Patient Safety & Quality Improvement Journal
http://psj.mums.ac.ir
PSQI

Incidence and Risk factors for Osteopenia of Prematurity in infants less than 32 weeks in Sulaimani Maternity Teaching Hospital

Banan Mohammed Nazdar[1]*, Alan Abdullah Abdulrahman[2]

1.Pediatric Neonatology, Department of Clinical Sciences, College of Medicine, University of Sulaimani, Sulaimani, Kurdistan Region, Iraq.
2. Branch of Clinical Sciences, College of Medicine, University of Sulaimani, Sulaymaniyah City, Kurdistan Region, Iraq.

ARTICLEINFO

Article type:
Research Paper

Article History:
Received: 26 Dec 2025
Accepted: 06 Jun 2026

Keywords:
Osteopenia of Prematurity, Preterm Infants, Very Low Birth Weight, Enteral Feeding, Total Parenteral Nutrition

ABSTRACT

Background:
This study aimed to determine the incidence and identify risk factors for osteopenia of prematurity in preterm infants born before 32 weeks of gestation.

methods:
This was a prospective cohort design in infants born before 32 weeks of gestation at Sulaimani Obstetrics and Gynecology Teaching Hospital in Iraq. All infants enrolled in the study were followed longitudinally. The target population included all preterm infants born at less than 32 weeks of gestational age, or weighing <1500g, and admitted to the Neonatal Intensive Care Unit (NICU) of the hospital. Maternal age, parity, pregnancy complications, antenatal steroid use, mod of delivery, Infant factors: gestational age, birth weight, Apgar score, respiratory support (need for mechanical ventilation, medications, and nutritional intake were measured. A p-value<0.05 was considered statistically significant.

Results:
The overall prevalence of OOP was 21.8%. Infants with OOP had significantly lower gestational age and birth weight (P≤0.001). Prolonged TPN duration (14.58±10.20 vs. 4.47±6.42 days; P≤0.006), delayed enteral feeding initiation (22.50±10.96 vs. 11.42±6.12 days; P≤0.005), and later supplementation (22.75±10.28 vs. 11.21±5.66 days; P≤0.005) were strongly associated with OOP. Higher rates of blood transfusion (83.3% vs. 31%; P≤0.005). Linear regression confirmed that lower gestational age (β=−0.553, P≤0.002), lower birth weight (β=−0.465, P≤0.001), and delayed enteral feeding (β=−0.534, P≤0.001) were significant independent predictors of OOP.

Conclusions:
OOP is prevalent in this cohort and is strongly linked to prematurity severity and postnatal nutritional practices. Early enteral feeding, minimizing prolonged Total parenteral nutrition, and vigilant biochemical monitoring (serum phosphorus and alkaline phosphatase) are critical preventive strategies.

► *Please cite this paper as:*
Nazdar B, Abdulrahman A. Incidence and Risk factors for Osteopenia of Prematurity in infants less than 32 weeks in Sulaimani Maternity Teaching Hospital. Journal of Patient Safety and Quality Improvement. 2026; 14(3): 169-181.
Doi: 10.22038/psj.2026.93837.1518

****Corresponding Author:*** E-mail: banan87@yahoo.com

Introduction

Metabolic bone disease of prematurity represents a spectrum of bone mineralization disorders in preterm infants (1). Osteopenia of prematurity (OOP) specifically denotes reduced bone mineral content relative to gestational age, typically manifesting as hypophosphatemia, elevated alkaline phosphatase, and radiological evidence of demineralization (2). This condition must be distinguished from osteoporosis, which describes a different pathophysiological process not applicable to the neonatal population studied herein (3).

The exact incidence of MBD has been reported differently in different centers, which may be due to a lack of consensus on the definition of MBD (4). MBD affects approximately 16 to 40 % of very low birth weight (birth weight less than 1,500 grams) and extremely low birth weight (birth weight less than 1,000 grams) infants (3). The prevalence of OOP in early postnatal life ranges from 2.5% to 50%, with higher incidence rates in extremely premature infants (5). Despite scientific and technological advances in the care of premature infants, the incidence of OOF remains high (6).

Risk factors for OOP include prematurity, low birth weight (1), Placental insufficiency, which occurs in preeclampsia and chorioamnionitis, impaired mineral transport in the uterus (7), late access to full enteral nutrition, Lack of calcium and phosphorus supplementation, inadequate vitamin D supplementation, and long-term use of parenteral nutrition (8). Identifying the risk factors for OOP will lead to the provision of specific therapeutic interventions for these premature infants and improve treatment outcomes (1).

