of preterm infants appears translucent and fragile. The level of integrity and protection provided by the skin is highly dependent on the gestational age at birth. The skin of preterm may not be able to perform most of its characteristic functions. This is because the outermost part of the skin, known as the stratum corneum, is thinner than that of full-term babies. The skin is usually found lacking in terms of temperature and moisture control. The skin of preterm infants may also lack the ability to protect the body from infection. Preterm infants can develop infection in almost any part of their body due to the fact their immune system is not fully developed.[18]

3.1.6 Cardiovascular system

Preterm babies experience a myriad of cardiovascular defects. Heartbeat commences on the 28 th day of fetal life, and the development of the heart is complete by the 42nd day. Hypotension and bradycardia are major abnormalities that occur in preterm infants. They are hallmark manifestations of immaturity of the cardiovascular system. Administration of pressors and normal saline or hydrocortisone can be soughed depending on the severity of the hypotension.[19]

3.1.7 Gastrointestinal system

Preterm infants have a higher chance of immature digestive systems. Usually, the digestive system of these infants is not structurally ready to absorb nutrients effectively. Formation and development of the gastrointestinal tract commence 28 days after conception and is fully formed by the 20th week of pregnancy. By the time the fetus can swallow and can suck milk, it is expected that the gastrointestinal system will be colonized with good bacteria. This allows for the administration of antibiotics due to infections in other parts of the body if necessary. However, this may affect the presence of bacteria in the gut. The introduction of probiotics such as bifidobacteria for gut development, is being considered and under research. Immaturity and lack of bacteria colonization of GIT affect feeding tolerance and food digestion. One major complication that can occur due to these pre-existing complications is necrotizing enterocolitis. This can be described as a severe disease that affects preterm infants. Hallmark symptoms include bloating, emesis of bile, decreased activity, bloody stool, failure of multiple organs, or death.[20]

4.0 Feeding and Nutrition Peculiarities in Preterm Infants

The presence of probiotic bacteria in the digestive tract of preterm infants is a vital foundation for the enforcement and development of the digestive system. Heavy colonization of the wrong type of bacteria in the gastrointestinal tract causes injury to the intestinal lining.

Preterm infants and low birth weight infants are predisposed to these conditions. In conditions where there are inflammation and infection of an infant's gut is called necrotizing enterocolitis. Breastfed pre-terms are less likely to develop this severe condition. Premature infants generally have immature immune and GIT systems. This may be due to delayed colonization of the gastrointestinal tract microbiota. Probiotics which encourage colonization of good bacteria have been established to provide health benefits when present in infants' gut. This reduces the chances of obesity, childhood infections and other atopic disorders.[21]

5.0 Factors that affect the gut of preterm infants

There are several factors that increase the risk of immature gut systems of pre-terms and its associated diseases. These factors include:

- Mode of delivery
- Use of corticosteroids during pregnancy
- Breastfeeding
- Use of antibiotic during delivery.

5.1.1 Mode of Delivery

The mode of delivery affects the health of an infant's GIT. Infants born through vaginal delivery generally have better gut microbial structure and gut microbiota. The birth canal where the fetus passes through is colonized by probiotics such as lactobacillus rhamnosus and reuteri. In contrast with infants born via c-section, the microbiota of these infants is similar to that of the mother's skin microbial flora. Therefore, infants birthed via vaginal delivery are exposed to more beneficial bacteria. This disparity between infants birthed through c-section vis-à-vis vaginal delivery reflects in the aberrations in their normal physiology and predisposition to diseases.[22]

5.1.2 Use of corticosteroids during pregnancy

Corticosteroids are used during pregnancy to treat hallmark symptoms of autoimmune diseases. Corticosteroids are termed risky when administered during birth and in pregnancy as it poses the threat of gut infections of preterm offspring. There is rising concern about how treatment using corticosteroids for autoimmune diseases affects the fetus during pregnancy and birth outcomes. Existing literature buttresses the fact that there is an association between cleft palate and the use of corticosteroids during pregnancy. A cleft palate affects the infant's ability to feed properly. Preterm births are also considered a risk outcome due to treatment using corticosteroids during pregnancy.[23]

5.1.2 Breastfeeding

Breast milk is composed of all the nutrients required for an infant's first 24 weeks of life. This includes water, minerals, carbohydrates, vitamins, proteins and fat. Breast milk is also made up of biomolecules that help fight against infections. Biological molecules such as immunoglobulin, white blood cells, whey proteins, and oligosaccharides. Protection from these agents in an infant is necessary as they help with the good health of the gut system of infants.[24]

5.1.3 Use of antibiotics during delivery

Exposure to antibiotics during pregnancy may predispose one to preterm birth. Administering antibiotics during pregnancy may lead to dysbiosis. Dysbiosis is a condition characterized by an imbalance in the community of microorganisms living together as a microbiome, particularly in the vagina. Studies have concluded a link between the microbiome of the mother's vagina and the microbial flora of the preterm infant's gut.[25]

