TÜRK PEDİATRİ ARŞİVİ
TURKISH ARCHIVES of PEDIATRICS

# Turkish Neonatal Society guideline for the follow-up of high-risk newborn infants

## Türk Neonatoloji Derneği yüksek riskli bebek izlem rehberi

Betul Acunaş[1], Sinan Uslu[2], Ahmet Yağmur Baş[3]

[1]Division of Neonatology, Department of Pediatrics, Trakya University, Faculty of Medicine, Edirne, Turkey
[2]Neonatology Clinic, Şişli Hamidiye Etfal Training and Research Hospital, İstanbul, Turkey
[3]Division of Neonatology, Department of Pediatrics, Yıldırım Beyazıt University, Faculty of Medicine, Ankara, Turkey

**Cite this article as:** Acunaş B, Uslu S, Yağmur Baş A. Turkish Neonatal Society guideline for the follow-up of high-risk newborn infants. Turk Pediatri Ars 2018; 53(Suppl 1): S180-S195.

### Abstract

Developments in perinatal and neonatal care have increased the survival rate of high-risk newborns but led to a rise in chronic diseases seen in these infants. A significant number of them attend primary and secondary health care centers after discharge; however, there are very few standard protocols for the long-term follow-up of these babies. Therefore, we aimed to establish a follow-up guideline that emphasizes on universal screening schemes and takes into consideration national data. The guide presented here provides brief recommendations for physicians in light of evidence-based data for the follow-up of high-risk newborn infants. The steps taken to monitor and solve the problems of all high-risk infants may vary. We hope the use of such a standard approach in evaluating each infant in daily routine will improve the life quality of these high-risk infants.

**Keywords:** Follow-up, guideline, high-risk, newborn

### Öz

Perinatal ve neonatal bakım alanındaki gelişmeler sonucunda riskli yenidoğanların yaşam oranı yükselmiş, ancak beraberinde bu bebeklerde görülen kronik hastalık oranı da artmıştır. Taburcu edildikten sonra birinci ve ikinci basamak sağlık merkezlerine başvuran hastaların önemli bir oranını oluşturmaya başlayan bu bebeklerin uzun süreli izleminin nasıl olması gerektiği ile ilgili ne yazık ki standart protokoller pek azdır. Bu nedenle evrensel izlem şemalarına ağırlık verdiğimiz ve ulusal verilerin de göz önüne alındığı bir izlem rehberi oluşturmayı amaçladık. Burada özetini sunduğumuz yüksek riskli bebek izlem rehberi uygulayıcıya kanıta dayalı veriler ışığında öneri niteliğinde bilgileri sunmaktadır. Tüm riskli bebekler için izlem ve sorunların çözümü için atılacak adımlar farklılıklar gösterebilir. Her bebeğin ayrı ayrı değerlendirildiği standart yaklaşımların güncel uygulamalarda kullanılmasının yüksek riskli bebeklerin yaşam kalitelerini artıracağını ummaktayız.

**Anahtar sözcükler:** İzlem, rehber, yenidoğan, yüksek risk

### Introduction

In parallel with the positive developments in the area of perinatal and neonatal care in our country, the survival rates of high-risk newborns improved substantially, but the rates of morbidity and chronic diseases observed in these babies have also increased. Although there are many protocols related to the follow-up of healthy babies, sufficient data are lacking concerning how high-risk babies should be followed up in the long term (1, 2). Specifying which steps and quality of care should high-risk babies receive and at which healthcare services will enable to initiate the necessary healthcare support in the early stages of life. An intervention performed timely and appropriately may prevent or display the majority of problems that have a high probability to occur in these babies [for example, laser photocoagulation for retinopathy of prematurity (ROP), using a hearing device in the early stage for hearing deficit]. With this objective we designed this guideline for the follow-up of high risk newborn infants to provide the following issues: how to plan the discharge of babies carrying risks in terms of long-term outcomes, who should follow them up, the content of the follow-up program; follow-up of growth and nutrition after discharge; neurologic and developmental follow-up; hearing

**Corresponding Author / Sorumlu Yazar:** Betül Acunaş E-mail / E-posta: betul.acunas@gmail.com

DOI: 10.5152/TurkPediatriArs.2018.01817

and ophthalmologic follow-up; immunization and other issues including follow-up of long-term problems such as bronchopulmonary dysplasia (BPD) and gastroesophageal reflux. This guideline provides brief recommendations to the implementers in the light of evidence-based data. We have tried to establish a follow-up guideline composed of global follow-up schemes mostly which includes national data as well. These recommendations do not encompass indispensable decisions because evidence or the country's conditions may be generally or locally insufficient in some issues. Therefore, it should be kept in mind that each patient should be addressed individually and evaluated considering the physician's and patient's present conditions. Medical and legal responsibility related to medical applications belongs to the implementer.

**Risk groups:** There is neither widely accepted standards related to follow-up programs after discharge of infants treated in neonatal intensive care units (NICU), nor are there any specified risk factors (3). The risk categories presented in Table 1 may be adjusted by each center in terms of experience, qualified teams, and technical-medical equipment opportunities.

**Plan before discharge:** The management plan for the process extending to discharge for high-risk newborns can be addressed in 3 steps, as specified below (1, 2, 4, 5):

### Determination of home discharge readiness of the infant

Those infants who have the following features can be safely discharged home:

- Stable vital signs in room environment up to at least 12 hours before discharge (respiratory rate < 60/min, heart rate 100-160 beats/min, axillary temperature 36.5-37.4°C);
- Adequate weight gain (<2 kg 15 g/kg/day, >2 kg 15-20 g/kg/day);
- Thermoregulation has been enabled at room temperature in an open bed and clothed;
- Fed sufficiently and appropriately without any cardiorespiratory problem;
- Sufficient respiratory control without apnea or bradycardia (absence of apnea and bradycardia in 5-8 days after discontinuation of caffeine treatment);
- Vaccinated adequately;
- Screening tests have been performed or planned (metabolic, hearing, retina, hip dysplasia);
- Individual home care plan has been prepared.

### Determination of readiness of the family and home environment

- Psychosocial states of family members are appropriate for discharge;
- Basic care competency of at least two people in the family; who will participate in the baby's care;
- Evaluation of the effect of the family's socioeconomic conditions on baby care (availability of phone that can be accessed 24-7, electrics, healthy drinking water, and an appropriate heating system);
- Presence of an appropriate home environment (too much furniture should not be placed in the baby's room, the room temperature should be kept at 22-24°C, the room should be naturally bright and aerated frequently, the bed should be placed in the mother's room, smoking should be strictly forbidden at home);
- An environment that will not cause burns, intoxication, and other accidents should be provided;
- Auxiliary power supply, if possible, to operate in case of potential interruption of power, which has vital importance for the use of medical devices during home care;
- Written consent of the family stating that all informing has been given clearly and in a comprehensible way and appropriate conditions have been provided;
- Parents should have gained training, skills and self-confidence in the following areas:
- Differentiation e of normal and pathologic signs,
- Basic information to monitor vital signs,
- Performing basic life support steps,
- Recognizeing important pathologic findings (e.g. fever, poor suck, vomiting, jaundice),
- Feeding competence (e.g. feeding with breastmilk/formula/orogastric feeding),
- Complience with hygiene rules (hand washing, cleaning and changing diapers),
- Providing basic care and monitor the baby (e.g. urine and stool properties, technique for relieving gas, skin care, umbilical care and genital area care, bathing, dressing, changing diapers),
- Having knowledge related to accident prevention and carrying a baby in a car,
- Having knowledge related to the doses of the drugs to be used at home, dosing frequency, preparation of drugs, storage conditions and potential toxicity findings,
- Being able to perform applications related to special care (Feeding with a gastric tube, use of home mechanical ventilation, aspirator, pulse oximeter, glucometer and oxygen tube, tracheostomy, shunt and wound care, physical therapy),

### Interview with the family before discharge and discharge epicrisis

- Before discharge, the child's status, expectations and follow-up process should be discussed and the family