There is no specific diagnostic method for MBD in premature infants. Clinical findings appear late and sometimes the diagnosis is missed. In fact, screening of individuals at risk for MBD is essential (3). Although the importance of early detection of MBD in premature infants is clear, there are significant differences in screening practices and facilities across regions. Infants with MBD had a lower gestational age and birth weight than control infants, and had longer durations of parenteral nutrition and hospitalization. Respiratory complications were significantly more common in high-risk infants compared with low-risk infants. Red blood cell transfusion is an independent risk factor for increased risk of MBD (6). The main clinical features of MBD in premature infants are elevated serum alkaline phosphatase (ALP) levels, hypophosphatemia, and skeletal hypomineralization (9).

Despite advances in neonatal care, the incidence of osteoporosis in preterm infants remains high, particularly in low-income settings where routine screening and preventive strategies may be limited. In Sulaymaniyah Maternity Teaching Hospital, there is a lack of comprehensive data on the prevalence of osteopenia in preterm infants and its associated risk factors. Prevention and early management of osteopenia can reduce short and long term complications like fracture and growth delay. It can provide basis for future managements of bone health more effectively in neonatal intensive care units. Without such data, it is challenging to develop effective strategies for its early detection, prevention, and management. Therefore, this study aimed to determine the incidence and identify risk factors for osteopenia of prematurity in preterm infants born before 32 weeks of gestation in this hospital and provide evidence that can inform clinical practices and neonatal care guidelines.

Materials and Methods

Study Design and Setting

This retrospective cohort study investigated the incidence and risk factors of osteopenia of prematurity in infants born before 32 weeks of gestation at Sulaimani Obstetrics and Gynecology Teaching Hospital.

Participants

The target population included all preterm infants born at less than 32 weeks of gestational age, or weighing <1500g, and admitted to the Neonatal Intensive Care Unit (NICU) of the hospital. Sample size was calculated using the formula for estimating a single proportion $n = Z^2p(1-p)/d^2$. Based on an anticipated OOP incidence of 22% from preliminary regional data, a sample of 55 infants provides 80% power to detect this prevalence with a 95% confidence interval width of ±11% ($Z = 1.96$, $p = 0.22$, $d = 0.11$). This sample size also allows detection of moderate effect sizes for key risk factors with acceptable statistical power.

Participants were included if they met the following criteria: Preterm infants born <32 weeks gestational age, birth weight <1500g, admitted to NICU within first 48 hours of life, and availability of complete medical records including biochemical and radiological data relevant to bone health.

Participants were excluded if they had: major congenital anomalies, infants with sever metabolic or renal disorders affecting bone health, infants transferred from other hospitals with incomplete data, and neonates who died before bone assessment could be completed.

Data Collection

Data were extracted from medical records of preterm neonates admitted to the NICU. Infants meeting inclusion criteria were identified, and their clinical parameters, laboratory values, and radiological findings were systematically reviewed to reconstruct their longitudinal clinical course from birth through bone health assessment. A structured data collection instrument was employed to extract pertinent maternal and neonatal variables, which included gestational age, birth weight, gender, multiple gestation, maternal health conditions, mode of delivery, and exposure to antenatal steroids. Additional neonatal parameters such as the duration of total parenteral nutrition (TPN), the timing of initiation of enteral feeding and supplementation, type of feeding, neonatal morbidities, and biochemical markers (specifically serum alkaline phosphatase and phosphorus levels) were also documented. The diagnosis of osteopenia of prematurity (OOP) was established based on radiological assessments and biochemical criteria. All data underwent thorough review and verification by the research team to ensure both accuracy and completeness prior to the execution of statistical analyses.

Statistical Analysis

Data were subjected to SPSS software, version 25.0. Descriptive statistics were employed to succinctly encapsulate the demographic and clinical characteristics of the cohort under investigation. Continuous variables were articulated as mean ± standard deviation (SD), while categorical variables were delineated as frequencies and percentages. The Chi-square test or Fisher's exact test was utilized to evaluate associations among categorical variables, whereas the independent sample t-test was implemented for the comparison of continuous variables across distinct groups.

A binary logistic regression analysis was conducted to elucidate independent risk factors correlated with OOP. Variables exhibiting a P-value ≤ 0.05 in the univariate analysis were incorporated into the multivariate model. Odds ratios (OR) along with 95% confidence intervals (CI) were computed to gauge the strength of these associations. A P-value ≤ 0.05 was deemed statistically significant for all analytical procedures undertaken.

Ethical Considerations

This investigation was undertaken in accordance with the ethical standards delineated in the Declaration of Helsinki. Ethical clearance was secured from the Ethics Committee of Sulaimani Teaching Hospital and the College of Medicine, University of Sulaimani (approval number: SUMH/REC/2023/187). Given that the study was retrospective and predicated on pre-existing medical records, the requirement for informed consent from parents or guardians was abrogated by the committee. All patient information was anonymized prior to analysis to uphold confidentiality and safeguard privacy. The data acquired were utilized exclusively for research objectives, and no identifying information was revealed in any publication or presentation derived from this research.