6.0 Refeeding syndrome in preterm infants

Refeeding syndrome in preterm infants can be explained as the misalignment of electrolytes, especially phosphorous. This happens sequel to the reintroduction or elevation of caloric availability after a time of absence or dearth in caloric consumption. Potassium and phosphorous are supplied via the placenta to the fetus and placental insufficiency may lead to fetal deficiencies. One of the reasons for poor fetal growth during pregnancy are nutritional deficiencies. It has become pertinent that aggressive and early parenteral nutrition be administered to severely low birth weight babies and premature infants.[26]

7.0 Causes of malnutrition in preterm infants

Malnutrition in preterm infants has pronounced long-term effects on their growth, metabolism, and neurodevelopment. Poor growth has been documented in premature infants, and this can be attributed to a couple of reasons, such as inadequate nutrient intake, low food storage, a deficit in standardized feeding practices, and immaturity of the gastrointestinal tract. Infants develop their nutrient stores throughout the entire period of the third trimester of pregnancy. Unfortunately, premature infants miss a few weeks or months in the uterus. They are therefore, birthed with depleted nutrient stores. This causes their nutritional need to be quite high. Parental illiteracy, family size, the

financial status of the parent, inadequate dietary intake, and inappropriate feeding habits affect the nutritional status of infants.[27, 28]

7.1 Identification of malnutrition in preterm infants

Malnutrition has been reported widely in premature infants. Both overnutrition and undernutrition can predispose to malnutrition and its negative effects. In order to identify malnutrition, early monitoring of infant nutritional status is recommended. Monitoring body weight and body composition via anthropometry, air displacement plethysmography (ADP), and dual-energy x-ray absorptiometry (DXA). Though some of these methods may be costly. They are precise in the assessment of body composition, hence nutritional status. Other approaches include dietary assessment and utilization of biochemical markers.[28]

7.1.1 Anthropometry

Anthropometry in infants can be described as the systematic measurement of the body of an infant. It is used to assess the weight, size, proportion, and body composition of infants. Body weight is one of the less complex parameters used in identifying malnutrition. After birth body weight is intricately associated with (Air displacement Plethysmography) ADP-determined fat-free mass. Infants can be classified according to their weight. Infants weighing above 4000 g are classified as overweight. Infants weighing below 2500 g are considered underweight. Body length is another parameter that indicates skeletal development and fat-free mass. This can be measured using tapes, or length boards. Head circumference as a parameter is more associated with the indication of brain development. Lack of increase in occipitofrontal development can be connected to prematurity-associated morbidity, brain atrophy, and post-hemorrhagic hydrocephalus. Body mass index is based on weight to length ratio. It helps to indicate the degree of body proportionality at birth and after birth.[29]

7.1.2 Biochemical Markers

There are a few significant biochemical growth markers for premature infants, namely, procollagen, bone-specific alkaline phosphatase, and osteocalcin. Procollagen peptidase can be described as an endopeptidase that plays a key role in the development of collagen. Procollagen quantitatively indicates type I collagen formation. Type I collagen is developed by proliferating osteoblasts. Hence, procollagen is an efficient marker of bone formation and growth. Bone-specific alkaline phosphatase is an alkaline phosphatase specific to the bones. It indicates the level of biosynthetic activity of cells responsible for bone formation. It is a responsive and efficient indicator of bone growth and metabolism. Osteocalcin is a 49-amino-acid peptide. It is produced by osteoblasts and released into the blood and bone matrix. Levels of osteocalcin increase when there is increased bone formation and growth. Osteocalcin is particularly elevated during the first year of life of a child. There is a direct correlation between growth rates and osteocalcin levels. An elevation or decline in osteocalcin level after repeated measurements will detect if a child is at a growth sprout or retarded stages of growth.[30,31,32]

7.1.3 Air displacement plethysmography

Air displacement plethysmography is a scientifically valid method for determining body composition. In infants air displacement plethysmography measures by assessing the body fat fraction in infants expressed in percentage. An electronic scale is utilized to determine the infants' mass. The complete body volume is determined by placing the subject in an enclosed vessel. Through the application of gas laws which are affected by pressure alterations in ratio to volume of air. This makes ADP a reliable technique for obtaining the percentage body fat in infants. It has also reflected reproducibility and accuracy in determining the percentage body fat in preterm and full-term infants.[33,34]

7.1.4 Dual energy x-ray absorptiometry

Dual energy x-ray absorptiometry measures bone mineral density using spectral imaging. It is used to monitor the development of the bones of preterm infants. A myriad of studies has certified the intricate and significant correlations between fat mass measured using dual-energy x-ray absorptiometry and fat mass measured with ADP. Twin films of the infants' forearm are taken via standard mobile x-ray at different x-ray energies. This technique affords the evaluation of the effect of diet on the total body composition and potential weight gain composition in preterm infants through their first week of life and beyond.[35,36]

