CONSENSUS

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International consensus on early rehabilitation and nutritional management for infants at high risk of neurological impairments

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INTRODUCTION

Infants at high risk of neurological impairment (IHRNI) refer to those with *in-utero*, perinatal, or postnatal high-risk factors that cause motor, cognitive, and/or language delays, abnormal muscle tone and posture, swallowing disorders, problematic behaviors, or any other clinical symptoms related to neurological damage.[1,2] Although it is too early to determine the long-term prognosis in the early stage, these infants are at risk of developing permanent neurological impairments, such as cerebral palsy, intellectual disability, and neurodevelopmental disorders.[1,2] The "early stage" mentioned in this consensus mainly refers to the stage from 0 to 2 years of adjusted age. An Australian cohort study found that the survival rate of extremely premature infants increased from 50% to 73% between 1991 and 2017. However, the incidence of neurodevelopmental disorders among these infants remained high and was

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inversely related to gestational age.[3] In the United States, a follow-up study of extremely premature infants indicated that 29.3% experienced moderate and 21.2% had severe neurodevelopmental impairments, with an incidence of 8.4% having moderate to severe cerebral palsy.[4] It is difficult to predict neurodevelopmental outcomes in early life. Consequently, the outcomes of IHRNI could vary from normal development to mild and severe neurological impairment. Despite the uncertainty, early intervention should be initiated when professionals identify neurological impairment-related clinical symptoms.[5] In addition, IHRNI might be susceptible to undernutrition, which not only impedes their neurodevelopment but also reduces their quality of life. Effective management of their nutritional needs might lead to significant improvements in the well-being of the entire family. To date, there is limited standardized guidance available for the early rehabilitation and nutritional management of these infants. As a result, the optimal timing for interventions might be overlooked, potentially compromising functional outcomes. This consensus, built upon currently available evidence and expert opinions, aims to provide effective recommendations for early rehabilitation and nutritional management of IHRNI.

METHODS

This consensus was led by the Rehabilitation Group of the Pediatrics Society of the Chinese Medical Association in conjunction with a panel of international specialists. A total of 62 specialists with expertise in early rehabilitation and nutritional management from China, the United States, the United Kingdom, and Belgium participated and decided upon 10 key clinical issues centered around early detection, rehabilitation intervention, and nutritional management of IHRNI. We subsequently conducted a comprehensive literature search on these issues in Pubmed/MEDLINE and Foreign Medical Retrieval System. Article selection prioritized systematic review (SR) related to the clinical issues, followed by randomized controlled trials (RCTs). If neither a suitable SR nor RCTs are available, the best evidence of a lower tier waschosen. When few or no studies directly address the population of IHRNI, and the corresponding clinical questions remain unresolved, research on conditions such as cerebral palsy, hypoxic-ischemic encephalopathy, prematurity risks, and neurodevelopmental disorders was considered.

The selected research evidence and recommendations were graded using the Oxford Center for Evidence-Based Medicine's method (Tables 1 and 2).[6] All proposed recommendations and pertinent content underwent two rounds of significance evaluation based on the Delphi method.[7] The initial round generated 60 recommendations derived from the 10 pre-determined clinical questions. These recommendations were then presented to the expert panel for evaluation via a questionnaire. Out of these, four recommendations did not achieve consensus. After incorporating new expert feedback, 14 recommendations were formulated in the second round, of which one did not gain consensus. After two rounds of Delphi assessment and expert group discussions, the final recommendations were consolidated. This consensus is officially registered on

TABLE 1 Levels of evidence

Level	Evidence
I	SR (with homogeneity[†]) of RCTs
	Individual RCT (with narrow confidence interval)
	All or none[‡]
II	SR (with homogeneity[†]) of cohort studies
	Individual cohort study (including low-quality RCT; e.g., < 80% follow-up)
	"Outcomes" research; ecological studies
III	SR (with homogeneity[†]) of case-control studies
	Individual case-control study
IV	Case-series (and poor quality cohort and case-control studies[§])
V	Expert opinion without an explicit critical appraisal, or based on physiology, bench research, or "first principles"

[†]Homogeneity means that a systematic review is free of worrisome variations (heterogeneity) in the directions and degrees of results between individual studies. Not all systematic reviews with statistically significant heterogeneity need to be worrisome, and not all worrisome heterogeneity needs to be statistically significant. As noted above, studies displaying worrisome heterogeneity should be tagged with a "-" at the end of their designated level.