Results

The gestational age mean ± SD of the infants with no OOP was 29.60 ± 1.720weeks whereas in OOP group it was 26.58 ± 2.23 weeks. The mean ± SD gestational age in the two groups was statistically different (P ≤ 0.001). The mean birth weight (± SD) of the No OOP group was 1172 ± 228.922 grams, and 888.33 ± 155.787 in the OOP group. The difference was found to be significant as well (P ≤ 0.001).

There were 19 (44.2%) males and 24 (55.8%) females in the No OOP and 8 (6.7%) and 4 (33.3%) males and females respectively in the OOP cohort. In the case of intrauterine growth restriction (IUGR), 3 (7%) infants in the No OOP and 2 (16.7%) of the OOP groups were affected. With regard to maternal factors, 16 (37.2%) mothers in the No OOP group had Multiple Gestation, and 27 mothers (62.8%) in the No OOP group did not. Conversely, the entire group of 12 (100 %) mothers of the OOP group no multiple gestations. Multiple gestations among the two groups differed statistically (P ≤ 0.027) (Table 1).

Table.1: Infant demographics of Prematurity in infants less than 32 weeks

Variable		Group		P-value*
		No OOP (n=43)	OOP (n=12)	
Gestational age (weeks)		29.60 ± 1.720**	26.58 ± 2.234	0.001
Birth weight (in grams)		1172 ± 228.922	888.33 ± 155.787	0.001
Gender	Male	19 (44.2%)&	8 (66.7%)	0.168
	Female	24 (55.8%)	4 (33.3%)	
IUGR	Yes	3 (7%)	2 (16.7%)	0.574
	No	40 (93%)	10 (83.3%)	
Multiple Gestation	Yes	16 (37.2%)	0	0.027
	No	27 (62.8%)	12 (100%)	
Mode of delivery	NVD	19 (44.2%)	9 (75%)	0.058
	Emergency CS	24 (55.8%)	3 (25%)	

*P-value based on Independent Samples t-test and chi square (Fisher exact test), ** Mean ± SD, & Frequency (%)

The mean ± SD maternal age of delivery in the No OOP was 31.42 ± 6.204years, and in the OOP group was 34.42 ± 7.179 years The maternal age of the two groups did not differ significantly. The No OOP group included 24 (55.8%) healthy, 8 (18.6%) diabetic, 3 (7.0%) diabetic and hypertension, 7 (16.3%) hypertension and 1 (2.3%) hypertension and preeclampsia in combination. 5 (41.7%) mothers in the OOP group were healthy, 2 (16.7%) had diabetes, 1 (8.3%) had both diabetes and hypertension, 1 (8.3%) had diabetes and preeclampsia, and 3 (25%) had hypertension. The maternal health conditions of the two groups did not differ significantly. The use of antenatal steroids was reported in 20 (46.5%) No OOP group mothers and 3 (25%) OOP group mothers. Also, 31 (72.1%) mothers in the No OOP group and 9 (75%) mothers in the OOP group had a history of receiving Calcium/Vit D during pregnancy, and there was no significant difference in the history of receiving Calcium/Vit D between the mothers in the two groups. (Table 2).

Table.2: Maternal and Antenatal history of Prematurity in infants less than 32 weeks

Variable	Group		P-value*
	No OOP	OOP	

		(n=43)	(n=12)	
Maternal age at delivery (in years)		31.42 ± 6.204**	34.42 ± 7.179	0.207
Maternal health conditions	Healthy	24 (55.8%)&	5 (41.7%)	0.469
	Diabetes	8 (18.6%)	2 (16.7%)	
	Diabetes/ Hypertension	3 (7%)	1 (8.3%)	
	Diabetes/ Preeclampsia	0	1 (8.3%)	
	Hypertension	7 (16.3%)	3 (25%)	
	Hypertension/ Preeclampsia	1 (2.3%)	0	
Antenatal steroid administration	Took steroid	20 (46.5%)	3 (25%)	0.321
	No. steroid	23 (53.5%)	8 975%)	
Maternal tonic use	Received Calcium/Vit D	31 (72.1%)	9 (75%)	N/S
	No taking Calcium/Vit D	12 (27.9%)	3 (25%)	

*P-value based on Independent Samples t-test and chi square (Fisher exact test), ** Mean ± SD, & Frequency (%)

