Factors associated with osteopenia in preterm infants via bone screening: a multicenter study. atlántico, 2023–2025

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Abstract

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Introduction: To determine the prevalence and associated factors of osteopenia in preterm infants through neonatal screening in healthcare institutions (*Instituciones Prestadoras de Salud*) in Atlántico, from 2023 to 2024. **Materials and Methods:** An observational, descriptive, cross-sectional study with exploratory data analysis. The population consisted of neonates < 36 weeks of gestation admitted to three intensive care units in Atlántico between December 2023 and 2024. The variables studied included sociodemographic, nutritional, and paraclinical data, as well as pharmacological treatment and complications. Data collection was performed by reviewing neonatal intensive care unit databases, assessing levels of alkaline phosphatase, phosphorus, and calcium after the fourth week of life. Data were tabulated in Excel and analyzed using Statgraphics 16 software. **Results:** An association was identified between osteopenia and low birth weight, lower gestational age, higher chronological age, corticosteroid use, and radiographic changes. **Conclusion:** The analysis of determinants revealed that lower gestational age, low birth weight, and pharmacological interventions were the primary factors associated with the development of metabolic bone disease of prematurity (osteopenia of prematurity).

INTRODUCTION

An estimated 15 million preterm infants are born worldwide each year; the preterm birth rate ranges between 5% and 18% of newborns, carrying a high potential for disability (Rsy & Lee, 2022). In Latin America, prematurity and low birth weight account for 60% of deaths in children under five years of age (Puello, 2021). In Colombia, the perinatal and neonatal mortality rate in 2023 was 13.6 deaths per 1,000 live births. Long-term impacts include alterations in anthropometric values, lower bone mineral density scores, risk of pathological fractures, and lower cognitive levels (Baş EK, 2022). Among the impairments in bone mineral density is osteopenia of prematurity, characterized by decreased mineralization due to mineral deficiencies and vitamin D deficits (Chacham, 2020).

Technological advancements have increased the survival of extremely preterm neonates, leading to the emergence of pathologies arising from artificial extrauterine growth (Galvis-Blanco, 2022; Mesa, 2022; Krithika, 2022; Yan-Mei, 2021). One such pathology is osteopenia, which can occur in 50% of very low birth weight newborns without adequate supplementation (Perrone, 2022; Lü K-L, 2023; Chinoy, 2020). The preterm newborn faces multiple complications due to organ immaturity and associated pathologies, forming a series of conditions that may induce the development of osteopenia (Wang, 2022). This condition can be screened using calcium, phosphorus, and alkaline phosphatase levels, which serve as sensitive indicators of bone metabolism;

their serum levels can be used as early markers to monitor bone metabolic status (Chen W, 2021; Bolívar VC, 2022; Boddu, 2022).

Calcium and phosphorus homeostasis is determined by multiple factors. Calcium is predominantly an extracellular ion, while phosphorus is intracellular; both are necessary for intracellular processes during infancy. Acting in conjunction with thyroid hormone levels, they are indispensable for proper bone development. Transient hypothyroxinemia of prematurity may be associated with the development of osteopenia of prematurity (Dursun M, 2022).

Consequently, any factor affecting this metabolism can lead to the disease. Examples include the use of medications such as corticosteroids, diuretics, and caffeine, the latter of which leads to excessive renal calcium loss (Kumar, 2022).

Mineral supplementation at basal levels in preterm infants does not correct osteopenia. The American Academy of Pediatrics recommends bone health screening starting at four postnatal weeks (Kavurt, 2021). The primary prevention strategy for osteopenia is the optimization of preterm nutrition, with an emphasis on mineral intake (Miller M, 2019).

MATERIALS AND METHODS

Following approval from the participating institutions, the attending physicians, and the Institutional Ethics Committee, a database search was conducted across three neonatal intensive care units in Atlántico. Serum levels of alkaline phosphatase, phosphorus, calcium, and vitamin D were determined for all preterm neonates with identified risk factors after four weeks of life who were admitted during the study period. Study variables, as well as inclusion and exclusion criteria, were rigorously evaluated. For eligible subjects, data were recorded using a pre-designed data collection form, subsequently tabulated in Microsoft Excel, and analyzed using Statgraphics version 16 software. Descriptive statistics, including frequency tables, pie charts, and X^2 tests, were employed. Results were presented in the form of tables and figures.

Regarding ethical considerations, in accordance with Article 11 of Resolution 8430 of 1993, this study is classified as "risk-free research," as it poses no threat to the physical integrity of the study population. Likewise, strict confidentiality and privacy were maintained for all evaluated documents and medical records.