[‡]Met when all patients died before the Rx became available, but some now survive on it; or when some patients died before the Rx became available, but none now die on it.

[§]Poor quality cohort study means that the study failed to clearly define comparison groups and/or failed to measure exposures and outcomes in the same (preferably blinded), objective way in both exposed and non-exposed individuals and/or failed to identify or appropriately control known confounders and/or failed to carry out a sufficiently long and complete follow-up of patients. By poor quality case-control study we mean one that failed to clearly define comparison groups and/or failed to measure exposures and outcomes in the same (preferably blinded), objective way in both cases and controls and/or failed to identify or appropriately control known confounders.

Abbreviations: RCTs, randomized controlled trials; SR, systematic review.

TABLE 2 Grades of recommendation

Grade	Level of evidence
A	Consistent level 1 studies
B	Consistent level 2 or 3 studies or extrapolations from level 1 studies
C	Level 4 studies or extrapolations from level 2 or 3 studies
D	Level 5 evidence or troublingly inconsistent or inconclusive studies of any level

the website of the International Practice Guideline Registry Platform under the registration number PREPARE-2023CN488.

CLINICAL QUESTIONS AND RECOMMENDATIONS

Clinical question 1: What are the primary factors influencing the prognosis of IHRNI?

Recommendation 1: The prognosis for IHRNI might worsen with more severe impairments in motor, cognition, eating, and nutritional status during the early stages. Additionally, the presence of more complex comorbidities at the early stage might negatively impact the prognosis further. Early detection and intervention could improve the prognosis. (Level I evidence, Grade A recommendation)

IHRNI often exhibit developmental delays, hypertonia, abnormal posture, and swallowing disorders at an early stage, issues that could profoundly affect their daily lives and social interactions over the long term. Straathof et al.[8] found that in infants with abnormal brain structure or those suspected of having neurological dysfunction clinically: (a) Over 90% exhibited delayed motor development during infancy, which becomes more pronounced with age; (b) Infants with better motor function tend to have better motor and social life skills during school age; (c) Improvements in motor function in infancy correlate with better cognitive function at school age. McGowan et al.[9] found that high-risk premature infants (those who presented with two or more conditions like bronchopulmonary dysplasia and brain injury) had a 3–4 times higher risk of delayed motor and cognitive development at age two compared to the low-risk group. In a follow-up study on extremely premature infants at 4–5 years of age, Rinat et al.[10] reported that those with early feeding difficulties demonstrated motor dysfunction in early childhood, which underscores the importance of early diagnosis and intervention of feeding and nutritional problems. Nutrition is crucial for infants' development during the first 1000 days and subsequent years. For instance, iron deficiency anemia at an early stage could adversely affect an individual's motor development and have a more pronounced impact on their cognitive development after the age of 5 years.[11,12] A survey found that 50.8% of children with cerebral palsy experienced undernutrition, and this was correlated with the severity of their condition.[13] Undernutrition is a common complication in IHRNI, and feeding problems are closely associated with motor and cognitive functions, highlighting the necessity of early detection and intervention of nutritional deficits.[14] Although precise data on the incidence of undernutrition in IHRNI is lacking, these infants are at increased risk of developing undernutrition. IHRNI often suffer from swallowing disorders, feeding difficulties, or digestive dysfunction resulting in deficiencies in nutritional intake while hypertonia exacerbates nutrient consumption. Undernutrition would further influence their neurodevelopment. Therefore, it is recommended to monitor the nutritional status of IHRNI and their functional development in motor, cognition, language, and feeding, aiming for the early detection of abnormalities and timely targeted interventions.[15]

Clinical question 2: How to detect IHRNI at an early stage?