The difference in infants morbidities was quite marked in the two groups (P ≤ 0.005). In No OOP group, 7 (16.3%) infants were free of comorbidities, 21 (48.8%) had respiratory distress syndrome (RDS), 3 (7%) had RDS/ CLD, 1 (2.3%) had Respiratory distress RDS/ CLD/ NEC, 1 (2.3%) mother RDS/ CLD/ Sepsis , 7 (16.3%) mother had Respiratory RDS/ NEC , 2 (4.7%) mother had RDS/ Sepsis and 1 (2.3%) mother had RDS/ IVH . In the OOP group, 3 (25.0%) mothers had RDS, 1 (8.3%) mother had RDS with CLD, 3 (25%) mothers had RDS with CLD with NEC and sepsis, 1 (3.8%) mother RDS/ CLD/ Sepsis, 2 (16.7%) mothers had RDS/ NEC and 2 (16.7%) mother had RDS/NEC /sepsis. The mean ± SD length of total parenteral nutrition (TPN) was 4.47 ± 6.41 days in the No OOP and 14.58 ± 10.20 days in OOP. The TPN duration in the two groups was found not to be similar (P<0.006) (Table 3).

Table.3: Neonatal factors of Prematurity in infants less than 32 weeks

Variable		Group		P-value*
		No OOP (n=43)	OOP (n=12)	
Neonatal morbidities	None	7 (16.3%) &	0	0.005
	Respiratory distress syndrome (RDS)	21 (48.8%)	3 (25%)	
	Respiratory distress syndrome (RDS)/ Chronic lung disease (CLD)	3 (7%)	1 (3.8%)	
	Respiratory distress syndrome (RDS)/ Chronic lung disease (CLD)/ Necrotizing enterocolitis (NEC)	1 (2.3%)	0	
	Respiratory distress syndrome (RDS)/ Chronic lung disease	0	3 (25%)	

	(CLD)/ Necrotizing enterocolitis (NEC)/ Sepsis			
	Respiratory distress syndrome (RDS)/ Chronic lung disease (CLD)/ Sepsis	1 (2.3%)	1 (3.8%)	
	Respiratory distress syndrome (RDS)/ Necrotizing enterocolitis (NEC)	7 (16.3%)	2 (16.7%)	
	Respiratory distress syndrome (RDS)/ Necrotizing enterocolitis (NEC)/ Sepsis	0	2 (16.7%)	
	Respiratory distress syndrome (RDS)/ Sepsis	2 (4.7%)	0	
	Respiratory distress syndrome (RDS)/ Intraventricular hemorrhage (IVH)	1 (2.3%)	0	
Use of diuretics	Used	5 (11.6%)	4 (33.3%)	0.092
	Not used	38 (88.4%)	8 (66.7%)	
Use of Caffein	Used	35 (81.4%)	12 (100%)	0.178
	Not used	8 (18.6%)	0	
Duration of total parenteral nutrition (TPN)		4.47 ± 6.416**	14.58 ± 10.202	0.006

*P-value based on Independent Samples t-test and chi square (Fisher exact test), ** Mean ± SD, & Frequency (%)

In the No OOP group, 4 (9.3%) infants were fed exclusively with breast milk, 18 (41.9%) received preterm formula, and 21 (48.8%) received a combination of breast milk and formula. In the OOP group, 3 (25%) infants were fed breast milk, 5 (41.7%) received preterm formula, and 4 (33.3%) received combination feeding. The type of nutrition during hospital stay did not differ significantly between the two groups. The mean ± SD time to start enteral feeding was 11.42 ± 6.12 days after birth in the No OOP group and 22.50 ± 10.96 days in the OOP group, showing a statistically significant difference (P ≤ 0.005). Similarly, the mean ± SD time to start nutritional supplementation was 11.21 ± 5.66 days in the No OOP group and 22.75 ± 10.28 days in the OOP group, with a statistically significant difference between the groups (P ≤ 0.003) (Table 4).

Table.4: Feeding and nutrition of Prematurity in infants less than 32 weeks

Variable		Group		P-value*
		No OOP (n=43)	OOP (n=12)	
Type of nutrition during hospital stay	Breast milk	4 (9.3%) &	3 (25%)	0.324
	Preterm formula	18 (41.9%)	5 (41.7%)	
	Combination	21 (48.8%)	4 (33.3%)	
Time of starting enteral feeding (postnatal age in days)		11.42 ± 6.123**	22.50 ± 10.959	0.005
Time of starting supplementation (in days)		11.21 ± 5.659	22.75 ± 10.279	0.003

*P-value based on Independent Samples t-test and chi square (Fisher exact test), ** Mean ± SD, & Frequency (%)

In the No OOP group, 10 (23.3%) mothers and OOP group, 5 (41.7%) mothers experienced a history of preterm rupture of membranes (PROM). 13 (31%) infants in No OOP group and 10 (83.3%) infants in OOP group had a history of blood transfusion which was also statistically significant (P ≤ 0.002). The radiological evaluation demonstrated that 8 (66.7 %) of the infants in the OOP group showed positive results of the osteopenia radiology, and 4 (33.3%) infants were without the osteopenia radiology. Meanwhile, all the infants in the No OOP cohort had negative radiological evidence of osteopenia. The result of osteopenia on imaging varied considerably among the groups (P ≤ 0.001). The mean ± SD ALP level of the infants in No OOP cohort was lower than 500 U/L. In OOP group, 4 (33.3%) infants had an ALP level of less than 500 U/L, and 8 (66.7%) neonates had above 500 U/L. The ALP levels between the two groups was statistically significant (P ≤ 0.001).

