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Case Report

Growth and development in an extremely low birth weight infant with osteopenia of prematurity: a case report

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Caring for extremely low birth weight (ELBW) infants remains a challenge in developing countries due to high morbidity and mortality rates. In Dr. Sardjito Hospital, Yogyakarta, the ELBW survival rate was 39.3%.[1] Expected outcomes of these ELBW survivors are increased risk of mortality during the infant period and short term as well as long term complications.[2] Osteopenia of prematurity is a comorbidity that can interfere with longterm growth and neurodevelopment.[3]

Osteopenia of prematurity is found in approximately 55% of babies with ELBW.[4] Antenatal demineralization is aggravated by improper nutritional interventions during perinatal care and post-discharge care. This comorbidity is asymptomatic in the infant's early life, but later contributes to linear growth failure, delayed teeth eruption, respiratory problems, and bone fractures in ELBW babies.[3] Early detection and prompt management of osteopenia of prematurity are needed for all ELBW infants. Here we present a case of an ELBW infant with osteopenia of prematurity who we observed for 18 months. The child underwent multidisciplinary interventions for modifiable prognostic factors to support optimal achievement of growth and neurodevelopment. **[Paediatr Indones. 2022;62:143-8 DOI: 10.14238/pi62.1.2022.143-8]**.

Keywords: *osteopenia of prematurity; extremely low birth weight infant; growth; development*

The case

We report here a small for gestational age female infant with ELBW who was born prematurely at 29 weeks to a primigravida mother with severe eclampsia. Her birth weight was 678 grams and she required hospitalization for 77 days. Her comorbidities during the neonatal period were hyaline membrane disease, neonatal sepsis, intraventricular hemorrhage, atrial septal defect, and feeding intolerance. Intensive care and monitoring helped the child survive the critical period.

By the time the infant was discharged from the perinatal ward, she suffered from osteopenia of prematurity. Her growth was below the 3rd percentile on the Fenton curve with a declined trendline in all her growth parameters. Her laboratory findings showed elevated alkaline phosphatase (ALP) at 1359 U/L (normal level <390 U/L), normal serum calcium at 2.39 mmol/L, normal serum phosphate at 2.4 mmol/L, and decreased 25-OH-vitamin D level at <3.0 ng/mL (normal level >30 ng/mL). The diagnosis of osteopenia of prematurity was established by the presence of growth failure accompanied by the high ALP level.

This prospective observational study was done to observe the growth and neurodevelopment of this

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preterm ELBW infant with osteopenia of prematurity, and to modify her prognostic factors. Such modifiable prognostic factors included infection, osteopenia, anemia, organ system sequelae, neurosensory impairment, as well as suboptimal caregiver attitudes and practices. **Table 1** shows the interventions and monitoring which were applied.

Planning for the interventions and monitoring checklist were kept by observer in a personal diary as a communication tool during the observation period. We encouraged the patient's mother and family to contribute by explaining that the expected outcome required family involvement; one simple way was to record their experiences in the diary, which was also maintained by the observer team. The diary also included information needed by the parents and family about premature birth implications,preventive care, a list of high calorie and protein foods, a table of weekly meals consumed, an immunization checklist, and the *World Health Organization (WHO)* growth chart.

During study period, the average monthly calorie index was 83.7% (target level >70%) and protein energy ratio (PER) was 10.3% (target level 8-12%) (**Figure 1**). At 8 and 14 months of age, the calorie index was not achieved due to infection and rehospitalization events, but then it went beyond the target, due to early detection and early intervention by the pediatric nutritionist. General and oral physiotherapy were done at the district hospital for her first year of corrected age, then continued daily at home. Playing outside the house and engaging in routine physical activity was encouraged.