Recommendation 2: Detailed neurological examination and developmental assessments should be performed for high-risk infants or infants who are suspected to have neurological impairments upon screening. Brain magnetic resonance imaging (MRI) and ultrasound should be conducted for individuals with abnormal examination. Early intervention and regular follow-up are recommended for those with detected neurological impairments. (Level I evidence, Grade A recommendation)

High-risk infants might include neonates and infants who were born prematurely, with low birth weight, a history of hypoxic-ischemic encephalopathy, or those who were treated at the neonatal intensive care unit (NICU) for other conditions. Infants with developmental delays might be identified by regular screening or caregiver reports. All of these infants should complete detailed neurological examination and developmental assessment. Further neurological imaging would be needed in cases with abnormal results.[1,16] The expert panel recommended Hammersmith Infant Neurological Examination (HINE) to be used since it has been shown to be a reliable and valid tool for detecting neurological impairment. It has a sensitivity of over 90% and a specificity of over 85% for predicting cerebral palsy.[1] HINE has also been shown to have a good predicting value of cognitive impairments.[17–19] In the neonatal period, Hammersmith Neonatal Neurological Examination (HNNE) could be used for detecting motor delay, but its sensitivity and specificity for neurological impairment are unclear.[20] As for motor performance, assessment tools that focus on abnormal features of neurological impairment and have good predictive values in long-term outcomes should be chosen. Prechtl's Assessment of General Movements (GMs) is recommended for assessing infants' spontaneous movement under the adjusted age of 5 months with 98% sensitivity and 91% specificity for predicting cerebral palsy.[1] In addition, the Test of Infant Motor Performance (TIMP) and Alberta Infant Motor Scale (AIMS) could help differentiate infants with delayed gross motor skills from typically developing peers. We also recommend regular follow-ups for both high-risk infants and infants with developmental delays using standardized assessments like Bayley Scales of Infant and Toddler Development III

(Bayley-III) and Griffiths Scale of Child Development, to track their development in motor, cognition, language, and social behaviors.[21] Neuroimaging, preferably brain MRI, is recommended when the infant is found to have abnormalities in neurological examination and functional assessments. A previous study found that abnormal brain MRI results 1 week after birth predicted a poor prognosis (neurological impairment or mortality) with a sensitivity of 85% and specificity of 86%–89%.[16] When brain MRI is not feasible, cranial ultrasound could be employed for those with open fontanelles.[22] However, a subsequent MRI should be conducted when possible. Early evaluation of social and emotional development is difficult since differences between typically developing infants and infants at high risk of neurodevelopmental disorders might not be easily identified before 6 months. We recommend the Communication and Symbolic Behavior Scales (CSBS) and Modified Checklist for Autism in Toddlers (M-CHAT) for early screening after the age of 6 months.[23] The NICU Network Neurobehavioral Scale (NNNS) might recognize neurodevelopmental delays and problematic behaviors during the neonatal period, especially in neonates at high risk of chemical exposure. Previous studies indicated that it also has predictive value for neurodevelopment and behavior at the age of 2 years.[9,24,25]