8.0 Nutritional guidelines and quality of nutrition required by pre-terms

Currently, there is no consensus on a standard nutritional guideline for preterm infants. Hence, there are glaring variations in practices from one geographical zone to another. One major challenge is the discrepancy between developed nutritional guidelines from reviews. There are a few reasons why this may happen. First are

the differences in the quality of nutritional guidelines recommended. Some reviews recommend mainly breast milk fortification, while others go a step further to recommend the intake of an array of nutrients such as enteral protein, glutamine, enteral and parenteral calcium, and parenteral macro and micronutrients. Another reason is the dearth of clear evidence for nutritional interventions in pre-terms. Most guidelines are made based off the judgement of specialists. This may have led to the variability among guidelines currently available. The final reason for significant variation may be disparities in the aims of the recommendations generated by the review. For instance, the aim of the review may be to develop an official guideline on parenteral administered nutrition or orally administered formulas.[37] Nutrition based guidelines for preterm infants usually differ based on their scope and priority. Some focus on physiological targets i.e. how best to simulate in-utero growth. Others focus on feasibility and safety in specific environments. Recommendations backed by the evidence-based results are those focused on human milk and early aggressive nutrition. Different organizations issue guidelines that vary in their nutrient targets and clinical approaches. Organizations such as ESPGHAN (European Society for Pediatric Gastroenterology, Hepatology and Nutrition) lays emphasis on "aggressive" targets to match third-trimester fetal growth. They recommend high protein intakes and specific fatty acids like DHA and ARA to support brain and eye development. The world Health Organization): Primarily targets low- and middle-income countries where resources like Parenteral Nutrition (PN) are scarce. Their guidelines emphasize Kangaroo Mother Care and the safety of "trophic" (small-volume) feeds to prime the gut and prevent infection. Guidelines of the American Academy of Pediatrics is a bit similar to ESPGHAN but often uses different thresholds for micronutrients. For example, the AAP suggests lower vitamin D targets compared to ESPGHAN's higher range. Nutritional recommendations are largely dependent on available resources in the given geographical or economical settings. While high income settings such as Europe prioritize optimal neuro-development low-income settings such as like Africa or Asia focus on more fundamental factors such as infection control and infant survival. Practical challenges peculiar to African neonatal units in regards to nutrition fortification that enhance infant survival include financial barriers, lack of access to relevant technology leading to infrastructural gaps, lack of well-trained health care professionals e.g. neonatal nutrition specialist. Finally cultural beliefs or myths associated with some settings within Africa may also pose a problem.[38]

8.1 Essential vitamins, nutrients and their functions in preterm infants

Proteins are high molecular weight macro and biomolecules that consist of one or multiple amino acid residues. Proteins are molecules with complex structures that carry out a lot of functions in cells. They are vital to the structure, function, and regulation of the human body. Proteins in preterm infants are responsible for regeneration and repair, neurodevelopment, immunity, weight gain, and lean body mass accumulation. Energy is needed for metabolism. The required energy consumption of an infant depends on the energy expenditure and feeding pattern. More energy consumption and use occur when there is rapid growth and physical activity. The recommended energy consumption by preterm infants is 110-135kcal/kg/day. Vitamin A is a fat-soluble nutrient composed of a class of chemically similar organic compounds such as carotenoid, retinol, ß-carotene, and retinyl-esters. Vitamin A is essential for healthy vision and immunity. It also plays a role in lung function, growth, reproduction, and development in preterm infants. Vitamin D is a group of fat-soluble compounds vital for enhancing the absorption of minerals such as calcium, phosphate, and magnesium. Vitamin D is a key nutrient required for bone development. Serum 25-hydroxy vitamin D (25OHD) is the standard biomarker for vitamin D in the human body. Apart from bone health, vitamin D plays a vital role in immune boosting, respiration, and neuromuscular function. Vitamin A is required in 1332-3330 IU whilst vitamin D is required in 400-1000 IU per kg weight of preterm infant. Iron is a fundamental mineral and a vital part of myoglobin and hemoglobin. Lack of iron leads to anemia. Preterm infants require higher levels of iron to meet the requirement of a growth spurt. Premature infants on a breast milk diet need iron supplementation as well. Iron is also known to play a key role in neuro-development. The ideal quantity of iron needed for an infant is 1-3mg/kg/day. Zinc is necessary for protein synthesis; hence it should be considered when placing infants on high protein diet. The required daily dose of zinc is 2-3mg /kg /day.[39, 40, 41]