At the end of the study, our patient had successfully caught up to her expected growth. Head circumference, body weight, and body length targets were reached at 2 months, 4 months and 14 months, respectively, of her corrected age. The body length target in our case is -2.78 SD, which is resulted from the expected final height for ELBW children and the genetic potential (**Figure 2**).The final height for age of ELBW children is 0.78 SD below median (95%CI -1.08 to -0.48) compared to normal weight baby, while the genetic final height based on a parent's height combining calculation was 150 cm + 8.5 cm, which was equal to 2 SD below median.

Laboratory parameters of osteopenia of prematurity as well as bone density scanning with dual energy X-ray absorptiometry (DXA) results revealed that the osteopenia of prematurity had resolved at 10 months of corrected age (**Table 1** and **Figure 3**).

Weight increment in our patient was greater than her height increment at the end of the follow-up, affecting her body mass index (BMI). This trend was similar to that of body composition results from DXA. While the fat mass percentage seemed lower compared to the baseline, it was actually increasing compared to her body surface area (BSA), as shown in **Figure 4**.

Neurodevelopmental achievement in our ELBW survivor was good according to her corrected age, in addition to her cognitive function and social adaptive behavior. Developmental screening of high-risk infants should be assessed monthly, as recommended, though we made some modifications in our case. We monthly screened the patient's development by online and did developmental screening with Denver-II test and capute scale test every 3 months to maintain good compliance and cost effectiveness since the patient lives in an urban area with low to middle economic status. The Bayley Scales of Infant Development-II examination was postponed due to the COVID-19

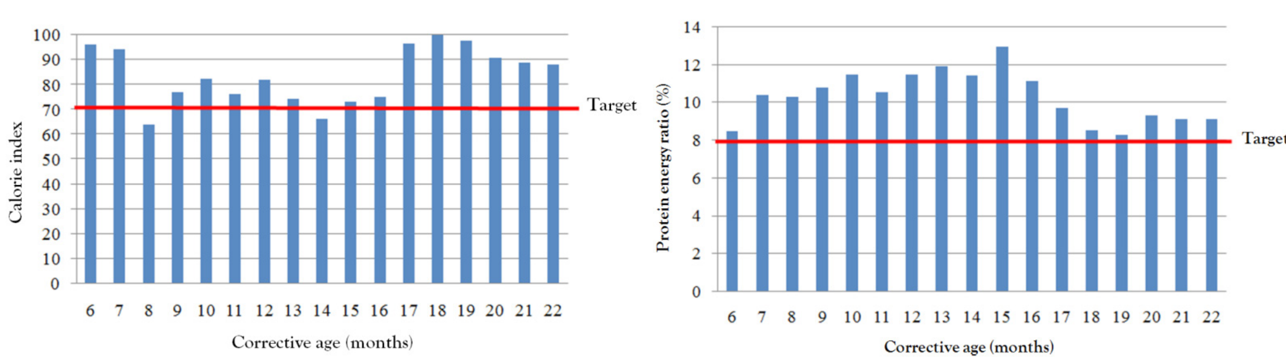

Figure 1. Calorie index and PER achievement over 22 months of corrected age.*Unachieved calorie index occurred when the patient suffered from infections