Among the assessment tools for neurological impairment, the GMs, HINE, and MRI are the most effective methods available for predicting cerebral palsy. Specifically, MRI performed at term corrected age had a sensitivity range of 86%–100% and specificity of 87%–97% in predicting cerebral palsy,[26] and MRI evidence of moderate to severe cerebral white-matter damage indicated severe cognitive impairment and cerebral palsy.[27] Cranial ultrasound findings of intraventricular hemorrhage levels III and IV have also been associated with severe cognitive impairment and paraventricular leukomalacia.[27] HINE combined with MRI could achieve a predictive value of 90% or greater for cerebral palsy.[1] A total HINE score below 57 at the adjusted age of 3 months or below 65 at 12 months indicates a risk of cerebral palsy, and a total score below 40 suggests a risk of severe cerebral palsy.[28] Further, HINE could anticipate subtypes of cerebral palsy as a total score of 50–73 along with an asymmetry score of 5 or above indicating hemiplegia, while a score below 50 indicates diplegia and quadriplegia.[28] In addition to cerebral palsy, a lower HINE score might also indicate potential developmental delay.[29] Romeo et al.[30] found that children who had stayed at the NICU for medical care were rarely able to achieve optimal scores among the same-aged infants at 3, 6, 9, and 12 months. The GMs combined with brain MRI could identify cerebral palsy with a predictive value of 95%–98%.[1,26] Infants who present with a series of cramped-synchronized general movements and the absence of fidget movements are at high risk of cerebral palsy.[31] A follow-up study on premature infants discovered that those with abnormal GMs results at 3 months exhibited worse motor and cognitive outcomes than infants with normal GMs.[32] The Bayley-III test could reflect delays in cognition, motor, language, adaptive behaviors, and social interaction. Once delays are detected, early intervention for these infants should be implemented. However, its efficacy in predicting development delays at late childhood or early school age is somewhat limited.[21] The risk for cerebral palsy increases if the infant exhibits abnormal GMs or HINE and is born with high-risk factors, or presents an abnormal brain MRI. For infants with normal brain MRI and without high-risk medical history, follow-up, and early interventions are still necessary if their GMs or HINE show anomalies.

Clinical question 3: Is early rehabilitation effective in enhancing functional outcomes for IHRNI?

Recommendation 3: Early rehabilitation might promote the development of motor and cognitive skills in IHRNI. It could effectively alleviate the severity of cerebral palsy, and reduce or prevent secondary complications associated with cerebral palsy. (Level I evidence, Grade A recommendation)

Early rehabilitation could enhance functional outcomes for IHRNI, notably in motor and cognitive functions. It might also reduce and prevent secondary complications and improve the prognosis for infants who are later diagnosed with cerebral palsy.[3] The fetal period and the first two years of life undergo active brain development and exhibit the highest degree of neuroplasticity, further emphasizing that early rehabilitation is pivotal for improving the prognosis of IHRNI.[16] Morgan et al.[33] demonstrated that the implementation of the goals-activities-motor enrichment approach could improve both motor and cognitive outcomes in high-risk infants with cerebral palsy. Eliasson et al.[34] discovered that introducing baby constraint-induced movement therapy (baby-CIMT) before the age of 12 months could enhance hand function in IHRNI, potentially leading to a better prognosis in manual ability. A study found that the CIMT might enhance the hand function of hemiplegic mice by promoting the remodeling of neurons, neurofilaments, dendrites/axon areas, and myelin in the motor cortex.[35] Dusing et al.[36] observed that early physical therapy based on parent-child interaction could enhance both motor and cognitive functions in children with motor delay.

Clinical question 4: What are the principles of early rehabilitation for IHRNI?

Recommendation 4: Early rehabilitation for IHRNI should be timely and specific, emphasizing the active involvement of the family. (Level I evidence, Grade A recommendation)

Based on current research evidence, effective early rehabilitation training for IHRNI should adhere to the following principles[5]: (a) Early initiation: Rehabilitation should begin as soon as neurological impairment is suspected to avoid missing the critical period of neuroplasticity; (b) Targeted and task-oriented training: Treatment should be selected based on infants' age, specific needs, and assessment results; (c) Active involvement of family: Modifying the family environment and enhancing interactions between family members and the infant could facilitate the emergence and development of motor, cognitive, behavioral, and other related skills.[37,38]

Clinical question 5: Which early interventions are effective for improving the outcome of IHRNI?