RESULTS

During the study period, 340 preterm infants were admitted to the units. After applying inclusion and exclusion criteria, a sample of 37 preterm infants was obtained. Within this population, 8.11% presented with Metabolic Bone Disease of Prematurity (Table 1). Regarding the sample characteristics, 59.45% of the infants were between 28 and 32 weeks of gestation, 43.24% had a chronological age ranging from 61 to 90 days, and 40.54% weighed between 1,000 and 1,500 grams. A significant correlation was observed between lower gestational age at birth ($p = 0.0055$) and lower weight for gestational age ($p = 0.0133$) with the risk of osteopenia of prematurity (Table 2, Figure 1, Table 3). Similarly, a significant correlation was found between higher chronological age ($p = 0.0012$) and the risk of osteopenia (Table 4, Figure 2).

Table 1.
Prevalence of Osteopenia in the Study Population

OSTEOPENIA	FREQUENCY	PERCENTAGE
NO	34	91.89%
YES	3	8.11%
TOTAL	**37**	**100%**

Source: Medical records database.

Table 2.

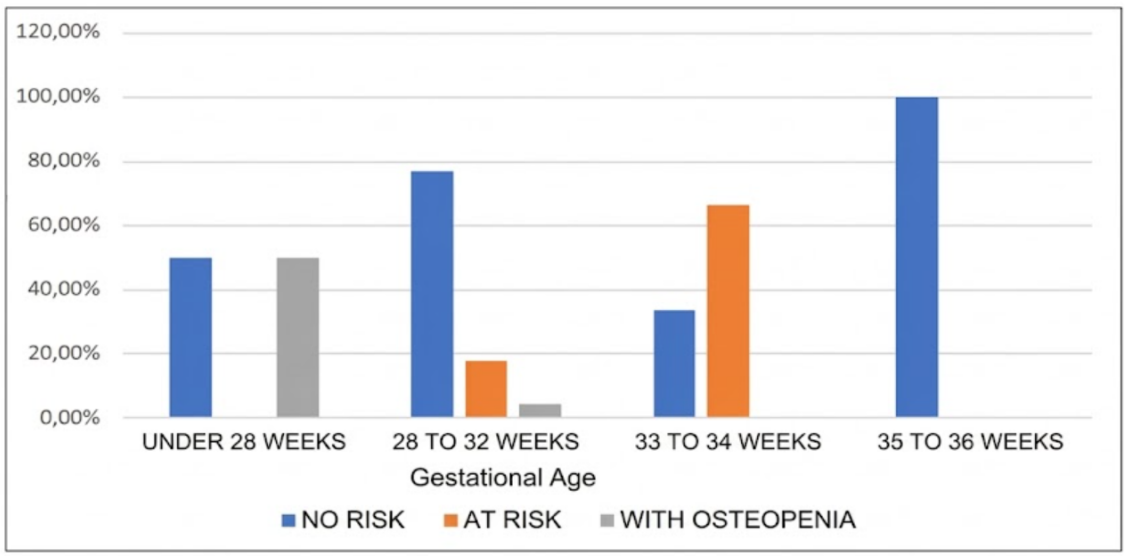
Relationship between Gestational Age and Risk of Osteopenia

GESTATIONAL AGE	NO RISK	AT RISK	WITH OSTEOPENIA	ROW TOTAL
< 28 WEEKS	2 (50.00%)	0 (0.00%)	2 (50.00%)	4 (10.81%)
28 TO 32 WEEKS	17 (77.27%)	4 (18.18%)	1 (4.55%)	22 (59.46%)
33 TO 34 WEEKS	1 (33.33%)	2 (66.67%)	0 (0.00%)	3 (8.11%)
35 TO 36 WEEKS	8 (100.00%)	0 (0.00%)	0 (0.00%)	8 (21.62%)
COLUMN TOTAL	**28 (75.68%)**	**6 (16.22%)**	**3 (8.11%)**	**37 (100.00%)**

p-value 0,005, X^2:18,293.
Source: Medical records database.

Figure 1.

Relationship between gestational age at birth and risk of osteopenia.



Source: Medical records database.

Table 3.

Relationship between Weight/Gestational Age and Risk of Osteopenia

WEIGHT/AGE	NO RISK	AT RISK	WITH OSTEOPENIA	TOTAL
APPROPRIATE	22 (88.00%)	1 (4.00%)	2 (8.00%)	25 (67.57%)
SMALL	6 (50.00%)	5 (41.67%)	1 (8.33%)	12 (32.43%)
COLUMN TOTAL	**28 (75.68%)**	**6 (16.22%)**	**3 (8.11%)**	**37 (100.00%)**

p-value 0,0133, X^2: 8,642.
Source: Medical records database.

Table 4.