The mean ± SD serum phosphorus level was 6.11 ± 0.79 mg/dL in the No OOP group and 3.45 ± 0.78 mg/dL in the OOP group which was statistically significant (P ≤ 0.001). According to the results, 43 infants (100%) infants in the No OOP group had been found to be at high risk of osteopenia, and in the OOP group, 8 (66.7%) and 4 (33%) infants were diagnosed with severe and mild osteopenia, respectively And the type of osteopenia in the two groups had a statistically significant difference (P ≤ 0.001). (Table 5).

Table.5: Feeding, nutrition and radiological evidence of osteopenia of Prematurity in infants less than 32 weeks

Variable		Group: No OOP (n=43)	Group: OOP (n=12)	P-value*
PROM	Yes	10 (23.3%) &	5 (41.7%)	0.274
	No	33 (76.7%)	7 (58.3%)	
Blood transfusion	Yes	13 (31%)	10 (83.3%)	0.002
	No	29 (69%)	2 (16.7%)	
Presence of radiological evidence of osteopenia	Positive radiological finding	0	8 (66.7%)	0.001
	Negative radiological finding	43 (100%)	4 (33.3%)	
Alkaline phosphate (ALP) level (U/L)	Less than 500	43 (100%)	4 (33.3%)	0.001
	More than 500	0	8 (66.7%)	
Serum phosphorus (mg/dl)		6.109 ± 0.786**	3.450 ± 0.775	0.001
Group	Sever osteopenia	0	8 (66.7%)	0.001
	Mild osteopenia	0	4 (33.3%)	
	high risk for osteopenia	43 (100%)	0	

*P-value based on Independent Samples t-test and chi square (Fisher exact test), ** Mean ± SD, & Frequency (%)

Fifty-five preterm infants born at less than 32 weeks' gestational age were divided into three groups according to their serum alkaline phosphatase (ALP) activity, serum phosphorus levels, and radiological findings. Infants with ALP > 500 IU/L, phosphorus < 4.5 mg/dL, and radiological evidence of bone changes were classified as Group 1 (severe osteopenia). Those with ALP < 500 IU/L, phosphorus < 4.5 mg/dL, and no radiological abnormalities were categorized as Group 2 (mild osteopenia). Infants with ALP < 500 IU/L and phosphorus levels between 4.5 and 5.0 mg/dL, irrespective of radiological findings, were designated as the high-risk-for-osteopenia group (Table 6).

Table.6: Category of Prematurity in infants less than 32 weeks

Group		No. %
Groups	Group 1: Sever osteopenia: ALP>500 + phosphorus < 4.5 + radiological finding	8 (14.5%)
	Group 2: Mild osteopenia: ALP < 500 + phosphorus < 4.5 with no radiological finding	4 (7.3%)
	Group 3: high risk for osteopenia: ALP < 500 + phosphorus > 4.5-5	43 (78.2%)

The mean ± SD time to initiation of enteral feeding was 26.00 ± 11.50 days after birth in the severe osteopenia group, 15.50 ± 5.80 days in the mild osteopenia group, and 11.42 ± 6.12 days in the high-risk group, showing a statistically significant difference among the three groups (P ≤ 0.001). Similarly, the mean ± SD age at initiation of mineral supplementation was 25.25 ± 11.35 days in the severe osteopenia group, 17.25 ± 6.08 days in the mild osteopenia group, and 11.21 ± 6.66 days in the high-risk group, also demonstrating a significant intergroup difference (P ≤ 0.001).

The type of nutrition during hospitalization differed significantly across the groups (P ≤ 0.001). In the severe osteopenia group, 3 (37.5%) infants received exclusive breast milk, while 5 (62.5%) were fed preterm formula. All infants in the mild osteopenia group received a combination of breast milk and formula. In the high-risk group, 4 (9.3%) infants were exclusively breastfed, 18 (41.9%) received only preterm formula, and 21 (48.8%) were given a combination of both feeding types.

A history of preterm rupture of membranes (PROM) was reported in 4 (50.0%) mothers of infants with severe osteopenia, 1 (25.0%) in the mild osteopenia group, and 10 (23.3%) in the high-risk group. Blood transfusion was required in 7 (87.5%) infants in the severe osteopenia group, 3 (75.0%) in the mild osteopenia group, and 13 (31.0%) in the high-risk group, a statistically significant difference among the groups (P ≤ 0.003) (Table 7).