Recommendation 5: The task-specified motor training, CIMT, and cognitive therapy have been proven effective (Level I evidence, Grade A recommendation). Speech and language therapy, developmental care in NICU, feeding support, and interventions to decrease comorbidities are also recommended, however, with less conclusive evidence of effectiveness. (Level II evidence, Grade B recommendation)

To improve the functional outcome of IHRNI, we recommend promoting motor, cognitive, language, and social skill development to prevent or mitigate secondary complications.[5,39] Based on the current evidence, the following interventions are recommended: (a) Task-specific motor training: This should be appropriately challenging, considering the patient's age and level of function. It should emphasize parental teaching to ensure that the exercises are performed regularly.[33,40–42] (b) Baby-CIMT and bimanual intensive training: These are the optimal interventions for infants at high risk of hemiplegia to improve manual ability. We suggest that infants at high risk of hemiplegia receive 30–60 minutes daily intensive baby-CIMT with active parental participation for at least 6 weeks.[34,43] (c) Cognitive therapy: This should be task-oriented and focus on parent-infant involvement within an interactive environment, and offer multimodal training (e.g., incorporating cognitive, language, motor, and social skills).[5,41,44] (d) Social interaction and communication skills: These should focus on face-to-face interactions, promoting the development of preverbal skills such as joint attention, emotional perception, and gestural communication. (e) Developmental care in NICU: Emphasis should be placed on involving parents through parent-neonate interaction, tactile therapy, Kangaroo skin-to-skin care, and breastfeeding. Fostering interprofessional collaboration across disciplines is crucial in supporting the implementation of developmental care in the NICU.[45,46] (f) Supported feeding: This includes functionally appropriate food texture, proper feeding posture, and an integrated approach to supporting oral feeding, which could help improve the efficiency and safety of feeding.[47,48] However, it is important to ensure safety and professional competency when providing developmental care in the NICU.

(g) Addressing comorbidities: It is very important to prevent or reduce comorbidities at the early stage, such as musculoskeletal problems, visual and auditory impairments, and sleeping disorders. This includes the incorporation of motor learning, ankle-foot orthoses, sensory-motor development, environmental adaption, and establishing daily routines.[5]

Clinical question 6: Could nutritional management optimize the body growth and neurodevelopment of IHRNI?

Recommendation 6: Nutritional management could prompt weight and height gain in IHRNI, and improve the development of motor, cognitive, language, and social-emotional skills. (Level II evidence, Grade B recommendation)

IHRNI are often affected by gastrointestinal complications, swallowing disorders, feeding difficulties, cognitive impairments, and hypertonia, which may cause insufficient nutritional intake and increased energy consumption. Consequently, the risk of undernutrition might be rising which could have detrimental effects on various systems, including the neurological, musculoskeletal, and immune systems. A multicenter prospective cohort study found that infants hospitalized due to acute diseases displayed a trend of improvement in neurodevelopmental outcomes along with their nutritional status at 6 months post-discharge, but infants in the group of severe emaciation and no improvement had decreased scores by an average of 1.8 points in neurodevelopmental assessment compared to their discharge baseline ($P < 0.001$).[49] Bhargava and colleagues found that undernutrition negatively impacts brain structure and neurodevelopmental outcomes, and targeted nutritional management could counteract these adverse changes in the brain and mitigate developmental delay, thereby contributing to the prevention of perpetual neurological impairments.[50,51]

Clinical question 7: How could we determine the nutritional management needs of IHRNI?

Recommendation 7: IHRNI should receive nutritional screenings on every hospital visit. Should a risk of undernutrition be identified, a comprehensive nutritional assessment and risk factors analysis should be conducted to determine their needs for nutritional management. (Level I evidence, Grade A recommendation)

Screening for risk of undernutrition

The screening for risk of undernutrition in IHRNI should be timely and efficient.[48] At present, most of the available