8.2 Current parenteral nutritional strategies for preterm infants

Intravenous feeding of dextrose, amino acids, and lipids, is recommended for severely preterm infants. Infants with hypoglycemia are administered a dose of dextrose

at 7 mg/kg/minute intravenously. Infant glucose levels should be monitored to avoid hyperglycemia. In the case of hyperglycemia, reduced dextrose infusion rates between 3 and 4 micrograms/minute/kilogram body weight are administered. It is important that premature infants get just the right amount of glucose to support physical and brain activity. The most important nutritional substance for growth is protein. Adequate amino acid intake is necessary for healthy growth and brain function. In cases of severely preterm infants, there is a direct relationship between amino acid administration and net protein level. Intravenous lipid infusions are necessary to prevent deficiency of essential fatty acids, especially docosahexaenoic acid (DHA). The ideal nutritional strategy for infants should include protein, vitamins, DHA and lipids. Readily available intravenous lipid products include soybean and fish oil. However, fish oil is preferable for preterm infant nutrition because it has both DHA, and tocopherol.[42, 43, 44]

8.3 Current oral formulations used in feeding preterm infants

The basic sources of oral nutritional needs for preterm infants are breast milk, breast milk fortifiers, and preterm formulas. Preterm infants have peculiar needs; they require extra calories for catch-up growth compared to full-term babies. Preterm infants need protein and fats for the development of the brain and organs. An appropriate amount of minerals and vitamins, as well as the right enzymes or probiotics as the case maybe is needed to attain ideal nutritional status. A preterm infant's stomach actively degrades proteins from milk with increasing breakdown across digestion time. Gastrin, gastrin-releasing peptide, and pepsin are secreted in the stomach for digestion of milk in preterm infants. There is a tendency for preterm infants placed on formula milk to develop necrotizing enterocolitis. It is, therefore, advisable that preterm infants be on a combination of breast milk and formula. In cases where formula cannot be afforded or accessed, breast milk fortifiers (containing nutrients and vitamins) may be administered along with human breast milk.[45,46] Tables 1 and 2, reflect the various milk formulas available in the market their components and pharmacological functions. Preterm formulas, including Dexolac®, Enfamil®, and Aptamil®, are densely formulated with medium chain triglycerides, whey protein, and DHA/ARA to address the high metabolic demands and nutritional gaps in preterm infants. These ingredients, combined with specialized minerals and vitamins, are crucial for promoting weight gain, preventing metabolic bone disease, and supporting neurodevelopmental outcomes.[45-50] Human milk fortifiers significantly enhance the nutritional profile of breast milk, making it more suitable for the unique needs of preterm infants. By boosting growth, immunity, and developmental outcomes, they play a crucial role in improving both short-term health and long-term quality of life for these vulnerable babies. Fortifiers enrich breast milk with additional macronutrients (energy, protein, fat, carbohydrate) that are often insufficient in preterm infants' diets. Fortifiers provide a broad spectrum of vitamins (A, C, D, E, K, B-complex, folate, biotin, pantothenic acid) and minerals (calcium, iron, zinc, magnesium, phosphorus, etc.), ensuring breast milk meets the higher nutritional demands of preterm babies. It enhances the nutrient density of breast milk without replacing its natural immunological and developmental benefits.[47]

Table 1: Current formulations and their primary ingredients[8, 9, 18, 48, 49, 50, 51, 52, 53]

PRETERM FORMULAS CURRENTLY AVAILABLE IN THE MARKET	CONTENTS			
	Vitamins	Minerals	Protein and amino-acids	Fats
Dexolac® Special care (Vegeterian formula)	Vitamins A, D, E, K, B and C. Folic acid and Niacin	Iodide, calcium, phosphorus, magnesium, sodium, potassium, chloride, iron, zinc, copper manganese and selenium	L-Cystine L-Histidine Taurine	Medium chain triglycerides, saturated fatty acid, mono-unsaturated fatty acid, trans fatty acids, cholesterol, alpha linoleic acid and linoleic acid.
Enfamil Neuro Pro ® (Premature)	Vitamins A, D, E, K, B6 and B12. Inositol, choline, Ascorbic acid, riboflavin (B2), folic acid, biotin, pantothenic acid.	Potassium, chloride, calcium, phosphorus, magnesium, iron, zinc, manganese, copper, iodine, selenium,	Taurine L-Carnitine Whey protein Soy lecithin	Sunflower oil, palm olein oil, coconut oil, soy oil, *mortierella alpina* oil and *schizochytrum* spp. oil.
SMA Gold® PREM2 (Preterm low birth weight infants)	Vitamins A, D, E, K, B6 and B12. Ascorbic acid, thiamin, riboflavin, niacin, folate, biotin and pantothenic acid.	Sodium, potassium, chloride, calcium, phosphorus, phosphate, Magnesium, iron, copper, manganese, selenium and iodide	Arginine, cystine, histidine, isoleucine, leucine, lysine, methionine, phenyl alanine, threonine, tryptophan, tyrosine, valine, aspartic acid serine, glutamic acid, proline glycine and alanine, whey protein.	Medium chain triglycerides, polysaturates, alpha linolenic acid (Omega3). Docosahexaenoic acid. Linoleic acid (Omega 6), arachidonic acid, S-N2 palmitate.
Pe- NAN® (Vegetarian formula)	Vitamin A, D, E, K and ascorbic acid. Folic acid, choline, biotin, inositol, thiamin, vitamin b12, riboflavin, niacin, pantothenic acid, pyridoxine.	Sodium, potassium, calcium, phosphorus, iron, magnesium, chloride, copper, zinc. Selenium, manganese, iodine, chromium. Molybdenum.	Taurine and L-carnitine	Saturated fat, mano-saturated fat, polysaturated, cholesterol, trans fat, docosahexaenoic acid (DHA), arachidonic acid, linolenic acid, linoleic acid.
Similac ® Neosure	Vitamin A, D, E, K and ascorbic acid. Folic acid, choline, biotin, inositol, thiamin, vitamin B12, riboflavin, niacin, pantothenic acid, pyridoxine.	Calcium magnesium iron zinc manganese phosphorus, copper, iodine, chloride, potassium, selenium.	Whey protein	Soy oil high oleic safflower oil, medium chain triglycerides, *alpina* oil and *schizochytrum* spp. oil.
Aptamil GOLD ® PRETERM	Vitamin A, D, E, K and ascorbic acid. Folate, biotin, inositol, thiamin, vitamin B5, B6, B12, riboflavin, niacin, pantothenic acid.	Calcium, phosphorous, sodium, potassium, chloride, magnesium, iron, zinc, manganese, copper, iodine, selenium.	Whey and casein	Saturated fat, medium chain triglyceride, Polyunsaturated fat, Linoleic acid Alpha linoleic acid, Arachidonic acid, Docosahexaenoic acid.