**Table 1. Risk categories**

| | High-risk (Level 3-4) | Moderate risk (Level 2) | Mild risk (Level 1) |
|---|---|---|---|
| Gestation week and birth weight | <1000 g<br><29 wk<br>SGA and LGA babies<br>Babies with fetal malnutrition | 1000-1500 g<br>29–34 weeks<br>Multiple pregnancies | Hospitalized in NICU with a birth weight of >1500 g and a gestational age of >34 wks<br>Late preterm<br>Early term |
| Central nervous system | Stage 3-4 ICH<br>Ventriculomegaly<br>Cystic PVL<br>Hydrocephaly<br>Perinatal asphyxia[a]<br>Convulsion<br>Cerebral infarction<br>Abnormal neurologic examination findings at the time of discharge<br>Need for advancedresuscitation at birth | Stage 2 ICH<br>Stage 2 HIE<br>Need for basic resuscitation at birth | Stage 1 ICH<br>Stage 1 HIE |
| Respiratory system | Prolonged (>7 days) MV<br>High frequency ventilation<br>BPD<br>Pneumothorax<br>Severe apnea | MV support (<7 days)<br>CPAP application | |
| Cardiovascular system | ECMO-iNO application<br>PPH<br>Shock requiring inotropic agents<br>Severe thrombosis | Catheter placement (umbilical central catheter or peripherally inserted central catheter) | |
| Infectious conditions | Severe sepsis<br>Meningitis<br>Nosocomial infection<br>Baby of HIV-positive mother<br>Intrauterine infections | Sepsis confirmed with culture | Clinical sepsis |
| Surgical problems | Diaphragm hernia<br>Tracheo-esophageal fistula<br>Duodenal atresia<br>Surgical NEC<br>PDA with surgical ligation<br>Laser applied ROP<br>Cardiac surgical diseases<br>Shunt operated hydrocephaly | NEC and PDA requiring medical treatment | Other surgical interventions (e.g. inguinal, umbilical hernia) |
| Other | Prolonged hypoglycemia<br>Prolonged hypocalcemia<br>Twin-to-twin transfusion<br>Jaundice requiring exchange transfusion<br>Bilirubin encephalopathy<br>Major congenital malformation<br>Metabolic/genetic diseases<br>Baby of mother with substance dependence | Hypoglycemia (≤25 mg/dL, >3 days)<br>Severe jaundice<br>Partial exchange transfusion<br>Inappropriate environmental conditions[b] | Transient hypoglycemia<br>Hypocalcemia<br>Jaundice requiring phototherapy |

BPD: bronchopulmonary dysplasia; CPAP: continuous positive airway pressure; ECMO: extracorporeal membrane oxygenation; HIE: hypoxic ischemic encephalopathy; ICH: intracranial hemorrhage; iNO: inhaled nitric oxide; LGA: large-for-gestational-age baby; MV: mechanical ventilation; NEC: necrotizing enterocolitis; SGA: small-for-gestational-age baby; PDA: patent ductus arteriosus; ROP: retinopathy of prematurity; PPH: persistent pulmonary hypertension; PVL: periventricular leukomalacia

[a]Patients with a 5th minute Apgar score of <3 who received therapeutic hypothermia treatment because of multiorgan failure and/or hypoxic ischemic encephalopathy

[b]Low socioeconomic status, very young or old mother, mother with psychological problems, mother who has not received prenatal care, mother with alcohol-drug habit

should be prepared for discharge in all aspects;

- The family's questions should be answered in a comprehensible way and written recommendations should be given;
- It is appropriate to use the "Neonatal Intensive Care Epicrisis Form" included in the Ministry of Health Healthcare Services Directorate's circular note (Number 2009/61) and the Directorate for Health Services' report (Date: 09.07.2015, Number 81595070/060.05/259).

## Who should follow up high-risk babies?

Families generally get closer and are attached to employees who work in NICUs. They like to see them in the follow-up after discharge and may not trust a new team or physician. Ideally, each neonatal intensive care unit should have a neonatal follow-up outpatient unit for high-risk babies and the main employees in this unit should be intensive care unit staff. However, follow-up methods can be specified individually for each baby and follow-up may be performed by different healthcare providers because of economic reasons in countries with disorganized and non-homogeneous demographic structures (e.g. residential area, hospital location, traffic, means of transport) and healthcare service areas, including our country (4-8).

***Low-risk babies:*** Pediatrician/primary care healthcare providers

***Moderate-risk babies:*** Follow-up should be performed by a team consisting of a neonatologist/pediatrician, child development specialist, radiologist, ophthalmologist, ear nose & throat specialist, pediatric clinical psychologist, and a social service specialist.

***High-risk babies:*** Follow-up should be performed by a team consisting of a neonatologist and child development specialist. In addition to the moderate-risk baby follow-up team, pediatric neurologist, genetics specialist, child speech therapist, pediatric endocrinologist, relevant surgeon (e.g. pediatric surgeon, neurosurgeon, orthopedist), pediatric cardiologist, physiotherapist, expert for nutrition of high-risk babies, and a special education specialist.

## Follow-up program for high-risk babies

All healthcare providers should be aware of developmental and medical follow-up guidelines for babies who carry risk. Although there are important differences in follow-up protocols according to the risk category of the newborn and relevant countries, regions and centers, the widely accepted judgement is that high-risk babies should be followed up at least up to school age (4, 8, 9).

High-risk babies carry risk in terms of somatic growth and in neurologic and developmental aspects. This risk increases further as the gestational week and birth weight decrease, though it shows great differences from center to center depending on care opportunities, experienced labor force, and infrastructure. Knowing that insufficient weight gain and growth predisposes to neurologic and developmental sequelae in the long term, and rapid growth predisposes to morbidity in adulthood, emphasizes the importance of follow-up of somatic growth. Mental retardation, cerebral palsy, behavioral problems and learning difficulties are observed considerably frequently in babies born with a gestational age below 28 weeks. However, it should be kept in mind that neurologic problems in particular will become more prominent and the signs will become clearer at 18-24 months and hopelessness or excessively positive expectations should not be presented to families. The importance of multidisciplinary follow-up should be specifically emphasized at each visit.

High-risk babies should be seen again within the first week (not exceeding 10 days) after discharge from the NICU. For problematic, small preterms infants (babies with insufficient weight gain or insufficient increase in head circumference, babies who are below the 3$^{rd}$ percentile on standard growth charts in the postmenstrual 40$^{th}$ gestational week or babies with chronic health problems such as BPD) the frequency of follow-up may be weekly or with intervals of 15 days until the baby becomes stable and achieves adequate growth. Although follow-up is generally recommended 7-10 days after discharge, at the adjusted 40$^{th}$ week or 1$^{st}$ month, monthly therafter during the first 3 months (if any problem is present, weekly-every 15 days), at the 6$^{th}$, 9$^{th}$, 12$^{nd}$ and 18$^{th}$ months, and at the age of 3 years, 5/6 years and 12 years, there is no official recommendation related to the frequency of follow-up after discharge for newborns who carry risk (1, 3).

## Follow-up of growth

Especially in preterm infants, growth rate is not only an indicator for somatic growth, but it also implies neurologic and developmental condition of these babies as well as health and nutritional states. The term "catch-up growth" indicates that the baby's weight, height and head circumference have reached the 50$^{th}$ percentile values for that age. The optimal growth rate is continuance of the postnatal growth of preterm babies at a speed equal to the expected growth in intrauterine life. However, the optimal growth model in the intrauterine period generally does not reflect the growth model experienced by a preterm infant (born at any gestational week) in the postnatal period. As the gestational week gets earlier, deviations from the optimal growth rate increase (10, 11).

Adjusted age is used in the follow-up of growth in preterm infants. The adjusted age should be based on the postconceptional 40$^{th}$ week. For example, the adjusted age of a baby who was born in the 30$^{th}$ gestational week and who is aged 20 weeks postnatally is calculated as follows: postconceptional age (30+20=50 weeks) – 40 weeks=10 weeks (12).

All these findings should be recorded in detail because they are important in terms of evaluation of an acute disease that may emerge in the future. It is recommended that adjusted age should be used for 24 months in the follow-up of weight and for 18 months in the follow-up of head circumference. It is not necessary to use adjusted age after the age of three years. In preterm infants, catch-up growth is achieved first by head circumference (in the first 6 months, secondly by weight (2-3 years of age), and thirdly by height (3-7 years of age) (3).

It is controversial as to which growth curves should be used in the follow-up of growth in preterm infants. Although environmental effects and metabolic requirements in postnatal life are very different from fetal life, intrauterine growth curves are frequently used in the evaluation of postnatal growth. The negative aspects of these curves are as follows:

- Difficulties in accurately specifying gestational age render standardization difficult;
- Considering multifactorial etiology of preterm delivery and inevitable variance optimal intrauterine growth of all preterms infants makes standardization questionable;
- Growth shows continuity whereas intrauterine growth curves are based on cross-sectional data. Postnatal longitudinal growth curves may be considered more realistic considering postnatal environmental conditions and the problems experienced by preterm babies; however, these curves are generally classified according to birth weight; they do not consider gestational age.
- Small-for-gestational-age (SGA) babies and infants with intrauterine growth retardation (IUGR) are evaluated together with appropriate-for-gestational-age (AGA) babies.
- They may not be reliable for different centers because they are constituted from data of infants from very different centers (differences in care, nutrition and experience), and short follow-up periods are present.