TABLE 3 Classification of undernutrition

Z score	Weight for age	Length for age	Weight for length
$-2<Z\leq-1$	Not applicable	Not applicable	Mild wasting
$-3<Z\leq-2$	Moderate underweight	Moderate stunting	Moderate wasting
$Z\leq-3$	Severe underweight	Severe stunting	Severe wasting

undernutrition risk screening tools are designed for inpatients, and their sensitivity across different conditions has not been adequately established. Taking into account the reliability, validity, and clinical application, we recommend the use of the Screening Tool Risk on Nutritional Status and Growth (STRONGkids) and the pediatric Subjective Global Nutritional Assessment to screen the undernutrition risk in IHRNI.[52–55]

Nutritional assessment

Body metrics measurement: Nutritional status is mainly reflected by anthropometry data, including weight, length, body mass index, skinfold thickness, mid-upper arm circumference, and head circumference. Supporting Information laboratory testing, such as serum protein levels, immune indicators, and trace element levels, could also be informative under the correct circumstances.[56] In line with the guidelines of the World Health Organization and incorporating the standards set by the American Society for Parenteral and Enteral Nutrition,[57,58] we suggest using *Z*-score to evaluate nutritional status, including weight-for-age *Z*-score, length-for-age *Z*-score, weight-for-length *Z*-score. Based on these measurements, undernutrition is categorized into wasting, stunting, and underweight (Table 3).

Risk factors: Factors leading to undernutrition in IHRNI could be grouped into two categories: (a) Factors affecting adequate nutritional intake and absorption, such as swallowing disorders, feeding difficulties, gastrointestinal dysfunction, gastroesophageal reflux, and anorexia, and (b) increased energy consumption due to conditions like hypertonia and comorbidities. Swallowing disorders and feeding difficulties are common in IHRNI. We recommend using the Neonatal Eating Assessment Tool (NeoEAT), the Neonatal Oral-Motor Assessment Scale, the Pediatric version of the Eating Assessment Tool-10 (PEDI-EAT-10), and the Ability for Basic Feeding and Swallowing Scale for Children to assess these problems.[59–63] The videofluoroscopic swallowing study and the fiberoptic endoscopic evaluation of swallowing are the gold standards for assessing swallowing function, as they offer precise evaluations of the anatomical structures and swallowing process.[48,64] Furthermore, we should also consider the infant's dietary patterns (such as daily intake, types of foods, length of time for feeding, and feeding intervals) and any history of gastrointestinal diseases or food allergies. This information aids in selecting appropriate feeding methods and food choices.

Clinical question 8: What is the optimal approach to providing nutritional support for IHRNI?

Recommendation 8: Nutritional support for IHRNI should be individualized. Critical components include careful evaluations of nutritional needs, choices of nutritional support methods, selections of enteral nutrition formulas, and providing feeding and swallowing support. (Level I evidence, Grade A recommendation)

Estimation of energy requirements

For infants under the age of 12 months, we suggest using indirect calorimetry to estimate energy needs. The daily energy intake should be equivalent to the Total Energy Expenditure (TEE) plus the energy required for deposition (TEE = 95 × weight [kg] − 126). The energy deposition requirements for different genders and related ages. From 0 to 3 months, boys require 180 kcal/day, while girls require 175 kcal/day. From 3 to 6 months, boys require 47 kcal/day, and girls require 60 kcal/day. From 6 to 9 months, the requirement for boys is 16 kcal/day, compared to 18 kcal/day for girls. From 9 to 12 months, boys' requirements rise slightly to 22 kcal/day, while girls' fall to 14 kcal/day.[65] Infants with mild undernutrition might receive an additional 20% of the daily energy intake, while infants with moderate undernutrition require an extra 40%, and infants with severe undernutrition need an extra 60%.[66,67] For neonates at risk of neurological impairment, the nutrient intake should be suggested by neonatologists since the neonates might have complex comorbidities.