Table 2: Ingredients of the various formulas available in the market and their key functions.

PRETERM FORMULAS CURRENTLY AVAILABLE IN THE MARKET	Immune system	Nutrients for Brain Development	Digestive Health	Growth and bone development	References
Dexolac® Special care (Vegeterian formula)	Vitamin A, C, E selenium and zinc.	Omega 3 and 6 fatty acids. Taurine, choline, Iron and Iodine	Lactose, whey protein and maltodextrin	Calcium phosphorous, magnesium and vitamin D	48 49
Enfamil Neuro Pro ® (Premature)	Vitamin A, D, E, K, Biotin, Ascorbic acid, Folic acid, Thiamin, Riboflavin, Vitamin E and Niacinamide.	*Mortella Alpina* oil and *schizochytrium* oil (source of (DHA and ARA), choline chloride and inositol.	Whey protein	Soy oil, whey protein coconut oil, medium chain triglycerides, calcium carbonate.	50
SMA Gold® PREM2 (Preterm low birth weight infants).	Vitamins A, D, E, K, B6 and B12. Ascorbic acid.	Iron, Vitamin D, Calcium, Omega 3.	S-N 2 Palmitate, Whey protein	Vitamin D and Calcium	51
Pre- NAN® (Vegetarian formula)	Vitamin A, D, E, K and ascorbic acid. Folic acid and vitamin B12.	Docosahexaenoic acid and Arachidonic acid (DHA-ARA)	Whey protein	Calcium and Phosphorous	52
Similac ® Neosure	Vitamin A, D, E, K and ascorbic acid. Folic acid, vitamin B12, riboflavin.	Docosahexaenoic acid (DHA) and lutein	Whey protein	Calcium and Phosphorous	53
Aptamil GOLD ® PRETERM	Vitamin A, D, E, K and ascorbic acid. Folate, vitamin B5, B6, B12. Prebiotic oligosaccharides (90% scGOS, 10% lcFOS)	Docosahexaenoic acid (DHA)	Whey protein	Calcium and Phosphorous	

Table 3: Some human milk fortifiers currently available and their ingredients.

Human Milk Fortifiers	CONTENTS	References
Cow & Gate Nutriprem Breast Milk Fortifier	MACRONUTRIENTS: Energy, Protein, Whey, Carbohydrate, Fat. VITAMINS: Vitamin A, Vitamin C, Vitamin E, Vitamin D, Vitamin K, Thiamin (B1), Riboflavin (B2), Niacin, Vitamin B6, Vitamin B12, Folic acid, Folate, Biotin, Pantothenic acid. MINERALS: Calcium, Chloride, Copper, Iodine, Iron, Magnesium, Manganese, Phosphorus, Potassium, Selenium, Sodium, Zinc.	54
SMA Breast Milk Fortifier	MACRONUTRIENTS: Energy, Protein, Whey, Carbohydrate, Fat. VITAMINS: Vitamin A, Vitamin C, Vitamin E, Vitamin D, Vitamin K, Thiamin (B1), Riboflavin (B2), Niacin, Vitamin B6, Vitamin B12, Folic acid, Folate, Biotin, Pantothenic acid MINERALS: Calcium, Chloride, Copper, Iodine, Iron, Magnesium, Manganese, Phosphorus, Potassium, Selenium, Sodium, Zinc.	54
Prolacta Bioscience human milk fortifiers	MACRONUTRIENTS: Protein, Carbohydrate, Fat. VITAMINS: Vitamin A, Vitamin C, Vitamin E, Vitamin D, Vitamin K, Thiamin (B1), Riboflavin (B2), Niacin, Vitamin B6, Vitamin B12, Folate, Biotin, Pantothenic acid MINERALS: Calcium, Chloride, Copper, Iodine, Iron, Magnesium, Manganese, Phosphorus, Potassium, Selenium, Sodium, Zinc.	55