When all data gathered in our country are evaluated, growth curves based on postnatal measurements published in a multi-center study conducted by the Turkish Neonatal Society, coordinated by Professor Aytuğ Atıcı, and in different studies conducted by other researchers from Turkey can be taken into consideration for growth follow-up. Since a more appropriate option does not yet exist a current growth curve may be used with knowledge of its limitations (13, 14).

To evaluate fetal growth, the Fenton growth curve, which includes growth curves for each gender beginning from the 22$^{nd}$ gestational week to the 50$^{th}$ week may be preferred (15). However Fenton growth curves cannot be considered compatible with postnatal adaptation (it ignores physiologic fluid loss in the first days of life), the accuracy of the height curves are questionable, and is not a good method for evaluation at the time of birth after the 36$^{th}$ gestational week. Therefore the multicentric, multiethnic, prospective INTERGROWTH-21$^{st}$ study conducted by The International Fetal and Newborn Growth Consortium, which excluded many maternal and neonatal problems, has aroused excitement. It is still not considered as a definite and widely accepted recommendation because validation studies have not been completed and includes only preterm babies below 33 gestational week (16, 17). On the other hand, Olsen's growth charts have been recommended for use to specify infants younger than 36 weeks as SGA, AGA or and large for gestational age (LGA). However, these charts are not considered appropriate for use after discharge (18).

It should be kept in mind that the growth curves in current use reflect growth references obtained as a result of postnatal measurements rather than growth standards, even though they have been revised and validated. Currently, the adjusted form of the Fenton growth curve may be used after discharge. The growth charts developed for female and male Turkish children from the standard growth curves developed in 2006 by the World Health Organization (WHO) may be used when the baby reaches term (40$^{th}$ gestational week) or 50$^{th}$ gestational week, (19, 20). Another approach is to use both charts at the 40$^{th}$ and 50$^{th}$ gestational weeks.

Practical points in follow-up of growth are as follows:
***Weight gain:*** Preterm infant (15-20 g/kg/day), mature infants (30 g/day for the first month, 20 g/day thereafter for 3-12 months).

***Increase in height:*** Preterm infants (0.8-1 cm/week), mature infants (0.75 cm/week in the first 3 months, subsequently, 0.5 cm/week for 3-6 months).

***Increase in head circumference (HC):*** Preterm infants s (1.0 cm/week for the 1-2 months, 0.5 cm/week in the 3$^{rd}$-4$^{th}$ months, average 0.7 cm/week), mature infants (0.5 cm/week in the first 3 months, subsequently, 0.25 cm/week).

The critical period is the first year for HC, the first 3 years for final height. Absence of catch-up in HC up to the 8$^{th}$ month and in height and weight at the age of 2 years, reductions in growth rate or growth percentile and excessive or little weight gain are red flags.

## Neurological and developmental follow-up

The basic objective of perinatal care is to keep the baby alive and to provide a qualified care and follow-up service in order to specify pathologic neurodevelopmental findings in the early stage and correct these findings in advancing life. The risk for neurologic and developmental disorders is increased in some cases, including mainly very small preterm infants whose chances for survival have gradually increased in recent years (21-23): low birth weight and gestational week; male sex, multiple pregnancy; central nervous system disorders (periventricular and intraventricular hemorrhage, periventricular leukomalacia, hydrocephaly, convulsion); presence of chorioamnionitis; problems including necrotizing enterocolitis, chronic lung disease and retinopathy of prematurity; sepsis and/or meningitis/ventriculitis accompanied by multiorgan failure; long-term postnatal use of glucocorticoids; inadequate growth; congenital anomalies; hypoxic ischemic encephalopathy and presence of abnormal neurological findings at the time of discharge; repeated painful interventions and recurrent exposure to general anesthetic substances; hyperbilirubinemia requiring exchange transfusion; recurrent apnea and bradycardia; need for resuscitation, mechanical ventilation (>7 days) and/or high frequency ventilation and/or oxygen; need for prolonged total parenteral nutrition; surgical interventions including patent ductus arteriosus (PDA), necrotizing enterocolitis (NEC) and shunt; maternal factors including poor socioeconomic status, depression, drug addiction, and pregnancy at a young age.

Points to be taken into consideration in neurologic and developmental follow-up of preterm infants who constitute a significant portion of babies carrying risk are as follows (24): adjusted age should be used up to the age of 2-3 years in evaluation; the earliest period to evaluate major findings is the adjusted 18-24 months; it should be understood that, unlike mature babies, development in preterm infants will not be regular; it should be kept in mind that a single isolated disorder may improve in subsequent periods; it should be remembered that prolonged hospitalization and medical problems may be the reason for persistence of hypotonicity in preterm infants and this condition may improve; it should be understood that follow-up of babies carrying risk should be realized in a multidisciplinary approach with team setup; all elements of this team should be specified by the physician who performs the follow-up and communication should be provided.

## Components of neurologic and developmental evaluation

***Neurological evaluation:*** It is recommended that standard neurologic and developmental evaluations be performed at all ages. Neurologic examinations include evaluation of gross motor function, tonus, reflexes, cerebellar functions, cranial nerves, and language development. Compliance with examinations and the ability to communicate are also included in the evaluation. For this objective, the Hammersmith neonatal neurologic examination method is included in guidelines as a simple and feasible test. While age-appropriate Amiel-Tison is used in neurologic evaluations, the Bayley Scale of Infant Development (BSID), and the Bayley Scale of Infant and Toddler (Bayley III) are standard tests that are most commonly used in specifying abnormal development in the first 2 years (24-26).

In recent years, the Guideline for Follow-up and Support of Development (GFSD) has been developed by Ertem et al. (27). This guideline is a brief test that can be understood easily by families and implementers and is used in the evaluation of development in infancy and early childhood.

***Imaging modalities:*** Developmental disorders of the brain can be evaluated using ultrasonography (USG), conventional and diffusion-weighted magnetic resonance imaging (MRI) and computed tomography (CT). Routine cranial ultrasonography is recommended for infants with a gestational age of <32 weeks and a birth weight of <1500 g. The most commonly used method is USG and its specificity is similar to MRI in detecting severe lesions [ventriculomegaly, cystic periventricular leukomalacia (PVL) and grade 3-4 hemorrhage]. MRI is more efficient in diffuse white matter anomalies and in visualizing cerebellar pathologies in the posterior fossa. Major limitations include differences in results depending on the operator for ultrasonography, exposure to radiation for CT, and high cost and need for sedation for MRI (25).

***Evaluation of gross motor skills:*** The Bayley scale is frequently used in the evaluation of gross motor skills. The Gross Motor Functions Classification System (GMFCS) is a reliable test for the evaluation of the severity of motor dysfunction in children with cerebral palsy and accuracy studies have been conducted for this test. Although classification system tests of gross motor functions are used from the age of 18 months, they are most frequently used at the age of 2-4 years, 4-6 years, and 6-12 years (25).

***Developmental evaluation:*** Frequently used developmental scales are development cards, Development Observation Card (DOC), the Trivandrum Developmental Screening Chart (TDSC), and the Denver Developmen-

tal Screening Test [the Ankara Developmental Screening Inventory (ADSI) has been adapted for Turkish children]. The Bayley Mental Development Index (MDI) and Bayley Psychomotor Development Index (PDI) can be used as general indicators of developmental status (25).

***Intelligence:*** Studies have shown that the intelligence score is 5-7 points lower in infants born with a birth weight of <2500 g compared with term infants. Using only the intelligence score may overlook the skills including verbal understanding and pursuing speech. Intelligence tests can be evaluated after the age of 3 years. Weschler's Intelligence Scale for Children-Revised (WISC-R) can be used between the ages of 6 and 18 years.

***Language and speech:*** Babies who have passed hearing tests in the neonatal period should be reevaluated at the age of 12 months. Speech and language skills can be evaluated using the "Language Evaluation Scale Trivandrum" (LEST) at the age of 1-2 years. The McArthur test is based on the observations of parents and used in babies aged ≥1 year. The guideline for "Follow-up and Support of Development" may be used in evaluations. The clinical evaluation of language fundamentals III is used in children aged ≥6 years (25, 26).

***Cognitive status and functional skills:*** The most commonly used scale in evaluating these two characteristics, especially in school-age children, is WISC-R.

***Evaluation of behaviors and visual motor skills:*** Children with attention-deficit and autism spectrum diseases frequently experience problems in skills including solving problems, organization and planning, copying, synthesis of perception, visual memory, and visual-motor function interaction. Other behavioral and psychological disorders are also observed more frequently in these children compared with the normal population. The Achenbach Child Behaviour Checklist (CBCL) can be used in detecting problems between the ages of 1.5 and 5 years. It is difficult to decide which method to choose in attention-deficit. Parental report is the easiest method (23, 25, 26).

