EDITORIAL

Assisted Physical Exercise for Preterm Neonates

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Metabolic bone disease (MBD) of prematurity, also known as osteopenia/ rickets of prematurity, is a major comorbidity in preterm, very low birth weight (VLBW) and chronically ill infants leading to deformities and even spontaneous fractures, if left untreated [1-3]. It is defined as reduced bone mineralization when compared to predicted level of bone mineral content of a fetus or neonate of similar gestational age or size along with biochemical markers and/or radiological findings [1]. The reported incidence varies from 16% in VLBW to 40% in extremely low birth weight (ELBW) neonates [2,3]. The key etiological factors remain inadequate calcium and phosphorous stores in the face of accelerated skeletal growth. Also, use of medications (steroids, caffeine), prolonged parenteral nutrition and immobilization in premature infants has shown to aggravate MBD [4,5]. MBD characteristically presents within 6-16 weeks after birth. Increased physical activity in preterm infants has shown to enhance bone mineralization along with better weight gain [4,6].

As the disease advances, biochemical abnormalities tend to increase significantly. These include hypocalcemia, hypophosphatemia, hyperphosphatasia and secondary hyperparathyroidism. Moreover, urinary phosphate wasting can ensue in these preterm neonates and vitamin D deficiency can also compound these effects [1-3]. On the other hand, biochemical derangements may or may not be associated with rachitic changes. Interestingly, MBD can also remain unidentified radiologically, as it needs profound loss of bone mineralization (>40%) to manifest characteristic radiological features. Some studies have evaluated bone mineral density, bone mineral content and whole-body lean mass in preterm neonates using bone densitometry by dual-energy *X*-ray absorptiometry (DXA) [1,4].

Newer studies propose that estimating bone Speed of sound (SOS) by quantitative ultrasound could predict bone turnover in preterm infants alongside standard biochemical markers [7-9]. Measuring bone SOS over mid-tibial shaft is a non-invasive tool that can indirectly depict bone strength. This was found to be higher in term neonates (median 3079 m/s) when compared to premature neonates (median 2911 m/s), in a study by McDevitt, *et al*. [7]. Many studies report good correlation between bone SOS and gestational age [7-11]. It was also seen that bone SOS was less in premature neonates who reached corrected age of full term neonates when compared to term neonates [8].

Majority of the preventive strategies for MBD target nutritional enhancement. However, the novel approach would be to focus on improving physical activity in these tiny neonates along with optimum nutritional supplementation, which might enhance bone metabolism and mineralization. Assisted physical exercise using passive range of motion of the extremities has shown to significantly increase the body weight, bone mineralization and osteogenesis. Some studies have shown that the exercise could attenuate the postnatal reduction in bone SOS [10,11].

The study by Shaw, *et al.* [12] in this issue of *Indian Pediatrics* is an open label randomized controlled trial, conducted in a level-3 neonatal unit from a tertiary care teaching hospital in Northern India. This is the first published study from India that evaluates the role of assisted physical exercise for enhancing bone strength in preterm infants as measured by quantitative ultrasound. This study has addressed two newer methods in predicting and preventing MBD in preterm neonates. First, they have used latest non-invasive methodology of estimating bone strength by measuring SOS in tibia, by quantitative ultrasound along with other metabolic work-up. Second, the authors evaluated the role of assisted physical exercise that aims to combat immobilization, one of the determinants of MBD. This collectively strengthens the study coupled with its high quality study design and methodology executed. The authors assessed the impact of daily assisted physical exercise conducted by mothers in stable preterm infants born at 27 to 34 weeks of gestation, from one week of postnatal age to term gestation on bone strength as estimated by tibial bone SOS at 40 weeks post menstrual age (PMA). The sample size was larger than previous randomized controlled trials [11,12]. The present study also included intrauterine growth restricted neonates when compared to the study by Litmanovitz, *et al*. [11], which comprised only appropriate for age neonates. This is much needed in Indian perspective when compared to western countries, as a sizable proportion of Indian neonates have intrauterine growth restriction. Captivatingly, the study had an exceptional follow up rate of 94%, which is difficult to achieve otherwise, and which was much higher than previous studies and the follow-up period was longer. Neonates in the exercise group received physical exercise and mothers were trained very meticulously, which also included video demonstration and mothers were provided with the videos containing standardized method, and the method was reassessed by the authors in periodic follow-up visits. Likewise, the authors have evaluated the primary outcome, SOS in left tibia with utmost precision.

Schulzke, *et al.* [4] concluded from their Cochrane review of eleven small randomized trials of moderate methodological and reporting quality that physical activity programs might lead to moderate bone mineralization and short-term growth in preterm neonates. As the effect size was small and the baseline risk of decreased bone mineralization and growth was low in their review, the clinical relevance of their results is unclear.

This study would make a path for further larger trials comparing the role of assisted physical exercise by mother in preterm neonates and its influence on their bone strength. Also, the results of this study would provide baseline data of tibial SOS by quantitative ultrasound for Indian neonates.

Funding: None; *Competing interests*: None stated.

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