Table.7: Feeding and nutrition of Prematurity in infants less than 32 weeks

Variable	Group			P-value*
	Sever osteopenia (n=8)	Mild osteopenia (n=4)	High risk for osteopenia (n=43)	

Time of starting enteral feeding (postnatal age in days)		26 ± 11.502**	15.50 ± 5.802	11.42 ± 6.123	0.001
Time of starting supplementation (in days)		25.25 ± 11.348	17.25 ± 6.076	11.21 ± 6.659	0.001
Type of nutrition during hospital stay	Breast milk	3 (37.5%) &	0	4 (9.3%)	0.004
	Preterm formula	5 (62.5%)	0	18 (41.9%)	
	Combination	0	4 (100%)	21 (48.8%)	
PROM	Yes. OOP	4 (50%)	1 (25%)	10 (23.3%)	0.241
	No. OOP	4 (50%)	3 (75%)	33 (76.7%)	
Blood transfusion	Yes	7 (87.5%)	3 (75%)	13 (31%)	0.003
	No	1 (12.5%)	1 (25%)	29 (69%)	

*P-value based on Independent Samples t-test and chi square (Fisher exact test), ** Mean ± SD, & Frequency (%)

Binary logistic regression analysis confirmed that lower gestational age (adjusted OR 0.48 per additional week, 95% CI 0.29–0.79, P = 0.004), lower birth weight (adjusted OR 0.99 per additional gram, 95% CI 0.994–0.999, P = 0.012), absence of multiple gestation (adjusted OR 3.82, 95% CI 1.15–12.68, P = 0.029), delayed initiation of enteral feeding (adjusted OR 1.18 per additional day, 95% CI 1.06–1.32, P = 0.003), and delayed mineral supplementation (adjusted OR 1.21 per additional day, 95% CI 1.08–1.36, P = 0.001) were significant independent predictors of OOP (Table 8).

Table 8: Independent predictors of osteopenia of prematurity identified by binary logistic regression analysis

Variable	Standardized Coefficients β	P-value*, CI: 95%
Gestational age (weeks)	- 0.553	0.002, - 0.061 – - 0.014
Gender	0.098	0.395, - 0.109 – 0.271
IUGR	- 0.118	0.366, - 0.544 – 0.204
Multiple Gestation	0.331	0.014, 0.064 – 0.538
Birth weight (in grams)	- 0.465	0.001, - 0.00 – - 0.001
Maternal age	- 0.089	0.473, - 0.022 – 0.010
Mode of delivery	0.267	0.051, - 0. 001 – 0.445
Type of nutrition during hospital stay	0.174	0.203, - 0.059 – 0.269
Time of starting enteral feeding	- 0.534	0.001, - 0.037 - - 0.014
Time of starting supplementation	- 0.577	0.001, - 0.040 - - 0.018

*P-value based on Binary regression

Discussion

The current study has been done to ascertain the incidence of osteopenia of prematurity (OOP) among infants whose gestation period is low (less than 32 weeks) and to determine the maternal and neonatal risk factors. The occurrence of OOP was determined as 21.8% in this study which is considered to be a major concern in handling high-risk babies. Statistical comparison indicated that there were considerable differences between the affected and unaffected groups of demographic risk factors, particularly, the low gestational age and low birth weight. Length of TPN and late initiation of enteral feeding were the most significant risk factors that were both found to be statistically significant risk factors in predicting OOP. Moreover, this complication was related to differences in neonatal comorbidities and a high rate of transfusion in the OOP group as the indicators of the severity of the underlying disease. The diagnosis was also associated with biochemical results with the mean serum phosphorus in the OOP category depicting hypophosphatemia, and ALP exceeding 500 U/L in at-risk infants.

In our study, 12 out of 55 (21.8) children with a gestational age of less than 32 weeks had osteopenia, 8 (66.7%) of which were severe cases and 4 (33.3%) mild cases. To a large extent, this observation is in line with other studies that have been conducted in other locations. In the study of D Angelika et al. (10) in 30 infants with less than 32 weeks and birth weight less than 1500 g, the prevalence has been stated to be 43%, which is more than our results. Such a difference might be explained by the fact that in the study phosphate supplementation in the parenteral nutrition was impossible, whereas in our study, it was local factors, including nutritional limitations, and comorbidities that were considered. In the study by MT Abd El Latif (11) close to the findings in the current study, that demonstrated a prevalence of 21.9% on less than 32 weeks of age and under 1500 grams of weight, which indicates the effect of low birth weight and late enteral nutrition, the role of low birth weight and late enteral nutrition is highlighted.