Table 1. Interventions toward modifiable prognostic factors

Modifiable prognostic factors	Baseline data (at age 3 months)	Interventions		Monitoring		Outcomes
Infection	No infection	Give adequate nutritional intake according to RDA with PER of 8-12% and micronutrient enrichment.[5,6]	Immunizations based on IPS recommendations, house environment modification based on Ministry of Health guideline.[7,8]	Monthly calorie index and PER index, monthly anthropometric measurements and nutritional status.	Daily health checklist, immunization checklist, and householdhealth environment checklist.	Two rehospitalizations due to infection in the first 2 years without prolonged length of hospital stay.
Osteopenia of prematurity with vitamin D deficiency	Growth failure, ALP 1359 U/L (normal <390 U/L), 25-OH-vitamin D <3.0 ng/mL (normal >30 ng/mL)		Vitamin D supplementation 400 IU/day and physical activity. Calcium and phosphate supplementation are given for hypocalcemia and hypophosphatemia.[9]		Evaluation of ALP, calcium, phosphate, and vitamin D every 6 months; DXA investigation at the beginning and end of observation (**Figure 3**)	Successful catch-up growth, ALP and 25-OH-vitamin D were in normal range at 10 months corrected age (ALP 287 U/L, 25-OH-vitamin D 44 ng/ml), BMD was in normal range (**Figure 3**)
Anemia of prematurity	Hemoglobin 10.2 g/dL, hematocrit 30.7%		Iron supplementation 2 mg/kg/day.[10]		Hemoglobin and erythrocyte index evaluation for next 3 months	Anemia has been resolved at 6 -month-old, with hemoglobin level at 13.9 mg/dL.
Neurosensory and neuro-developmental impairment	No ROP, normal OAE examination	Child development stimulation.[11] Early intervention for any suspicious results from developmental screening.		Denver-II test and Capute scale screening every 3 months, OAE evaluation, BERA examination, visual function screening, M-CHAT screening		Neurosensory function was normal, development was appropriate to the corrected age, and no behavioral disorder.
Caregiver attitude and practice	Not yet assessed	Comprehensive and continuous education, and assess for any psychosocial change.[11] Create a premature baby community and hold a togetherness event.		Attitude and practice questionnaire at the beginning of observation, a month after interventions, and follow up as needed.[11-14]		Appropriate caregiver attitude and practice.

ALP=alkaline phosphatase; BERA=brainstem evoked response audiometry; DXA=dual energy x-ray absorptiometry; IPS=Indonesian Pediatric Society; M-CHAT=modified checklist autism in toddler; OAE=otoacoustic emission; PER=protein energy ratio;RDA=recommended daily allowances; ROP=retinopathy of prematurity

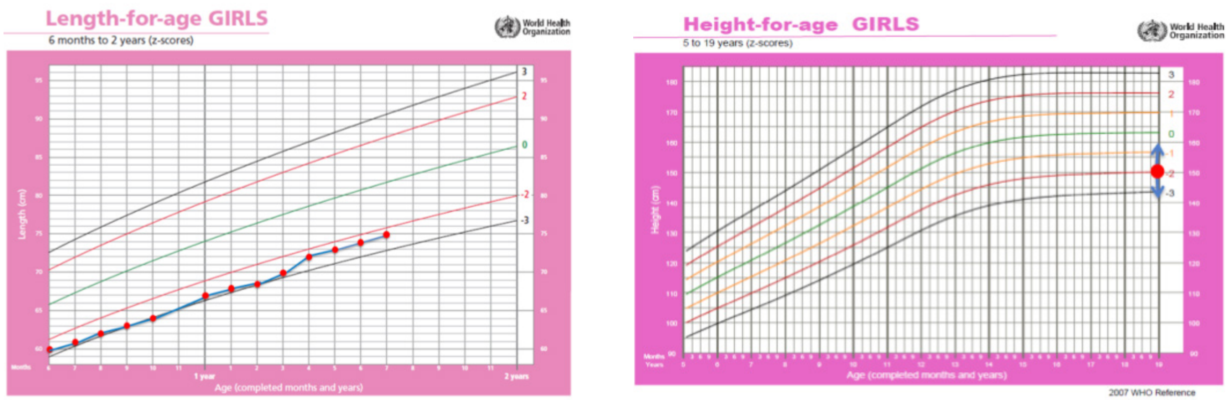

Figure 2. Catch-up for length was achieved at 14 months corrected age (left) according to the final height target (right).