9.0 Preventing malnutrition in preterm infants - Recommendations

Nutrition is vital for building immunity, growth, and metabolism. In preterm infants' proper nutrition has been known to prevent suboptimal growth. Suboptimal head growth leads to a decline in psychomotor and mental skills, and high chances of autism and cerebral palsy. World Health Organization's recommendations for the nutrition of preterm infants start with prompt initiation of feeding after preterm birth. Mother's Own Milk (MOM) is a "gold standard" for preventing NEC and sepsis. If MOM is unavailable, donor human milk is strongly preferred over formula for babies under 1.5 kg.

Fortification of human milk, especially infants that are very preterm is viable as clinical evidence shows that babies fed with fortified breast milk have higher IQ scores and more advanced white matter development long term. Table 3, enumerates the major human milk fortifiers available and their key ingredients. Administration of micronutrients such as Iron, Zinc, Vitamin D, E, K, and A. Subsequently, the administration of probiotics aids GUT maturity and improves digestion is under consideration.[56, 57]

10.0 Key Conclusions

- Preterm infants in neonatal care units face environment-based challenges that do not exist in the third trimester in the uterus.
- The organs of preterm infants are not fully developed and may most likely be lacking in the ability to support life outside the uterus. These organs make up systems and put up a fight for infancy survival alongside the intensive care provided by health professionals and parents.
- Optimal nutrition is necessary for the survival of preterm infants. Early and proper feeding (supply of essential vitamins and nutrients) is necessary to increase chances of infant survival.
- Breastmilk is the most reliable and effective source of nutrition for preterm infants.

e 12 line 4-7 should please read...

Fortification of human breast milk, (to improve its quality) especially infants that are very preterm, can be a viable option.

- In cases where human breast milk cannot be assessed, oral formula milk with similar whey: casein ratios similar to breast milk can be administered as nutritional source to preterm infants.

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CONFLICT OF INTEREST
None declared.

11.0 REFERENCES

1. Mabrouk A, Abubakar A, Too EK, Chongwo E, Adetifa IM (2022). A scoping review of preterm births in sub-Saharan Africa: burden, risk factors and outcomes, *International Journal of Environmental Research and Public Health* 19(17):10537.
2. Tekeba B, Techane MA, Workneh BS, Zegeye AF, Gonete AT, Ahmed MA, Wassie YA, Wassie M, Kassie AT, Ali MS, Mekonen EG, Tamir TT, Tsega SS (2024). Determinants of preterm birth among reproductive age women in sub-Saharan Africa: evidence from demographic and health survey data, *PLoS One* 19(6): e0305810.
3. Omwenke IW (2026). Determinants of preterm birth in sub-Saharan Africa: a systematic review with evidence from Nigeria, *Journal of Clinical and Metabolism Studies* 10(3).
4. Rodriguez S, De La Cruz D, Neu J (2024). Nutrition strategies to prevent short-term adverse outcomes in preterm neonates, *BMJ Nutrition, Prevention & Health* e000801(1):1-8
5. Keikha M, Kelishadi R (2022). Comment on determinants of malnutrition among children: a systematic review, Nutrition 102:111722.
6. Gonete AT, Alemu TG, Mekonnen EG, Takele WW (2021). Malnutrition and contributing factors among newborns in Gondar Hospital, *BMJ Open* 11(11): 1-10.
7. Gidi NW, Mekasha A, Nigussie AK, Goldenberg RL, McClure EM, Worku B (2020). *Preterm nutrition and clinical outcomes, Global Pediatric Health* 7(1):1-7.
8. Wiechers C, Bernhard W, Goelz R, Poets CF, Franz AR (2021). Optimizing early neonatal nutrition in premature infants, *International Journal of Environmental Research and Public Health* 18(14):7544.
9. Hay WW (2018). Nutritional Support Strategies for the Preterm Infant in the Neonatal Intensive Care Unit, *Pediatric Gastroenterology, Hepatology & Nutrition* 21(4):234-247.
10. Behrman RE, Butler AS (2007). Mortality and acute complications in preterm infants. In: Preterm birth: causes, consequences, and prevention. Washington DC: National Academies Press.
11. Kramer MS (2000). The contribution of mild and moderate preterm birth to infant mortality. Fetal and Infant Health Study Group of the Canadian Perinatal Surveillance System, *Journal of the American Medical Association* 284(7):843-849.
12. World Health Organization (2024). Preterm birth. Available at: www.who.int/news-room/fact-sheets/detail/preterm-birth. Accessed December 28, 2024.
13. Ryan JG, Dogbey E (2015). Preterm births: a global health problem, MCN: *The American Journal of Maternal/Child Nursing* 40(5):278-283.
14. Johnson S, Gilmore C, Gallimore I, Jaekel J, Wolke D (2015). The long-term consequences of preterm birth: what do teachers know? *Developmental Medicine & Child Neurology* 57(6):571-577.
15. Boyle E, Johnson S, Draper E, Manktelow B, Seaton S, Evans T, Paneth N (2014). Neonatal outcomes and delivery of care for infants born late preterm or moderately preterm: A Prospective population-based study, *Archives of Disease in Childhood: Fetal and Neonatal Edition* 99(1): A39.
16. Modrzejewska M, Kot J (2016). Changes in the central nervous system of prematurely born children, *Acta Ophthalmologica Polonica* 118(1):55-58.
17. Frezza S, Catenazzi P, Gallus R, Gallini F, Fioretti M, Anzivino R (2019). Hearing loss in very preterm infants: should we wait or treat? *Acta Otorhinolaryngologica Italica* 39(4):257-262.
18. Kim JH (2023). Providing Optimal Nutrition to Very Low Birthweight Infants in the NICU, *NeoReviews* 24(5): e271-e284.
19. Vrselja A, Pillow JJ, Black MJ (2021). Effect of Preterm Birth on Cardiac and Cardiomyocyte Growth and the Consequences of Antenatal and Postnatal Glucocorticoid Treatment, *Journal of Clinical Medicine* 10(17):3896.