***School-age evaluation:*** The evaluations performed during this period include growth, parent-teacher questionnaire, attention-deficit, school performance, behavioral problems, quality of life, self-confidence, and academic success. In high-risk babies, problems are observed frequently in the school-age period. The Bende-Gestalt" test (BG), Wide Range Achievement Test (WRAT), WISC-R, and 'human figure drawing' are the criteria used for evaluation in the school-age period (23, 25, 26).

**Table 2. Fluid and macronutrient requirement in babies fed enterally**

| | Target (kg/day) | Target (for 100 kcal) |
|---|---|---|
| Fluid, mL | 135–200 | |
| Energy, kcal | 110–135 | |
| Protein, g | | |
| BW <1.5 kg | 4.0-4.5 | 3.6-4.1 |
| BW >1.5 kg | 3.5-4 | 3.2-3.6 |
| Lipid, g | 4.8-6.6 | 4.4-6 |
| Carbohydrate | 8-10 mg/kg/min | 10.5-12 g |

BW: body weight

## Nutritional follow-up after discharge

Adequate enteral nutrition cannot be provided because of problems including respiratory distress and gastrointestinal system immaturity in the first days of life in small preterm babies. Energy requirement is increased because of hypoxic acidosis, hypotension, and infections, especially in infants with a birth weight of <1500 g and a gestational age of <32 weeks. When extrauterine weight gain in preterm infants was compared with fetal growth, a great difference was found. Ninety-seven percent of babies who have a birth weight of <1500 g at the postmenstrual 36$^{th}$ week and 99% of the babies with a birth weight of <1000 g are discharged with a body weight below the 10$^{th}$ percentile (28, 29).

An inability to meet protein and energy requirement in the early stages causes postnatal malnutrition in these babies. If malnutrition is not corrected in this period, which is critical for brain growth, negative effects may be observed on the development of the central nervous system. It has been shown that preterm infants fed with breastmilk have better psychomotor development at 18 th month compared with preterms fed with preterm formula. When small preterm infants in particular are exclusively breastfed, however, they cannot reach the targets shown in Table 2 and growth and development do not occur at the expected level (29, 30).

Fortified breastmilk has a positive impact on weight gain, protein intake indicators, growth rate and bone mineralization. Therefore, breastmilk should be fortified when daily breastmilk reaches 80-100 mL/kg in very-low-birth-weight (VLBW) preterm infants (birth weight <1500 g). With this fortification, the protein content increases by 1 g/dL, the fat content increases by 0.6 g/dL, and the carbohydrate content increases by 1 g/dL. The calcium content becomes 90 mg/dL and the phosphorous content becomes 45 mg/dL. When fortified breastmilk is given with

an amount of 140-160 cc/kg/day, 3.6-4.1 g/kg/day protein and 110-130 kcal/kg/day calories will be provided to the baby (28, 29).

VLBW preterm infants (birth weight <1500 g) are fed with fortified breastmilk or preterm formula if breastmilk is absent during follow-up in the neonatal care unit. Currently, studies emphasize that the strategy of continuing preterm style nutrition in these babies after discharge from the neonatal unit gives more favorable outcomes, especially in terms of neurologic aspects (31).

According to the European Society for Paediatric Gastroenterology Hepatology and Nutrition (ESPGAN) 2006 recommendations, breastfeeding should be continued in preterm infants if they have appropriate weight for the postmenstrual age (10-90$^{th}$ percentile) and are fed with breastmilk at the time of discharge. If they are fed with preterm formula, they may continue with standard formula with long-chain polyunsaturated fatty acids (LCPUFA) after they reach term (PM 40$^{th}$ week) (32). For preterm infants who have lower weight by the postmenstrual age (below the 10$^{th}$ percentile) and/or who have a BUN value of <10 mg/dL at the time of discharge: breastmilk and fortifier or breastmilk and preterm formula (2-3 meals/day) may be given. Infants whose growth parameters achieve the 50$^{th}$ percentile by the adjusted age may continue only with breastmilk if their biochemical indicators are within the normal limits. If breastmilk is absent, preterm formula can be given up to the postmenstrual 40$^{th}$ week. After the postmenstrual 40$^{th}$ week, feeding can be continued with postdischarge formula up to the 52$^{nd}$ week (can be used up to the adjusted age of 6-9 months). When the growth parameters reach the 50$^{th}$ percentile by adjusted age (10$^{th}$ percentile for babies who were SGA at birth), one may switch to standard term formula (28, 33).

Studies proposing that accelerating growth would lead to metabolic problems by increasing fat content in the body composition in the long term should also be considered. Red flags indicating that nutrition is insufficient in preterm infants are weight gain <15-20 g/kg/day, increase in height <1 cm/week, increase in head circumference <1 cm/week, phosphorous <4.5 mg/dL, alkaline phosphatase >450 IU, BUN <10 mg/dL, prealbumin <10 mg/dL, sodium <133 mmol/L, ferritin <50 mcg/L, and 25 (OH) Vitamin D <50 nmol/L (20 ng/dL) (33).

Although optimal micronutrient requirements for preterm infants have not been fully specified, it is recommended that vitamin D at a dosage of 200-400 IU/day should be initiated in VLBW babies in the first weeks of life and the dosage should be increased to 400 IU/day when the body weight reaches >1500 g and full enteral feeding begins (28, 34). Oral iron prophylaxis is recommended especially for infants who are fed with fortified (in our country, iron supplementation is absent in breastmilk fortifiers) or unfortified breastmilk and who were born with a birth weight of <1500 g. Ferritin levels may be measured before initiating iron prophylaxis because these babies receive frequent blood transfusions. The Turkish Neonatal Society Nutrition Group recommends that iron supplementation should be initiated at a dosage of 2-3 mg/kg/day in the 2$^{nd}$ week at the earliest (ideally in the 6-8$^{th}$ weeks) and continued until the 12-15$^{th}$ month (28, 33). According to the final recommendations, daily requirements of preterm infants in terms of other micronutrients are as follows: calcium 120-160 mg/kg; phosphorous 60-90 mg/kg; magnesium 8-15 mg/kg; copper 150-200 mg/kg; zinc 2 mg/kg. Evidence related to oral multivitamin and mineral supplementation in preterm babies fed with breastmilk or formula is insufficient and there are no definite recommendations. It has been reported that multivitamins can be given to VLBW babies who are fed with unfortified breastmilk until the age of 6 months or until the body weight reaches 2000 g. Most vitamins and minerals are sufficient in preterm formulas and fortified breastmilk (28, 29, 33).

## Hearing follow-up

Hearing loss is the most common congenital disorder with an incidence of 1-3 in 1000 live births. Screening of newborn babies in terms of hearing deficit is an important public health service. It has been shown that early detection of hearing loss and performing the necessary intervention before the age of 6 months enable these children to catch up with their peers who have normal hearing, in terms of speech and language development. The tests used for screening include otoacoustic emission screening (OAE) and auditory brainstem response screening (ABR), and these tests evaluate the peripheral auditory system and the cochlea (35).

In the screening program in our country, OAE has been used as the primary test in the screening of healthy newborns. If the baby could not pass this test, ABR was used as the second screening test. However, it was decided to apply the ABR screening protocol in babies who have no risk factors with the circular published by the Republic of Turkey Ministry of Health General Directorate of Public Health on November 24$^{th}$, 2017 (Figure 1) (36). Hearing screening tests must be performed in the first 72 hours or before babies are discharged from hospital and/or at the

time of discharge. The objective is to complete screening tests in the first month, to complete further tests in the 3rd month in babies with suspicious hearing loss, and to provide treatment and rehabilitation within the 6th month in babies with hearing loss (35).

In those infants who carry risk in terms of hearing loss (Table 3), the primary hearing test is performed with ABR. If the baby fails the test, ABR is repeated (35). In babies who fail the retest, audiologic evaluation should be performed in 3 months. Babies who have one or multiple risk factors in terms of hearing loss are reevaluated before the age of 24-30 months even if they pass the primary screening tests (36, 37). Infants whose hearing loss becomes definite are also evaluated in terms of visual function and genetic counseling is provided for these babies. After this stage, special education programs are applied under supervision of expert educators to teach hearing, language, and speech (35).