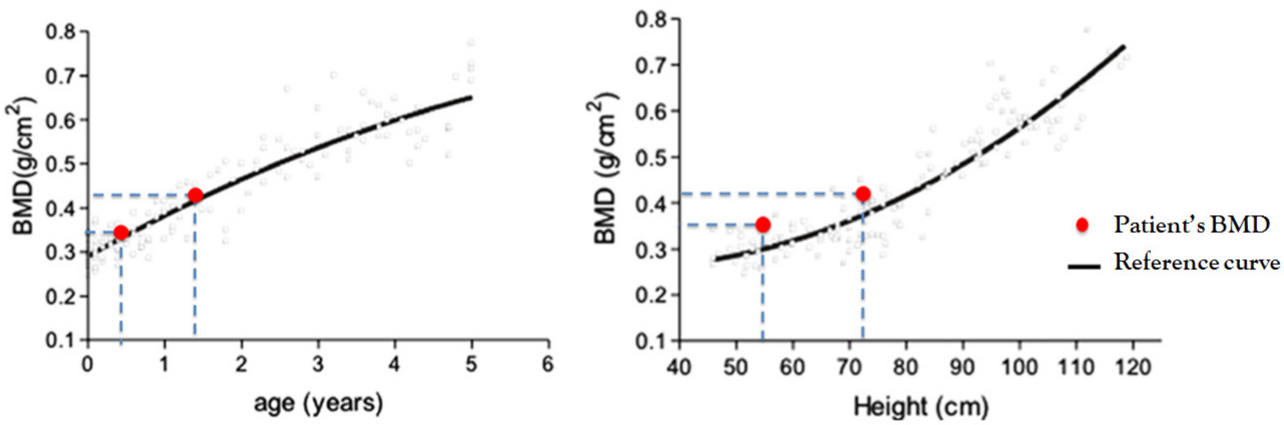

Figure 3. Bone mineral density (BMD) of the patient was in line with the reference curve[15]

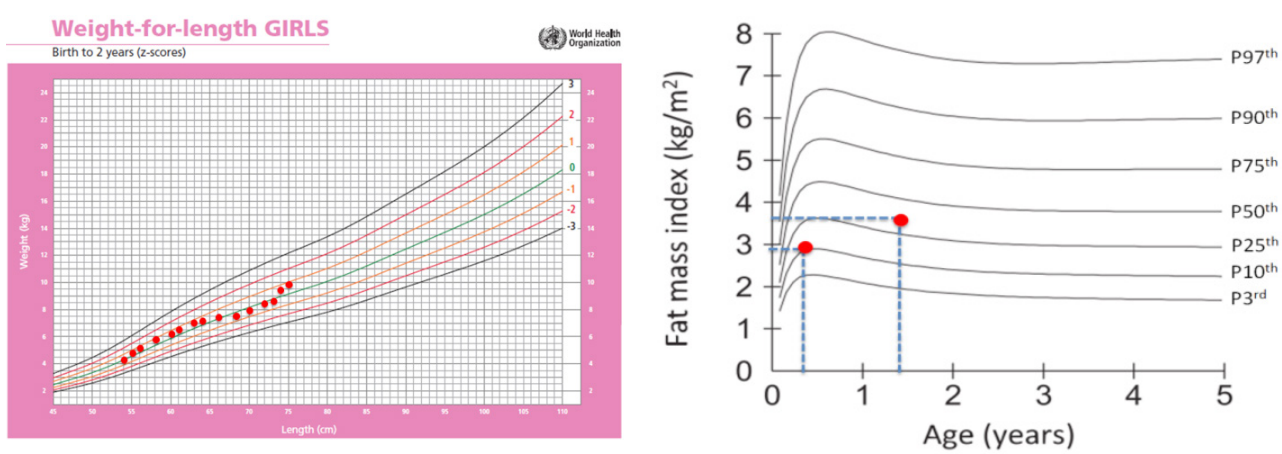

Figure 4. BMI (left) and fat mass index (right) increased due to slower height increment[16]

pandemic. The Conner's screening test was scheduled at age of 36 months to detect any signs of attention-deficit/hyperactivity disorder (ADHD).

