

## EDITORIAL

## Osteopenia of the preterm newborn

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**O**steopenia is of relatively recent and growing interest in the preterm newborn. It is also known as rickets of prematurity or metabolic bone disease of prematurity. According to the report on premature births of the World Health Organization (WHO), 10% of births worldwide occur before 37 weeks of gestation.<sup>1</sup> It has also been reported that during recent decades a significant increase in the rate of survival of preterm infants has been seen. At the same time, this has increased the emerging conditions such as osteopenia of prematurity, which can occur in up to 30% of infants born before 28 weeks of gestation. The prevalence depends on gestational age, weight and type of nutrition. It is present in 55% of premature newborns with a weight of <1000 g and in 23% of infants with weight <1500 g at birth. There is a significant difference in the presentation of this condition between the premature newborns fed with breast milk, due to the low content on some occasions of minerals and vitamin D in maternal milk vs. those fed with formulas designed for pre-term children with a high content of these minerals (40% vs. 16%, respectively).

Osteopenia of the newborn is characterized by a reduction of bone mineral content with or without changes of rickets and is caused both by severe nutritional deficiencies as well as biomechanical factors. It occurs during the 10<sup>th</sup> and 16<sup>th</sup> weeks of life, but it may not be detected until there is severe demineralization (between 20% and 40%

of mineral bone loss).<sup>2</sup> There are multiple factors in addition to the prematurity itself, with the consequent mineral deprivation to which the mother makes a significant contribution during the last trimester of pregnancy, leading to this syndrome. Prolonged periods of parenteral nutrition, immobilization, treatment with medications such as steroids, diuretics and others have a direct effect on mineralization. The clinical picture varies from a silent condition up to florid pictures of rickets with multiple fractures.

In spite of this being a common disease, there are important controversies in the literature with relationship to the methods of detecting infants at risk as well as their interpretation.<sup>3</sup> The levels of alkaline phosphatase, calcium and serum phosphorus are used independently or in combination for detecting cases with deficiencies. However, there is no agreement on the acceptable cut-off levels or of the time in which these determinations should be made. The same occurs with X-rays because there is also no consensus on the interpretation of the images for diagnosis and follow-up of osteopenia. Studies with dual-energy absorption x-rays (DEXA) are considered by many groups as the gold standard because it is an already validated technique. It has some limitations because the technology is basically available only in research centers, and it is difficult to perform studies outside of these centers. Another limitation is the difficulty in keeping patients completely still because movements produce artifacts and complicate results interpretation. The use of quantitative ultrasonography has also been evaluated, although there is controversy. Whereas some groups have shown a decrease of sound attenuation in preterm infants 24 to 31 weeks of gestation, others find no correlation between this method and serum markers.

The most important question in these cases would be: What is the impact of osteopenia of the premature on the health of these patients? In the short term, the most

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frequent complications without timely treatment are fractures of the long bones and ribs, with an incidence that varies between 10 and 32%. With supplementation of these minerals with vitamin D in the diet, osteopenia of prematurity and fractures are resolved and, apparently in the short term, there are no consequences. However, there are some follow-up studies at 5 to 7 years to be taken into account because it has been reported that preterm children treated with steroids for chronic lung disease have a significant difference from those premature infants who were not treated with dexamethasone, both in density as well as in bone mineral content measured by DEXA. Other studies have shown a lower bone mineral density (BMD) in preterm children vs. children who were born at term. They conclude that there is a decrease in the peak bone mass of premature infants. It has also been shown that apparently healthy children who suffer fractures have a significant difference in BMD. These studies that demonstrate changes in bone mineralization in children and adolescents have led some authors to hypothesize that early osteoporosis in adulthood may be related to deficiencies of mineralization in early life. Prevention of osteopenia of the preterm NB and its timely treatment should be the primary objective in intensive care units. All children who weigh <1500 g, with a gestation age <28 weeks, who receive parenteral nutrition for >4 weeks or who receive treatment with diuret-

ics or steroids should be monitored for this condition. Despite the controversies in the levels of markers, these should be used with clinical judgment and monitored weekly (calcium, phosphorus and alkaline phosphatase) for follow-up. Together with the markers, both DEXA and quantitative ultrasound can assist in the follow-up to observe changes in bone mineralization. An adequate intake of calcium, phosphorus and vitamin D and performing passive exercises can prevent abnormal activity of bone remodeling and maximize potential growth in preterm infants. More research is required to obtain a consensus on early diagnosis and follow-up protocol of these cases in order to reduce the short- and long-term complications that may appear.

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