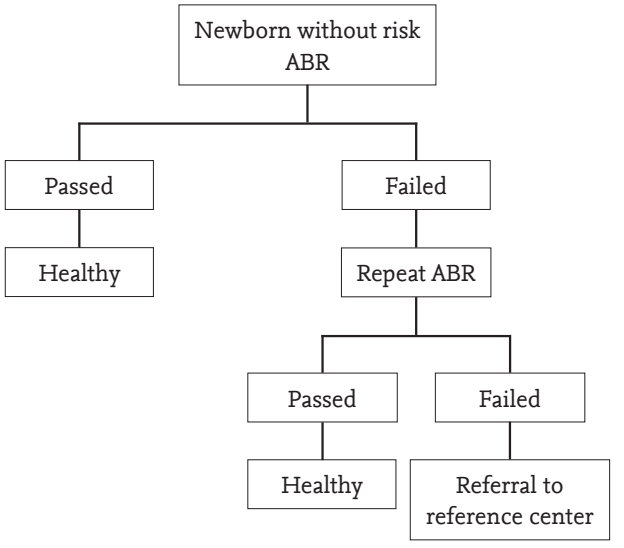


**Figure 1. Republic of Turkey Ministry of Health Public Health Agency hearing follow-up flowchart**
ABR: auditory brainstem response

## Ophthalmologic follow-up of preterm infants

Retinopathy of prematurity (ROP) is a developmental vascular proliferative disease of the immature retina, the etiology and pathogenesis of which are not fully known. Although many etiologic factors have been considered in the development of ROP, the best known risk factors include low birth weight and gestational age. Oxygen treatment is another important risk factor in the development of ROP (38). According to the 2013 recommendations of the American Academy of Pediatrics and the American Academy of Ophthalmology, screening is recommended in babies born with a birth weight (BW) of ≤1500 g and/or with a gestational age of ≤30 weeks, and in babies with a gestational age (GA) above 30 weeks and a birth weight of 1500-2000 g who have clinical problems and need cardiopulmonary support (39).

In the Turkey Retinopathy of Prematurity Guideline prepared by the Turkish Neonatal Society and Turkish Ophthalmology Society in 2016, screening was recommended in all babies with a gestational age of ≤32 weeks

**Table 3. Risk factors for hearing loss**

- Presence of a familial history of hearing loss in childhood
- Prenatal factors: Maternal drug addiction, drugs given to the mother during pregnancy (e.g. aminoglycoside, isotretinoine), lack of follow-up during pregnancy
- Perinatal infections (e.g. TORCH infections, zika virus, HIV, syphilis)
- Bacterial-fungal sepsis/meningitis
- Use of ototoxic drugs (e.g. aminoglycoside, diuretic)
- Perinatal asphyxia, difficult labor (for example: Apgar score of <6 at the 5th minute)
- Being hospitalized in NICU for 5 days and longer (e.g. prematurity)
- Mechanical ventilation treatment for 5 days and longer
- Persistent pulmonary hypertension, treatment with ECMO
- Birth weight ≤1500 g
- Infant of diabetic mother, hypothyroidism
- Hyperbilirubinemia requiring exchange transfusion
- Neurodegenerative diseases
- Craniofacial anomalies, e.g. outer ear or ear canal anomalies, skin folds.
- Syndromes and genetic diseases with hearing loss
- Trauma

or a birth weight of ≤1500 g and in babies with a gestational age of >32 weeks or a birth weight of >1500 g who have undergone cardiovascular supportive treatment or in preterm babies who are considered risky in terms of development of ROP by a physician monitoring the baby (40). The first ophthalmologic examination should be performed at the postmenstrual 31st week in babies born with a gestational age below 27 weeks and in the postnatal 4th week in babies born with a gestational age of ≥27 weeks (2). Classification of the disease is made according to the International Classification of Retinopathy of Prematurity (ICROP). The international classification system is based on 3 clinical variables (41): **1-Localization:** To specify involvement of the disease, the retina is divided in 3 regions (zones) where the optic nerve is the center; **2-The degree of vascular proliferation (stage):** The disease is divided into 5 stages according to the degree of vascular proliferation; **3-The degree of extension:** The retinal surface is divided into sectors of 30° (clock hours). In this way, it can be found to which clock hour the disease has extended. Increased tortuosity in the arterioles and dilated venules in the posterior retinal pole is defined as "plus" disease. Presence of "plus" disease is an indicator of severity of ROP and may be associated with opacification in the vitreous, iris vessel dilatation and reduced pupillary reactions. In the new terminology, this picture is expressed as aggressive posterior ROP. It should be treated urgently. If the first examination reveals that retinopathy has developed, a follow-up schedule is established according to the severity and progression of the disease. A monitoring period of 1-3 weeks is required until the retinal vessels reach the oro serrata in all zones (39). The objective of treatment is ablation of the avascular peripheral retinal areas. This procedure is performed with diode laser photocoagulation. The criteria for laser photocoagulation in retinopathy of prematurity (Type 1 ROP) were specified by the multi-center Early Treatment for Retinopathy of Prematurity (ETROP) study group (42). Medical interventions should be initiated as soon as possible in cases of aggressive posterior ROP and in 48-72 hours at the latest in cases of non-aggressive ROP (38).

Bevacizumab (Avastin®), ranibizumab (Lucentis®), aflibercept (Eylea®) and pegaptanib (Macugen®) are anti-vascular endothelial growth factor (VEGF) monoclonal antibodies, and use of these antibodies in the treatment of ROP is an alternative method. They are administered as intravitreal injections. Although laser photocoagulation is the gold standard in the treatment of ROP, use of anti-VEGF agents has the following advantages: They can be applied more easily, a rapid response is obtained when they are used, they can be used in cases where the cornea is opaque and the vitreous is cloudy and the pupil is not dilated, and they do not cause narrowing in the visual field and recurrence and refraction disorders occur less frequently (38, 43). Potential disadvantages include transient reduction in serum VEGF levels and brain, lung, heart, and kidney injury. In addition, they may disrupt normal retinal vascularization. The American Academy of Pediatrics emphasized that bevacizumab might be considered in zone I grade 3 ROP+ "plus" disease, but stated that further studies were needed in terms of the dose, optimal timing, safety, and efficiency (39). Peripheral vascularization slows down in babies in whom anti-VEGF has been administered; follow-up up to the age of 2-3 years is important because possible activations have been reported in the long-term (38, 43). Anti-VEGF alone or in combination with laser treatment may not always be able to prevent retinal detachment. In cases of total or subtotal retinal detachment, surgical treatments including scleral indentation and vitrectomy are performed (38).

Infants who have had retinopathy may develop late complications including myopia, amblyopia, strabismus, glaucoma, retinal detachment, nystagmus, cataracts, and optic atrophy. In addition, the frequency of strabismus, amblyopia and refractive disorder is increased in children who were born prematurely independent of development of retinopathy. Therefore, it is recommended that preterm babies should undergo full ophthalmologic evaluations at the age of 9-12 months, 2-3 years, and before school age (38, 40).

## Immunization

Preterms infants (<37 weeks) and/or newborns infants with low birth weight (<2500g) carry increased risk in terms of morbidity and hospitalization because of many conditions that can be prevented by vaccination. Independent of the birth weight and gestational age, they should be vaccinated at the same time and according to the same schedule as term babies (excluding hepatitis B and BCG vaccines). If the baby is clinically stable and gaining weight, vaccination is initiated at the chronologic age of 60 days and a full dose is given. Vaccination may be extended to 2-3 days to prevent multiple injections on the same day (44-46).

**Hepatitis B immunoprophylaxis:** Seroconversion following Hepatitis B vaccination may be lower than expected in babies born with a birth weight below 2000 g (44).

**Maternal HBsAg (-):**

- In babies with a birth weight (BW) of ≥2000 g, the first dose of hepatitis B vaccine is administered at birth, the 2nd dose is administered at the end of the 1st

month, and the 3rd dose is administered at the end of the 6th month.
- In babies with a birth weight (BW) of <2000 g, the first dose of hepatitis B vaccine is administered one month after birth or at the time of discharge, the second dose is administered one month after the 1st dose, and the 3rd dose is administered six months after the 1st dose.

**Maternal HBsAg (+):**
- If the birth weight is ≥2000 g, the 1st dose of hepatitis vaccine and hepatitis B immunoglobulin (HBIG) are administered to the baby in the first 12 hours of life. The 2nd dose is administered at the end of the 1st month, and the 3rd dose is administered at the end of the 6th month. Anti-HBs and HBsAg tests should be performed between the 9th and 15th months.
- In babies with a birth weight of <2000 g, the 1st dose of hepatitis B vaccine and HBIG are administered at the first 12 hours of life. The first dose at birth is not considered as part of the routine immunization scheme of 3 doses because the baby's BW is below 2000 g. At the end of the first month, a 3-dose hepatitis B immunization scheme is initiated. Anti-HBs and HBsAg tests should be performed between the 9th and 15th months.

**Maternal HbsAg unknown:**
- The HBsAg test is performed in the mother. In babies with a birth weight above 2000 g, one may wait up to one week for the result. If the HBsAg test result in mothers of babies below 2000 g is not obtained in 12 hours, one must act as if the mother is HbsAg (+). Vaccine and HBIG are administered to the baby in 12 hours. If the result is obtained in 12 hours, the above mentioned recommendations are pursued.