Maternal attitudes and practices in descriptive form were documented by the questionnaire that was adapted from the *Infant and Young Child Feeding*

Questionnaire for the Assessment of Knowledge, Attitude and Practices among Child Care Providers (IYCF-CCPQ), *Kangaroo Mother Care Questionnaire* from the *Shavazi-Abbasi Study*, and premature care items from the *WHO* and *American Academy of Pediatrics (AAP)*.[11-14] Questionnaire results revealed that the baby's mother was coping well with her child's needs and did not require further psychological intervention.

Discussion

Catch-up growth in a baby born small for gestational age with ELBW tends to be slower than in normal birth weight babies. Catch-up growth can continue for up to 36 months of corrected age.[17] Length is the last growth parameter to be caught up in ELBW infants. The final height for age of ELBW children is 0.78 SD below median (95%CI -1.08 to -0.48) compared to normal weight baby, and it should be considered to define target length/height in every ELBW children along with genetic potential.[18,19]

Weight increment in ELBW should not exceed 0.67 SD in order to prevent increasing BMI to a level (+2-3 SD) that could lead to metabolic and cardiovascular disorders.[18] Nutritional status in ELBW infants, furthermore, should also include body composition assessment by DXA, since it provides fat and lean mass comparison, in addition to monthly index measurements of calories and PER. This approach is more comprehensive as anthropometric measurements are not able to predict total fat mass percentage.[18]

Many factors can interfere with the growth of ELBW infants, one of which is osteopenia of prematurity. An osteopenia of prematurity diagnosis can be established by elevated ALP >900 U/L without hypophosphatemia, with 88% sensitivity and 71% specificity. If it is concurrent with decreased serum phosphate <1.8 mmol/L, the sensitivity increases to 100%.[4] Fortified human milk supplementation is recommended for ELBW infants who have reached full enteral feeding.[9] In a limited-resource facility, hindmilk wasshown to increase premature baby weight.[20] Infant formula is an alternative source of nutrition if human milk supplement is unavailable or if giving expressed hindmilk still results in suboptimal growth; however, supplementation with formula may be associated with low bioavailability of calcium and phosphate. Their absorption is determined by vitamin D; thus, vitamin D supplementation at 400 IU/day is recommended for ELBW infants.[9]

Infection is the most common etiology of rehospitalization in ELBW survivors in the first two years. Respiratory tract infections account for 42.1% of such rehospitalization cases. Infections in other organ systems account for 8.1%.21 Smaller lung volume, narrow airways, greater chance of trapped air, and high airway reactivity contribute to the high risk of respiratory tract infections, despite complete immunization, proper hygiene practices, and healthy environments. Extended hospital length of stay (LoS) is another outcome of rehospitalization events. Early detection of symptoms by the mother and proactive interventions were shown to prevent prolonged LoS in our ELBW patient. Median LoS for rehospitalization events in a previous cohort study was 3.7 + 2.6 days,[21] compared to 2 days and 5 days LoS for our patient. Hence, our patient did not have prolonged hospital LoS.

Support for parents, especially psychologically, is essential to the care of premature infants. When a patient is discharged from perinatal care, parents should have sufficient education to build their confidence, readiness, and trust, in addition to long-term communication with medical advisors.[2] Peer group meetings with parents of premature infants and togetherness events are also an effective way to make a positive psychological impact.[11]

In conclusion, despite their poor postnatal history and likelihood of concurrent comorbidities, with comprehensive intervention and monitoring, ELBW infants with osteopenia of prematurity are able to optimally grow and develop as well as normal birth weight infants. Presence and maintenance of a premature infant diary as a communication tool is also an effective way to support expected outcomes. Intervention and monitoring by medical advisors and family are required through childhood, due to the ongoing risk of morbidity. Appropriate caregiver attitudes and practices, in spite of low socioeconomic and/or background knowledge, should also be assessed periodically in order to ensure that interventions are properly implemented, as seen in this case.[11]

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