For infants aged 1–2 years, the target energy intake = (basal metabolic rate [BMR] × muscle tone × activity level) + growth energy requirement.[68,69] For decreased muscle tone, multiply the BMR by 0.9; for normal muscle tone, multiply by 1.0; for increased muscle tone, multiply by 1.1. For the activity level, if the infant is active in a lying position, multiply by 1.1; if the infant is assisted in moving or crawling, multiply by 1.2; if the infant can walk independently, multiply by 1.3. The additional energy required for growth is recommended to be 35 kcal/day. The BMR could be calculated using the following gender-specific formulas:

$$\text{Forboys : BMR}\left(\text{kcal/day}\right) = (0.167 \times \text{weight}\left[\text{kg}\right] + 15.174 \times \text{height}\left[\text{cm}\right]) - 617.6$$

$$\text{Forgirls : BMR}\left(\text{kcal/day}\right) = \left(16.252 \times \text{weight}\left[\text{kg}\right] + 10.232 \times \text{height}\left[\text{cm}\right]\right) - 413.5$$

Selection of approaches and formulas for nutritional support

Oral feeding is the preferred method for infants with good feeding safety. We suggest improving their eating efficiency through training in feeding skills and swallowing. Tube feeding is recommended for infants with a risk of aspiration, or taking too long to feed, or those with severe swallowing disorders, insufficient energy intake, stunted growth (below the 5th percentile for length-for-age), and signs of no weight gain over 3 months.[48] If tube feeding is anticipated to last under 6 weeks, the nasogastric tube is the usual choice. For those infants experiencing gastroesophageal reflux, aspiration, vomiting, and delayed gastric emptying, transitioning to a nasojejunal tube might be warranted. For tube feeding extending beyond 6 weeks, we suggest using the gastrostomy tube for feeding, although this decision is ideally made in a multidisciplinary setting involving the pediatrician, dietician, speech therapist, occupational therapist, psychologist, and parents. In the presence of complications like gastroesophageal reflux, aspiration, vomiting, and delayed gastric emptying, a transition to a gastrostomy jejunal tube, or jejunostomy tube might be necessary. For infants with either temporary or permanent gastrointestinal dysfunction, or an inability to swallow, absorb, or digest food, parenteral nutrition should be considered a viable alternative when its complications are insufficiently considered.[70]

For malnourished infants without severe milk protein allergy, we recommend that: (a) For breastfed infants, supplement with nutrient-dense formula (~100 kcal per 100 mL) or preterm infant formula (~75 kcal per 100 mL) in addition to adequate breast milk; (b) For infants receiving breast milk via bottle, consider adding a milk fortifier or supplementing with nutrient-dense formulas to provide extra energy; (c) For those on the regular formula, transition gradually to a nutrient-dense formula increase energy intake. Utilizing nutrient-dense formulas could provide IHRNI with additional energy without increasing the load on their gastrointestinal capacity, which is beneficial since these infants commonly experience swallowing disorders, reduced feeding efficiency, and gastrointestinal dysfunction.[71] Throughout the nutritional support process, continuous monitoring and communication with caregivers are essential. If any adverse reaction occurs, we suggest conducting symptomatic treatment and adjusting nutritional support plans accordingly. Infants with severe milk protein allergy should receive extensively hydrolyzed formula or amino acid formula under the guidance of a nutritionist. Between 5 and 8 months of age, IHRNI should begin receiving complementary food except for those diagnosed with food allergies who should avoid certain allergenic foods. The food types and textures should be gradually introduced and kept to their age as the infants show increased oral motor and swallowing capacities.

Feeding therapy

The aims of feeding therapy are to enhance the safety and efficiency of feeding, facilitate the transition from tube to oral feeding, increase infants' nutritional intake, support optimal growth, and ultimately improve their overall quality of life.[46,72,73] We recommend: (a) Modifying food texture by increasing viscosity to prevent aspiration; (b) Optimizing feeding posture by having the infants properly supported with slight neck flexion; (c) Implementing oral sensory-motor experience to improve feeding skills; (d) Using nipples and bottles with slower flow and proper pacing for safe feeding; (e) Helping caregivers to utilize above approaches at home.

Clinical question 9: What are the best approaches to promote early rehabilitation and nutritional support when managing IHRNI?