**BCG vaccine:** Vaccination is performed according to the chronologic age in babies born after the 34th gestational week. In preterm infants born before the 34th gestational week, the vaccine is administered after the baby completes postconceptional 34 weeks and the chronologic age is at least 2 months on condition that the body weight has reached 2000 g (44).

**DaBT-IPV-Hib and conjugated pneumococcus vaccines:** These vaccines are administered fully when preterm babies reach a chronologic age of 60 days (independent of birth weight and gestational age), if the medical status is stable and regular weight gain is present. In babies in whom apnea occurs at the time of the first dose, it is recommended that the infant should be under supervision for 48-72 hours after the 2nd dose in a healthcare institution (47).

**Measles, rubella, mumps, and chickenpox vaccines:** These vaccines are administered at the 12nd month (44).

**Influenza vaccine:** In babies carrying moderate and high risk, influenza vaccine is administered twice with an interval of one month after the 6th month. In the flu season, it is recommended that influenza vaccines should be administered to the parents of high-risk babies aged younger than 6 months living in the same house and to individuals who are in close contact. In addition, Tdap (tetanus attenuated diphtheria and acellular pertussis) is recommended to be administered depending on the vaccination status (44, 45).

**Rotavirus vaccine:** Preterms infants carry high risk in terms of hospitalization because of viral gastroenteritis in the first year of life. Therefore, it may be recommended to families, although it is not a routine vaccine included in our country's immunization scheme. It is a live oral vaccine. The first dose of rotavirus vaccine should be administered between the postnatal 6 weeks and 14 weeks and 6 days (postnatal 42-104 days). Vaccination should be completed before the chronologic age of 8 months (44, 45). In preterm infants with an adjusted age of 32 weeks and above (mean 34 weeks), vaccination can be performed as in term babies. The American Academy of Pediatrics recommends that vaccination should be initiated after discharge in babies hospitalized in intensive care units. One should be cautious in terms of contact with other infants if rotavirus vaccine has been administered in the final 2-3 weeks in rehospitalized babies (48).

**Respiratory syncytial virus (RSV) prophylaxis:** Fifty percent of the babies who develop BPD are rehospitalized because of pulmonary reasons (pneumonia, RSV infection) in the first year of life. Prophylaxis with palivizumab, which is a monoclonal antibody, should be administered in these patients in RSV season in the first 2 years. There is no need to wait for vaccination after administration of palivizumab (44, 49) The Turkish Neonatal Society 2018 RSV prophylaxis recommendations are shown on Table 4 (49).

It is recommended that babies who will receive RSV prophylaxis should be given an appointment on the same day in order to minimize waste in use of palivizumab. Palivizumab should be administered in 5 doses at most with an interval of one month throughout the RSV season (between October and March).

## Others

Some features should be noted while performing physical examinations during follow-up of babies discharged from

**Table 4. Turkish Neonatology Society 2018 recommendation for RSV prophylaxis with Palivizumab**

| Chronological age at the beginning of RSV season | | | |
|---|---|---|---|
| Condition | ≤3 month | <12 month | 12-24 month |
| Premature <29 weeks | | Prophylaxis | No |
| Birth weight <1000 g | | Prophylaxis | No |
| Premature 29-32 weeks* | Prophylaxis | No | No |
| BPD** | | Prophylaxis | No |
| BPD treated in the previous 6 months*** | Prophylaxis | Prophylaxis | |

*All premature infants with a gestational age between 29 0/7-31 6/7 weeks who are less than 3 months old chronologically at the RSV season

** Bronchopulmonary dysplasia (BPD); <32 0/7 weeks old who received more than 21% oxygen therapy for at least 28 days

*** Those infants with BPD who received steroids, oxygen, bronchodilator, diuretic therapy in the previous 6 months should achieve RSV prophylaxis also in the second year of life

the neonatal intensive care unit. Pulse and respiratory values should be evaluated considering gestational age and adjusted age. Blood pressure measurement is especially important in patients who develop BPD and in whom umbilical arterial catheters have been placed. Flattening in the temporal region of the head may be observed in relation to prematurity or long hospitalization periods and generally improves up to the age of 3-4 years. Small calcium deposits forming in the intravascular access and intervention areas do not cause any problem, but may remain for years. Families can be informed that most scars in the intervention areas will recover and very little scar will be left. Plastic surgeons should be consulted if scars leading to functional or cosmetic problems are present. Capillary hemangiomas are common in preterms infants and families should be informed that these hemangiomas may become larger and deeper in the first year and disappear in subsequent years. A nasal deformity due to nasal continuous positive airway pressure (CPAP) may develop; it is appropriate to consult otorhinolaryngology or plastic surgery if it causes purulent secretion and infection. The anterior fontanelle closes between the adjusted age of 6 and 19 months. In addition, preterm babies should be examined in terms of undescended testis and consulted up to the age of one year (50-53). Other points that should be noted in the follow-up are as follows:

**Respiratory problems:** In babies discharged from the neonatal intensive care unit, long-lasting respiratory problems may also occur after discharge. The most common problem in preterm newborns is BPD. In addition, the risk for reactive airway disease and respiratory infections are increased in these babies.

**Bronchopulmonary dysplasia:** In babies with bronchopulmonary dysplasia, lung function may be abnormal, especially in the first year of life and these babies may need home monitorization and supportive treatment. Obtaining and recording cardiorespiratory indicators (respiratory rate and heart rate, blood pressure, oxygen need, chest radiography and echocardiography to determine the presence of pulmonary hypertension), which will constitute the basis for home monitoring at the time of discharge, is important especially for infants with moderate-severe BPD. If the infant is receiving oxygen at home, it is very important to keep the oxygen saturation at or above 95% and not to let it reduce below 90% because hypoxia may lead to mortality, pulmonary hypertension, cor pulmonale, insufficient weight gain, and increased airway resistance. Metabolic requirements are increased in these babies; adequate energy needs to be provided (150 kcal/kg/day may be needed) and any upper respiratory tract infection may easily extend to the lower respiratory tract and this is the most common reason for rehospitalization in the first 1-2 years after discharge. The family should be told that they need to keep the baby away from ill individuals and from crowded places, visitors should be decreased, contact with cigarette smoke should be avoided, and the importance of hand washing should be emphasized. Exposure to respiratory viruses should be avoided. Therefore, RSV and influenza prophylaxis is important (see immunization). After the age of two years, most respiratory and nutritional problems will improve (50-53).

**Follow-up of apnea:** Apnea of prematurity develops in approximately 25% of preterm newborns and usually improves before discharge from hospital or by the 40$^{th}$ week. However, apnea episodes may last longer in some babies. If a baby is ready to be discharged, but has mild apnea (apnea lasting >15 seconds not accompanied by bradycardia or desaturation that does not require intervention), the infant may be discharged with cardiorespi-

ratory home monitoring, which can be continued until the postmenstrual 43-44th week. If apnea is more severe, the baby should not be discharged and home monitoring should not be recommended. Monitors used at home recognize heart rate and chest movements and oxygen saturation measurement is optional. It should be kept in mind that these devices detect central apnea directly, but they may miss obstructive apnea where chest movements continue if bradycardia or desaturation does not develop. In addition, there is no evidence indicating that home monitoring will prevent sudden infant death syndrome (SIDS) (50-53).

**Gastroesophageal reflux (GER):** Gastroesophageal reflux is observed considerably frequently in infants and especially in preterm newborns. The frequency is rather high (65%) in preterm babies with a birth weight of <1000 g. GER disappears with maturation at about one year of age. When gastroesophageal reflux leads to morbidity, this is called GER disease and this causes growth retardation, apnea, feeding problems, loss of appetite and irritability. The association of gastroesophageal reflux with apnea, chronic lung disease, and growth retardation has not been fully proven. The value of specific diagnostic tests is variable and depends on the clinical picture. History and physical examination may sometimes be sufficient for making a diagnosis of GER disease and initiating treatment. In the treatment of GER in newborns, non-pharmacologic methods are preferred primarily and these methods include frequent feeding with small amounts, feeding in the right lateral position, and switching to the left lateral position one hour later, increasing the consistency of foods, using hypoallergic formula, and changing the mode of feeding. If GER does not improve with these precautions, the baby should be evaluated by a pediatric gastroenterologist. If this is not possible, one focuses on decreasing esophageal acid exposure with H2 receptor antagonists or proton pump inhibitors. However, one should be cautious in terms of adverse effects while using these drugs. Prokinetic agents are not recommended because they have limited benefit and significant adverse effects (54).