In addition, in the study by AM Saleem et al. (12) aimed to examine the radiographic changes of the wrist and arm and compare it to the assessment of ALP as a predictor of MBD, the probability of OOP was similar to that of the present study. Nevertheless, the incidence of OOP varies across different studies, including the incidence of OOP of 12 per cent in the study by E Ruiz et al. (13) in Colombia and the incidence of OOP of 52 % in the research by BS Hekimooglu (14) in Turkey. Nonetheless, these similarities and differences denote that OOP is an international issue of concern in premature infants care and cannot be restricted to a particular geographical area.

The findings of the present study clearly indicate that demographic and clinical risk factors clearly associated with defective bone mineralization were also prevalent in this population. The difference in gestational age and birth weight was significantly different between infants with and without OOP. Infants born with OOP were three weeks earlier and had lesser birth weights, and the mean gestational age, and mean birth zone were higher in the non-OOP group. This difference supports the pathophysiology of OOP underlying the idea that as prematurity and low birth weight increase, mineral reserves become lower, and the dependence on postnatal nutritional support increases to achieve the required mineralization levels, which is achieved in utero (15, 16). Babies of these gestational ages (26 weeks on average) have literally lost the chance to build calcium and phosphorus throughout the third trimester and are now vulnerable to reduced bone density (17).

Linear regression analysis showed the significance of GA as the risk factor of osteopenia and the incidence of osteopenia increases with a decrease in GA; these results are consistent with the research of Debere et al. (2022) and Alda et al. (2025) (18, 19), who resulted in lower GA as the key predictor of OOP. A higher GA is therefore considered to be a protective factor. Birth weight was also reported to be a significant determinant of child-bearing OOP, with increased birth weight being associated with low osteopenia risks. This finding is consistent with the previous studies (20, 21), which found that infants born with VLBW have a comparatively increased risk of OOP.

The findings of the current investigation demonstrated that the duration of reliance on TPN was markedly prolonged in the OOP cohort, nearly threefold compared to the non-OOP cohort. This observation aligns with the conclusions drawn from the research conducted by D Angelika et al. (22), which posited that prolonged TPN serves as the most significant acquired risk factor for OOP. Another scholarly work indicated a relative risk of 5.40 for TPN exceeding 15 days (10), potentially attributable to the constraints associated with the physical solubility of calcium and phosphorus within TPN formulations that hinder the comprehensive fulfillment of skeletal mineral requirements (23), or the absence of mechanical intestinal stimulation through enteral nutrition (EN), which may adversely affect mineral absorption and the stimulation of osseous growth (24). These results underscore the critical necessity of clinical protocols aimed at the prompt initiation of enteral feeding and the mitigation of TPN reliance.

The assessment of OOP frequently necessitates an integrative approach encompassing clinical, biochemical, and radiological evaluations (25). This investigation validated the effectiveness of these biomarkers through the quantification of phosphorus and ALP concentrations in neonates. The findings indicated that the serum phosphorus and ALP concentrations exhibited significant disparities between the two cohorts. The average serum phosphorus concentration was notably reduced in neonates categorized within the OOP group compared to those in the non-OOP group. This observation may hold considerable significance, as diminished serum phosphorus is recognized as one of the most robust biochemical indicators of OOP, while phosphorus deficiency constitutes a critical element in the pathophysiology of metabolic bone disease of prematurity (MBDP) (26, 27).

Infants in the non-OOP group had an ALP level below 500 U/L, about 2/3 of the infants who received OOP had higher levels than 500 U/L. This statistically significant difference supports the use of 500 U/L as an effective discriminant to identify infants at increased risk as a part of this population (28).

The only paradoxical finding in this analysis was that OOP cases in infants whose mothers had a history of more than one birth were non-existent. Usually, the multiples are associated with heightened prematurity and intrauterine growth restriction only risk factors of OOP (29, 30). This inability is probably associated with the stochasticity of sampling in a small population, and a small sample size. Therefore, bigger regional studies should be done to expand on this counter-intuitive relationship. The findings of this research clearly were able to establish the main factors that were modifiable in the postnatal period.

Among the main limitations of this study was one of the not so large sample groups of infants with OOP. This weakness especially those in the estimation of maternal risk determinants spurred a reduction in statistical power that would be necessary to establish more tenuous associations and therefore could have concealed the establishment of bona fide maternal risk determinants. In addition to that, the unicenter nature of the study implied that the derived results were conditional upon the definite managerial and therapeutic protocols used in the discussed NICU. The significantly high rate of late enteral feeding suggests the urgency of evaluation and possible revision of local programs that regulate the process of feeding intolerance management.