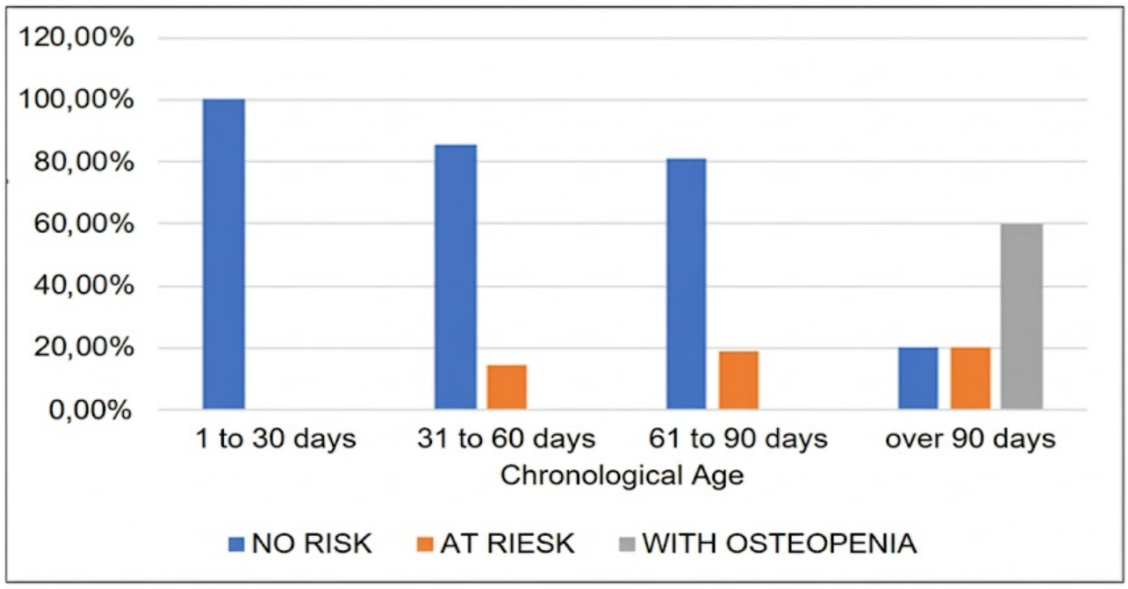
Relationship between Chronological Age and Risk of Osteopenia

CHRONOLOGICAL AGE	NO RISK	AT RISK	WITH OSTEOPENIA	TOTAL
1 TO 30 DAYS	2 (100.00%)	0 (0.00%)	0 (0.00%)	2 (5.41%)
31 TO 60 DAYS	12 (85.71%)	2 (14.29%)	0 (0.00%)	14 (37.84%)
61 TO 90 DAYS	13 (81.25%)	3 (18.75%)	0 (0.00%)	16 (43.24%)
OVER 90 DAYS	1 (20.00%)	1 (20.00%)	3 (60.00%)	5 (13.51%)
COLUMN TOTAL	**28 (75.68%)**	**6 (16.22%)**	**3 (8.11%)**	**37 (100.00%)**

p-value 0,0012, X^2: 22,121
Source: Medical records database.

Figure 2.

Relationship between chronological age and risk of osteopenia.



Source: Medical records database.

Regarding pharmacological management, 59.46% of the population received parenteral nutrition for more than 10 days, 29.73% received caffeine for 15 to 28 days, and 27.03% received glucocorticoids for more than 10 days. A statistical correlation (p = 0.0015) was found between glucocorticoid use and the risk of osteopenia (Table 5). Regarding diuretics, 16.22% of infants received them for 15 to 30 days, with hydrochlorothiazide being the most common (27.03%). Antiepileptic drugs were administered to 24.32% of the study population for more than 30 days.

Table 5.

Relationship between Days of Corticosteroid Therapy and Risk of Osteopenia

STEROID DAYS	NO RISK	AT RISK	WITH OSTEOPENIA	ROW TOTAL
0 DAYS	13 (86.67%)	2 (13.33%)	0 (0.00%)	15 (40.54%)
1 - 3 DAYS	5 (100.00%)	0 (0.00%)	0 (0.00%)	5 (13.51%)
4 - 10 DAYS	1 (14.29%)	3 (42.86%)	3 (42.86%)	7 (18.92%)
> 10 DAYS	9 (90.00%)	1 (10.00%)	0 (0.00%)	10 (27.03%)
COLUMN TOTAL	**28 (75.68%)**	**6 (16.22%)**	**3 (8.11%)**	**37 (100.00%)**

p-value 0,0015, X^2: 21,434.
Source: Medical records database.

For the diagnosis of osteopenia of prematurity based on serum levels, 83.78% of the study population presented normal calcium levels, while 56.76% showed high phosphorus levels. Concerning bone radiographic alterations and the risk of osteopenia, a statistically significant relationship was found (p = 0.0030), where radiographic changes detected 100% of the neonates with osteopenia of prematurity (Table 6).

Table 6.