**Sudden infant death syndrome (SIDS):** Death that cannot be explained with full autopsy in babies aged below one year, examination of the place of death, and evaluation of the clinical history is defined as SIDS. Low birth weight and/or low gestational age are the most important risk factors and the highest risk occurs in the postmenstrual 50-52nd weeks. It is thought that a maturational delay related to the development of the nervous system and cardiorespiratory control, a triggering event including airway obstruction accompanying brainstem anomaly or an anomaly in serotonin signalization may be involved in the mechanism. Other risk factors include exposure to cigarette smoke, maternal age <20 years, sleeping in the prone position, soft bed, and excessive warming. The incidence of SIDS has decreased by fifty percent with placing babies in the supine position for sleep. Families should be informed of the following precautions: 1-Lay the baby in the supine position, avoid laying the baby in the prone position; letting babies sleep on their sides is not recommended either; 2-The baby's bed should be solid and have a regular surface, it should be a special bed for babies, do not use airbeds; 3-Do not use pillows and wool blankets before the age of one year; 4-Put the baby close to the lower end of the bed without covering their head, cover the baby only up to the chest and compress the bed lining and blanket under the bed; 5-Do not allow soft toys in the bed; 6- Do not attach objects including safety pins or amulets on the baby's clothes, which may be harmful, 7- Keep the baby in the same room with you at night during the first 6 months, but do not share the same bed; 8- Starting from pregnancy, do not smoke and do not let the baby get in contact with smokers after birth (including the father); 9-Do not keep the baby in very hot-very cold environment (50-53).

**Osteopenia:** Osteopenia has been reported in 55-60% of babies with a birth weight <1000 g and in 23% of babies with a birth weight of 1000-1500 g. Osteopenia of prematurity is observed more frequently in babies who have received long-term total parenteral nutrition and who use drugs that affect bone mineral metabolism, in infants of diabetic mothers, and in SGA babies. Clinically, osteopenia is observed between the 6th and 12nd months and is frequently asymptomatic. However, it may be manifested with reduction in weight gain and growth retardation, rachitis, fractures, and pain with touching. Severe clinical findings including respiratory difficulties due to weak thoracic wall compliance or an inability to wean from ventilator may also be present. Osteopenia of prematurity should be suspected when low serum Ca-P and high alkaline phosphatase (ALP) are present. An ALP value of >800 IU/L or a P value of <3.5 mg/dL suggests severe osteopenia. Some investigators have reported that ALP levels may be used for screening. If ALP is >900 IU/mL, its sensitivity is one hundred percent. Early initiation of enteral feeding, keeping the period of parenteral feeding short, supporting breastfeeding, and using special preterm formulas may decrease osteopenia. Adequate vitamin D intake is also essential (400-1000 IU). Exercises increases bone mineral content. In the follow-up of patients with osteopenia, Ca, P, and ALP are measured monthly until the 6th month and every 3 months thereafter (55).

**Umbilical and inguinal hernia:** Both umbilical and inguinal hernias occur frequently in preterm newborns. Umbilical hernia occurs in 75% of babies with a birth weight of 1000-1500 g. Although the majority regress spontaneously at the age of 2 years, surgical closure may be considered if it still persists at the age of 4 years or if it is >2 cm and/or abdominal pain accompanies. Although the risk for strangulation is low, umbilical hernia persisting beyond 4-6 years of age may undergo surgery for cosmetic reasons. Inguinal hernia may develop in 30-42% of babies with a birth weight of 500-1000 g, in 10% of babies with a birth weight of 1000-1500 g, and in 3% of babies with a birth weight of 1500-2000 g. The risk is higher with male sex and long-term mechanical ventilation. Surgical repair is essential before strangulation occurs because it does not regress spontaneously. Surgery is mostly performed before discharge from the NICU when the body weight reaches 1800-2000 g.

**Dental problems:** Both preterm and term newborns who have had critical illness have increased risk in terms of dental problems. In addition, problems including V-shape palate, deformation in the cutting tips, dental loss, and sulcus in the palate may develop in newborns who have remained intubated for a long period. Therefore, the American Academy of Pediatric Dentistry Infant Oral Health Guideline recommends that infants have their first dental examination at the age of 12 months and optimal fluorine intake be provided by way of drinking water or drops administered systemically when the postmenstrual age reaches 6 months (56).

**Infant car seat or bed:** Use of baby safety seats in cars is recommended for newborns and infants in many countries of the world including our country in order to prevent mortality and morbidity related to motor vehicle accidents. Infant car safety seats specific for babies with a three or five-point harness should be used. The seat should be installed to face the rear of the car and in the backseat of the car. An adult who will be monitoring the baby face-to-face should be present beside the baby. Putting baby-blanket rolls on both sides of the baby and placing a rolled diaper or baby-blanket below the belts may prevent friction and injury. In addition, preterm newborns and especially those with a body weight of ≤2000 g before discharge experience desaturation, apnea, and bradycardia with a higher rate in car safety seats or beds compared with term newborns. Therefore, the American Academy of Pediatrics published a revised guideline in 2009 (57). According to this guideline: 1- Preterm babies and mature, but hypotonic infants (e.g. Down syndrome), babies who have undergone cardiac surgery or who have micrognathia (e.g. Pierre Robin sequence) should be placed in a baby car seat and monitored in terms of apnea, bradycardia or oxygen desaturation; 2-The test should last for 90-120 minutes (30 min after feeding); 3-Failure criteria: a-Apnea ≥20 s, desaturation (<90% longer than 10 s or <93%) + bradycardia (≤80/min for longer than 10 s) during a monitoring period of at least 90 minutes, b-Disruption in respiratory pattern. If the baby fails this test, the test is repeated in a car safety bed. If the baby fails the test also in the safety bed, it should be evaluated further and reviewed medically (57-59).

## Conclusion

A summary guideline that can be used by primary and secondary healthcare providers in the follow-up of high--risk newborns and that will also be helpful for tertiary care healthcare providers, has been presented in view of evidence-based data as much as possible. Steps to take for follow-up and solution of problems for all high-risk babies may show variance. Standard approaches where individualized methods are chosen by evaluating each baby separately will increase the quality of life for high-risk babies and improve the families' and community's moral force.

**Conflict of Interest:** No conflict of interest was declared by the authors.

**Financial Disclosure:** The authors declared that this study has received no financial support.

**Çıkar Çatısması:** Yazarlar çıkar çatışması bildirmemişlerdir.

**Mali Destek:** Yazarlar bu çalışma için mali destek almadıklarını beyan etmişlerdir.

## References

1. Vohr BR, O'Shea M, Wright LL. Longitudinal multicenter follow-up of high-risk infants: why, who, when, and what to assess. Semin Perinatol 2003; 27: 333-42.
2. O'Shea M. Changing charecteristics of neonatal follow-up studies. Neuroreview 2001; 2: e249-55.
3. Vohr BR. Neonatal follow up program in the new millenium. Neuroreview 2001; 2: e241-8.
4. Vohr BR, Msall ME. Follow-up of high risk infants. In: Vergara ER, Bigsby R, (eds). Developmental and therapeutic interventions in the NICU. 1st ed. Baltimore: Paul H Brokes Publishing 2004.p.267-92.
5. Follow up of high risk newborns. NNF Clinical Practice Guidelines. pp 217-252 (www.nnfpublication.org)
6. Köksal N. Düşük doğum ağırlıklı bebeklerin izlemi. İçinde: Yurdakök M, Erdem G, (editörler). Neonatoloji. 1st