20. Indrio F, Neu J, Pettoello-Mantovani M, Marchese F, Martini S, Salatto A (2022 Development of the Gastrointestinal Tract in Newborns as a Challenge for an Appropriate Nutrition: A Narrative Review, *Nutrients* 14(7):1-15.
21. Bresesti I, Salvatore S, Valetti G, Baj A, Giaroni C, Agosti M (2022). The Microbiota-Gut Axis in Premature Infants: Physio-Pathological Implications, Cells 11(3):379.
22. Zhang C, Li L, Jin B, Xu X, Zuo X, Li Y (2021). The Effects of Delivery Mode on the Gut Microbiota and Health: State of Art, *Frontiers in Microbiology* 12:724449.
23. Bandoli G, Palmsten K, Forbess Smith CJ, Chambers CD (2017). A Review of Systemic Corticosteroid Use in Pregnancy and the Risk of Select Pregnancy and Birth Outcomes, *Rheumatic Disease Clinics of North America* 43(3):489-502.
24. Maurya P, Yadav L (2015). Physiological basis of breastfeeding, *International Journal of Medical Sciences* 8(1-2):60-67.
25. Nguyen MH, Fornes R, Kamau N, Danielsson H, Callens S, Fransson E (2022). Antibiotic use during pregnancy and the risk of preterm birth: a population-based Swedish cohort study. *Journal of Antimicrobial Chemotherapy* 77(5):1461-1467.
26. Bradford CV, Cober MP, Miller JL (2021). Refeeding Syndrome in the Neonatal Intensive Care Unit, *Journal of Pediatric Pharmacology and Therapeutics* 26(8):771-782.
27. Pereira-da-Silva L, Virella D, Fusch C (2019). Nutritional Assessment in Preterm Infants: A Practical Approach in the NICU, *Nutrients* 11(9):1-18.
28. Goldberg DL, Becker PJ, Brigham K, Carlson S, Fleck L, Gollins L (2018). Identifying Malnutrition in Preterm and Neonatal Populations: Recommended Indicators, *Journal of the Academy of Nutrition and Dietetics* 118(9):1571-1582.
29. Casadei K, Kiel J (2024). Anthropometric measurement. In: StatPearls. Treasure Island: StatPearls Publishing.
30. Bhandari V, Fall P, Raisz L, Rowe J (1999). Potential biochemical growth markers in premature infants, *American Journal of Perinatology* 16(7):339-349.
31. Crofton PM, Shrivastava A, Wade JC, Stephen R, Kelnar CJH, Lyon AJ (1999). Bone and collagen markers in preterm infants: relationship with growth and bone mineral content over the first 10 weeks of life, *Pediatric Research* 46(5):581.
32. Kanbur NO, Derman O, ?en TA, Kinik E (2002). Osteocalcin. A biochemical marker of bone turnover during puberty, *International Journal of Adolescent Medicine and Health* 14(3):235-239.
33. Valencia ME, Villegas-Valle RC (2012). Body fat measurement. In: Preedy VR, ed. Handbook of anthropometry. New York: Springer:397-413.
34. Ma G, Yao M, Liu Y, Lin A, Zou H, Urlando A (2004). Validation of a new pediatric air-displacement plethysmograph for assessing body composition in infants, *American Journal of Clinical Nutrition* 79(4):653-660.
35. Yumani DFJ, De Jongh D, Lafeber HN, Van Weissenbruch M (2021). A comparative study using dual-energy X-ray absorptiometry, air displacement plethysmography, and skinfolds to assess fat mass in preterms at term equivalent age, *European Journal of Pediatrics* 180(3):919-927.
36. Pieltain C, De Curtis M, Gérard P, Rigo J (2001). Weight gain composition in preterm infants with dual energy X-ray absorptiometry, *Pediatric Research* 49(1):120-124.
37. Embleton ND (2022). Fifteen-minute consultation: ABCDE approach to nutritional assessment in preterm infants, *Archives of Disease in Childhood - Education and Practice Edition* 107(5):314-319.
38. Devarajalu P, Kumar J, Dutta S, Attri SV, Kabeerdoss J (2024). Gut microbiota of preterm infants in the neonatal intensive care unit: a study from a tertiary care center in northern India, *Frontiers in Microbiology* 15:(1329926)1-8.
39. Ilardi L, Proto A, Ceroni F, Morniroli D, Martinelli S, Mosca F (2021). Overview of Important Micronutrients Supplementation in Preterm Infants after Discharge: A Call for Consensus, Life 11(4):1-13.
40. Kumar RK, Singhal A, Vaidya U, Banerjee S, Anwar F, Rao S (2017). Optimizing Nutrition in Preterm Low Birth Weight Infants-Consensus Summary, *Frontiers in Nutrition* 4:(20)1-9.
41. Chauhan SS, Sarkar PD, Bhimte B (2011). Prematurity and Related Biochemical Outcomes: Study of Bone Mineralization and Renal Function Parameters in Preterm Infants, *Biochemistry Research International.* 2011:740370.
42. Deriba BS (2021). Nutritional-Related Predictors of Preterm Birth in North Shewa Hospitals, Central Ethiopia: A Case-Control Study. Pediatric health, *Medicine and Therapeutics* 12:315-324.
43. Meiliana M, Alexander T, Bloomfield FH, Cormack BE, Harding JE, Walsh O (2024). Nutrition guidelines for preterm infants: A systematic review, *Journal of Parenteral and Enteral Nutrition* 48(1):11-26.
44. Jayatissa R, Bekele A, Kethiswaran A, De Silva AH (2012). Community-based management of severe