Relationship between Presence of Radiographic Alterations and Risk of Osteopenia

RADIOGRAPHIC ALTERATIONS	NO RISK	AT RISK	WITH OSTEOPENIA	ROW TOTAL
NO	28 (77.78%)	6 (16.67%)	2 (5.56%)	36 (97.30%)
YES	0 (0.00%)	0 (0.00%)	1 (100.00%)	1 (2.70%)
COLUMN TOTAL	**28 (75.68%)**	**6 (16.22%)**	**3 (8.11%)**	**37 (100.00%)**

Statistical Significance: p-value 0.0030, $X^{2:}$ 11.648.
Source: Medical records database.

Regarding comorbidities associated with prematurity and the development of osteopenia, 29.73% of preterm infants presented necrotizing enterocolitis, 18.92% presented Grade III bronchopulmonary dysplasia (BPD), and 16.22% presented Grade II

BPD. No significant correlation was observed between the grade of BPD and the risk of osteopenia (p = 0.0683); however, these remain contributing factors to the development of the condition.

Among the infants studied, 89.19% initiated enteral feeding between the first and second day of life, and 62.16% were fed preterm infant formula. This is relevant as mineral content in breast milk, particularly for extremely preterm infants, is often insufficient, thereby increasing the risk of osteopenia.

DISCUSSION

This study determined the prevalence and factors associated with metabolic bone disease of prematurity (MBDP) through neonatal bone screening in three institutions between 2023 and 2025. Out of 340 preterm infants, screening was completed for 37 who met the selection criteria. It was found that 8.11% of this population presented with MBDP. These results are not consistent with the studies by Krithika or Lee, where MBDP occurred in 55% of extremely low birth weight infants (Krithika, 2022; Lee, 2022).

Regarding gestational age, MBDP occurred most frequently in the range of 28 to 32 weeks (61.11%). Concerning the relationship between gestational age at birth and the risk of osteopenia, a representative association was found with lower gestational age (p = 0.0055); results showed that 66.67% of patients at risk of osteopenia had a gestational age between 33 and 34 weeks. These findings are compatible with the studies by Perrone, where 47% of preterm infants under 28 weeks, 29% between 28 and 31 weeks, and 11% over 32 weeks developed MBDP (Perrone, 2022).

In relation to weight for gestational age, the most frequent indicator was adequate for gestational age (67.67%), and birth weight was primarily between 1000 and 1500 grams (40.54%). A significant association was found between weight for gestational age and the risk of osteopenia (p = 0.0133), where 41.67% of patients at risk of osteopenia were small for gestational age. These results are compatible with the studies by Hekimoğlu, who found that MBDP is associated with 69.2% of preterm infants with a birth weight of less than 1000 grams (Hekimoğlu, BS 2023).

A significant association was found between chronological age and osteopenia (p = 0.0001), identifying that 60% of preterm infants with osteopenia were older than 90 days. This result coincides with the studies by Hekimoğlu, which found that 88.5% of preterm neonates with MBDP were older than 14 days (Hekimoğlu BS, 2023).

Regarding radiographic changes, these were absent in 97.3% of the cases. However, a significant association was found between radiographic changes and osteopenia (p = 0.0006), as 100% of patients with osteopenia exhibited radiographic alterations. This result correlates with the studies by Kavurt S, which found that 50% of preterm neonates with MBDP showed radiological changes at 4 weeks of life (Kavurt, 2021).

Regarding the duration of corticosteroid use, the majority were administered for an interval of more than 10 days (27.03%). A significant association was found between the days of corticosteroid therapy and the risk of osteopenia (p = 0.0015), as 42.86% of patients at risk of osteopenia received corticosteroids for 4 to 10 days. These results coincide with the studies by Wang, where the use of corticosteroids increased the risk of osteopenia by 40% to 50% in preterm infants (Wang, 2022).

CONCLUSIONS

The present study contributes to the understanding of metabolic bone disease of prematurity (MBDP) by providing key information for the design of prevention

strategies.

Through neonatal bone screening, the prevalence and several factors associated with MBDP in newborns were determined. A lower prevalence of MBDP was identified compared to that reported in international studies, which may be attributed to a lack of screening across the majority of the susceptible population. This finding underscores the clinical importance of requesting screening studies for preterm infants at high risk for osteopenia.

The analysis of associated factors revealed that lower gestational age at birth, small weight for gestational age, higher chronological age, and the use of medications such as glucocorticoids are the primary influencers in the development of MBDP.

Regarding radiographic changes, it was found that all preterm neonates with osteopenia exhibited bone radiographic alterations. No statistically significant relationship was found concerning calcium and phosphorus levels, highlighting the importance of conducting composite screening as recommended by the American Academy of Pediatrics.

Finally, it is acknowledged that methodological limitations, such as the sample size of the study population, may have influenced the results. Consequently, further research is suggested to evaluate MBDP longitudinally and to analyze its prevalence and underlying determinants in greater depth.

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