ed. Ankara: Alp Ofset 2004.p.254-63.
7. İnce Z. Prematüre bebeğin taburcu olduktan sonra büyüme izlemi, beslenme ve aşılamasında kanıta dayalı uygulamalar. Çocuk Dergisi 2009; 9: 167-71.
8. American Academy of Pediatrics. Committee on fetus and newborn. Hospital discharge of the high-risk neonate. Pediatrics 2008; 122: 1119-26.
9. Korkmaz A. Prematüre bebeklerde uzun süreli izlemin temel ilkeleri. Clinic Pediatri 2010; 5: 6-9.
10. Dusick AM, Poindexter BB, Ehrenkranz RS, Lemons JA. Growth failure in the premature infant: can we catch up? Semin Perinatol 2003; 27: 301-10.
11. Lemmons JA, Bauer CR, Oh W, et al. Very low birth weight outcomes of the National Institute of Child health and human development neonatal research network, January 1995 through December 1996. NICHD Neonatal Research Network. Pediatrics 2001; 107: E1.
12. Griffin IJ. Growth management in premature infants. In Uptodate, Abrams SA, Motil KJ (Eds), UpToDate, Wolters Kluwer, 2017.
13. Atıcı A. Intrauterine growth curves for neonates born in Turkey: Ministry of Health and Turkish Society of Neonatology Multicenter Study. Turkish Society of Neonatology Bulletin 2011; 23: 41-51.
14. Salihoglu O, Karatekin G, Uslu S, Can E, Baksu B, Nuhoglu A. New intrauterine growth percentiles: a hospital-based study in Istanbul, Turkey. J Pak Med Assoc 2012; 62: 1070-4.
15. Fenton TR, Kim JH. A systematic review and meta-analysis to revise the Fenton growth chart for preterm infants. BMC Pediatrics 2013; 13: 59.
16. Villar J, Cheikh Ismail L. International fetal and newborn growth consortium for the 21st century (INTERGROWTH-21st). International standards for newborn weight, length, and head circumference by gestational age and sex: the Newborn Cross-Sectional Study of the INTERGROWTH-21st Project. Lancet 2014; 384: 857-68.
17. Villar J, Giuliani F, Bhutta ZA, et al. International fetal and newborn growth consortium for the 21(st) Century (INTERGROWTH-21(st)). Postnatal growth standards for preterm infants: the Preterm Postnatal Follow-up Study of the INTERGROWTH-21(st) Project. Lancet Glob Health 2015; 3: e681-91
18. Olsen IE, Groveman SA, Lawson ML, et al. New intrauterine growth curves based on United States data. Pediatrics 2010; 125: e214.
19. Borghi E, De Onis M, Garza C, et al. Construction of the World Health Organization child growth standards: selection of methods for attained growth curves. Stat Med 2006; 25: 247-65.
20. Gökçay G, Furman A, Neyzi O. Updated growth curves for Turkish children aged 15 days to 60 months. Child Care Health Dev 2008; 34: 454-63.
21. Volpe J. Neurologic outcome of prematurity. Arch Neurol 1998; 55: 297-300.
22. Stephens BE, Vohr BR. Neurodevelopmental outcome of the premature infant. Pediatr Clin North Am 2009; 56: 631-46.
23. Latal B. Prediction of neurodevelopmental outcome after premature birth. Pediatr Neurol 2009; 40: 413-9.
24. American Academy of Pediatrics. Follow-up Care of High-Risk Infants. Pediatrics 2004; 114: 1377.
25. Syennes AR. Developmental outcome. In: MacDonald MG, Seshia MMK, (eds). Avery's neonatology pathophysiology and management of the newborn. 7th ed. Philadelphia: Wolters Kluwer; 2016.p.1157-68.
26. Allen MC. Neurodevelopmental outcomes of premature infants. Curr Opin Neurol 2008; 21: 123-8.
27. Ertem IO, Dogan DG, Gok CG, et al. A guide for monitoring child development in low- and middle-income countries. Pediatrics 2008; 121: e581-9.
28. Schanler JS. Approach to enteral nutrition in the premature infant. In Uptodate, Abrams SA, Motil KJ (Eds), UpToDate, Wolters Kluwer, 2017.
29. Ramel SE, Georgieff MK. Nutrition. In: MacDonald MG, Seshia MK, (eds). Avery's neonatology. Pathophysiology and management of the newborn. Philadelphia: Wolters-Kluwer; 2016.p.280-97.
30. Agostoni C, Buonocore G, Carnielli VP, et al. Enteral nutrient supply for premature infants: commentary from the European Society of Paediatric Gastroenterology, Hepatology, and Nutrition Committee on Nutrition. J Pediatr Gastroenterol Nutr 2010; 50: 85-91.
31. Adamkin DH. Postdischarge nutritional therapy. J Perinatol 2006; 26: S27-S30.
32. ESPGHAN Committee on Nutrition. Feeding premature infants after hospital discharge: a commentary by the ESPGHAN Committee on Nutrition. J Pediatr Gastroenterol Nutr 2006; 42: 596-603.
33. Kültürsay N, Bilgen H, Türkyılmaz C. Türk Neonatoloji Derneği prematüre ve hasta term bebeğin beslenmesi rehberi, 2014.
34. Abrams SA and the Committee on Nutrition. Calcium and Vitamin D requirements of enterally fed premature infants. Pediatrics 2013; 131: e1676–83.
35. Adcock LM, Freysdottir D. Screening the newborn for hearing loss. In: Uptodate, Abrams SA, Duryea TK, (eds). UpToDate, Wolters Kluwer, 2017.
36. Türkiye Cumhuriyeti Sağlık Bakanlığı Halk Sağlığı Genel Müdürlüğü Ulusal Yenidoğan İşitme Taraması Uygulama Rehberi, 2017
37. US Preventive Services Task Force. Universal screening for hearing loss in newborns: US preventive services task force recommendation statement. Pediatrics 2008; 122: 143-57.
38. Coats DK. Retinopathy of prematurity: Treatment and prognosis. In: UpToDate, Garcia-Prats, JA, Saunders RA, (eds). UpToDate, Waltham, MA, 2017.
39. American Academy of Pediatrics, American Academy of Ophthalmology; American Association for Pediatrics

Ophthalmology and Strabismus. Screening examination of premature infants for retinopathy of prematurity. Pediatrics 2013; 131:189-95.
40. Koc E, Bas AY, Özdek Ş, ve ark. Türkiye Prematüre Retinopatisi Rehberi, 2016.
41. International Committee for the Classification of Retinopathy of Prematurity. The ınternational classification of retinopathy of prematurity revisited. Arch Ophthalmol 2005; 123: 991-9.
42. Good WV, Early Treatment for Retinopathy of Prematurity Cooperative Group. The early treatment for retinopathy of prematurity study: structural findings at age 2 years. Br J Ophthalmol 2006; 90: 1378-82.
43. Mintz-Hittner HA, Kennedy KA, Chuang AZ, BEAT-ROP Cooperative Group. Efficacy of intravitreal bevacizumab for stage 3+ retinopathy of prematurity. N Engl J Med 2011; 364: 603-15.
44. Jill E. Baley. Schedule for immunization of premature infants. In: Martin RJ, Fanaroff AA, Walsh MC, (eds). Fanaroff and Martin's neonatal perinatal medicine- diseases of the fetus and newborn. Missouri; Mosby Elservier; 2015.p.1839-40.
45. Saari TN, American Academy of Pediatrics Committee on Infectious Diseases. Immunization of premature and low birth weight infants. American Academy of Pediatrics Committee on Infectious Diseases. Pediatrics 2003; 112:19198.
46. Bonhoeffer J, Siegrist CA, Heath PT. Immunisation of premature infants. Arch Dis Child 2006; 91; 929-35.
47. Flatz-Jequier A, Posfay-Barbe KM, Pfister RE, Siegrist CA. Recurrence of cardiorespiratory events following repeat DTaP-based combined immunization in very low birth weight premature infants. J Pediatr 2008; 153: 429-31.
48. American Academy of Pediatrics Committee on ınfectious diseases. Prevention of rotavirus disease: Updated guidelines for use of rotavirus vaccine. Pediatrics 2009; 123: 1412-20.
49. Türk Neonatoloji Derneği. Palivizumab ile RSV proflaksisi önerileri. 11 Temmuz 2018. http://www.neonatology.org.tr/
50. Stewart J. Care of the neonatal intensive care unit graduate. In: UpToDate, Abrams SA, Kim MS, (eds). UpToDate, Wolters Kluwer, 2017.
51. Mc Court MF, Griffin CM. Comprehensive primary care follow-up for premature infants. J Pediatr Health Care 2000; 14: 270-9.
52. Ritchie SK. Primary care of the premature infant discharged from the Neonatal Intensive Care Unit. MCN Am J Matern Child Nurs 2002; 27: 76-85.
53. Verma RP, Sridhar S, Spitzer AR. Continuing care of NICU graduates. Clin Pediatr 2003; 42: 299-315.
54. Czinn SJ, Blanchard S. Gastroesophageal reflux disease in neonates and infants: when and how to treat. Paediatr Drugs 2013; 15: 19-27.
55. Harrison CM, Gibson AT. Osteopenia in premature infants. Arch Dis Child Fetal Neonatal Ed 2013; 98: F272-5.
56. American Academy on Pediatric Dentistry Clinical Affairs Committee-Infant Oral Health Subcommittee, American Academy on Pediatric Dentistry Council on Clinical Affairs. Guideline on infant oral health care. Pediatr Dent 2008-2009.p.30-90.
57. Bull MJ, Engle WA, Committee on Injury, Violence, and Poison Prevention and Committee on Fetus and Newborn, American Academy of Pediatrics. Safe transportation of premature and low birth weight infants at hospital discharge. Pediatrics 2009; 123: 1424.
58. Davis NL. Car seat screening for low birth weight term neonates. Pediatrics 2015; 136: 89.
59. Arya R, Williams G, Kilonback A, et al. Is the infant car seat challenge useful? A pilot study in a simulated moving vehicle. Arch Dis Child Fetal Neonatal Ed 2017; 102: F136.