Recommendation 9: IHRNI often presents with multiple functional complications or comorbidities. A comprehensive approach involving an interprofessional medical team—including specialists in rehabilitation, pediatrics, neonatology, neurology, neurosurgery, gastroenterology, and nutrition—is essential. This team should collaborate to establish a management routine, ensuring the timely provision and enhancing the efficiency of early rehabilitation and nutritional support. (Level I evidence, Grade A recommendation)

In this interprofessional medical team, the rehabilitation department plays a pivotal role in this process. During consultations, rehabilitation professionals should thoroughly review the infant's medical history, clinical symptoms, and growth pattern; conduct early detection of neurological impairment and undernutrition; be involved in formulating early rehabilitation plans and nutritional management plans through interdisciplinary collaboration; support the delivery of parent education; follow up with infants and their caregivers. Furthermore, if the infant manifests other comorbidities, such as sensory impairments, or gastrointestinal diseases, a referral to the specialists should be initiated. Rehabilitation professionals should facilitate inter- and intra-disciplinary communication that centered around the infant's primary needs, and promote joint

decision-making to prioritize intervention so as to offer effective and holistic solutions.

Clinical question 10: How should regular follow-ups for IHRNI be conducted?

Recommendation 10: IHRNI should have monitoring of the motor, cognitive, and language development every 1–3 months, particularly at months 1, 3, 6, 9, 12, 18, and 24. Functional outcomes should be assessed with follow-ups until at least age 2. For advanced motor skills, language, cognitive, and behavioral development, follow-ups might extend to age 6 or school age. (Level I evidence, Grade A recommendation)

Given neuroplasticity and treatment effects, it is recommended to evaluate the motor, cognitive, growth, and other functional outcomes of IHRNI at 2 years of age or beyond. Liu et al.[74] observed that cognitive performance at 6 months in infants with very low birth weight was not a reliable predictor for cognitive status at 24 months, and found that cognitive interventions could enhance their functional outcomes. Kalstabakken et al.[75] in the longitudinal study on high-risk infants, noted that cognitive performance at 1 year only served as a general predictor for cognition at 2 years and preschool age. This underlines the importance of continued follow-ups through school age to cater to the child's evolving functional needs. There is also evidence suggesting interrelations among different domains. Early motor capabilities could predict cognitive functions, while cognitive and language capacities are indicative of school-age intelligence levels.[76]

For IHRNI, neurological assessments, early interventions, and nutritional management should be conducted immediately after birth. IHRNI should undergo follow-ups every 1–3 months, which include evaluating the implementation of the interventions, comparing therapeutic efficacy, and addressing parental queries. We should also pay attention to neurodevelopmental performance in months of significant milestone changes (1, 3, 6, 9, 12, 18, and 24 months of age). The clinical trajectories of these infants are often variable, and their prognoses would be more clearly understood and predicted by the age of 2 or after. Therefore, early rehabilitation and nutritional management should be monitored and tracked until at least the age of 2. Beyond this age, prognosis could be predicted, and decisions on whether to continue treatments and the frequency of follow-ups could be made. Milestones of higher level skills in motor, language, cognition, and behavior may need to be monitored till age 6 or school age.

LIMITATIONS AND FUTURE DIRECTION

At present, challenges persist in both the early and accurate identification of IHRNI and in the standardized implementation of early rehabilitation and nutritional management. Mastery of the latest strategies, combined with ongoing research evidence, is crucial to addressing these challenges. This consensus offers practical suggestions for early detection, rehabilitation, and nutritional management for IHRNI. The aim is to ensure that those at risk, including but not limited to infants with cerebral palsy, do not miss the optimal window of opportunity for early intervention, thus improving their functional outcomes. Notably, much of the current research focuses on infants at high risk of cerebral palsy, making this consensus more emphasized on this group, which inherently presents certain limitations. Additionally, this consensus primarily addresses recommendations for undernutrition, a prevalent issue among IHRNI. Yet, issues related to overweight, obesity, and trace element deficiencies warrant further exploration and research.

THE EXPERT PANEL

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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