and moderate acute malnutrition during emergencies in Sri Lanka: challenges of implementation, *Food and Nutrition Bulletin* 33(4):251-260.

45. Cilieborg MS, Boye M, Sangild PT (2012). Bacterial colonization and gut development in preterm neonates, *Early Human Development* 88(Suppl 1): S41-S49.
46. Cong X, Xu W, Janton S, Henderson WA, Matson A, McGrath JM (2016). Gut Microbiome Developmental Patterns in Early Life of Preterm Infants: Impacts of Feeding and Gender, *PLoS One* 11(4): e0152751.
47. Yu Y, Lu L, Sun J, Petrof EO, Claud EC (2016). Preterm infant gut microbiota affects intestinal development, *American Journal of Physiology-Gastrointestinal and Liver Physiology* 311(3): G521-G532.
48. Danone India (2025). Dexolac special care. Available at: www.danone.in/products/dexolac-special-care/. Accessed December 27, 2025.
49. Enfamil (2025). Enfamil NeuroPro EnfaCare formula. Available at: www.enfamil.com. Accessed December 27, 2025.
50. SMA HCP (2025). SMA Gold Prem 2. Available at: www.smahcp.co.uk. Accessed December 27, 2025.
51. Amazon (2025). Nestlé nutrition infant formula. Available at: www.amazon.in. Accessed December 27, 2025.
52. Similac (2025). NeoSure infant formula. Available at: www.similac.com. Accessed December 27, 2025.
53. Nutricia (2025). Aptamil Gold+ preterm formula. Available at: www.nutricia.com.au. Accessed December 27, 2025.
54. Westland S (2020). Human milk fortifiers. First Steps Nutrition Trust.
55. Prolacta Bioscience (2024). Product nutrition information. Available at: www.prolacta.com. Accessed December 28, 2024.
56. Salas Lorenzo I, Chisaguano Tonato AM, De La Garza Puentes A, Nieto A, Herrmann F, Dieguez E (2019). The Effect of an Infant Formula Supplemented with AA and DHA on Fatty Acid Levels of Infants with Different FADS Genotypes: The COGNIS Study, *Nutrients* 11(3):1-16.
57. Lamport L, Hartman C, Codipilly C, Weinberger B, Schanler R (2019). Effects of Nutrition supplementation and osmolality, *Journal of Parenteral and Enteral Nutrition* 43(6):809-814.