Conclusion

The results of this study showed that the incidence of OOP was to be 21.8% that matches the world neonatal and population health statistics. The results highlight that very low birth weight and the low gestational age are the main demographic risk factors. More to the point, the researchers have also determined modifiable postnatal determinants, namely, the length of TPN and the major delays in the commencement of enteral feeding and supplementation. Also, there was a strong correlation between OOP and repeated blood transfusion requests and severity of co-morbid neonatal morbidities, such as combinations of RDS, chronic lung disease, NEC, and sepsis, which revealed the necessity of more intensive clinical care. The paper also showed that biochemical monitoring is useful in the diagnosis of OOP, and the results of serum ALP and phosphorus levels are reliable indicators of early diagnosis and screening.

Acknowledgments

Our sincere gratitude goes out to all those who contributed their time, effort and expertise to make this study a success.

Conflict of interest

All authors declare no conflict of interest.

Data availability

On demand, the data from the research is made available to the corresponding author.

Authors' contributions

Each author contributed equally in this research work.

Funding

Not applicable.

References

1. Ukarapong S, Venkatarayappa SKB, Navarrete C, Berkovitz G. Risk factors of metabolic bone disease of prematurity. Early human development. 2017;112:29-34. doi: 10.1016/j.earlhumdev.2017.06.010.
2. Rustico SE, Calabria AC, Garber SJ. Metabolic bone disease of prematurity. Journal of clinical & translational endocrinology. 2014;1(3):85-91. doi: 10.1016/j.jcte.2014.06.004.
3. Faienza MF, D'Amato E, Natale MP, Grano M, Chiarito M, Brunetti G, et al. Metabolic bone disease of prematurity: diagnosis and management. Frontiers in pediatrics. 2019;7:143. doi: 10.3389/fped.2019.00143.
4. Gaio P, Verlato G, Daverio M, Cavicchiolo ME, Nardo D, Pasinato A, et al. Incidence of metabolic bone disease in preterm infants of birth weight< 1250 g and in those suffering from bronchopulmonary dysplasia. Clinical Nutrition ESPEN. 2018;23:234-9. doi: 10.1016/j.clnesp.2017.09.008.
5. Costa R, Franco C, Santos N, Maio P, Vieira F, Antunes S, et al. Metabolic Bone Disease of Prematurity in Very Low Birthweight Infants: Retrospective Observational Study. Acta Médica Portuguesa. 2019;32(7-8):536-41. doi: 10.20344/amp.10994.
6. Avila-Alvarez A, Urisarri A, Fuentes-Carballal J, Mandiá N, Sucasas-Alonso A, Couce ML. Metabolic bone disease of prematurity: risk factors and associated short-term outcomes. Nutrients. 2020;12(12):3786. doi: 10.3390/nu12123786.
7. Chin LK, Doan J, Teoh YS, Stewart A, Forrest P, Simm PJ. Outcomes of standardised approach to metabolic bone disease of prematurity. Journal of paediatrics and child health. 2018;54(6):665-70. doi: 10.1111/jpc.13813.
8. Chen W, Yang C, Chen H, Zhang B. Risk factors analysis and prevention of metabolic bone disease of prematurity. Medicine. 2018;97(42):e12861. doi: 10.1097/MD.0000000000012861.
9. Yan-Mei C, Xin-Zhu L, Rong Z, Xi-Hong L, Xiao-Mei T, Ping-Yang C, et al. Expert consensus on clinical management of metabolic bone disease of prematurity (2021). Zhongguo Dang dai er ke za zhi= Chinese Journal of Contemporary Pediatrics. 2021;23(8):761-72. doi: 10.7499/j.issn.1008-8830.2105152.
10. Angelika D, Etika R, Mapindra MP, Utomo MT, Rahardjo P, Ugrasena DIG. Associated neonatal and maternal factors of osteopenia of prematurity in low resource setting: A cross-sectional study. Annals of Medicine and Surgery. 2021;64. doi: 10.1016/j.amsu.2021.102235.
11. Abd El Latif MT, Abougabal AMSH, Saad KM, Akl HAA. Cross-sectional study of osteopenia of prematurity and associated risk factors. Alexandria Journal of Pediatrics. 2018;31(2):67-75. doi: 10.4103/ajop.Ajop_16_18.
12. Saleem AM, Alsayed LM, Ahmed IA, Rezk NA. Biochemical Markers and Radiological Findings in Premature Osteopenic Neonates. The Egyptian Journal of Hospital Medicine. 2022;87(1):2038-45. doi: 10.21608/ejhm.2022.232262.
13. Ruiz E, Piamonte DE, Gómez DT, Díaz LA, Pérez LA. Incidence of metabolic bone disease in neonates under 32 gestational weeks at the Hospital Universitario de Santander in Colombia. Biomédica. 2024;44(1):35-44. doi: 10.7705/biomedica.6926
14. Hekimoğlu BS. Risk factors and clinical features of osteopenia of prematurity: Single-center experience. Trends in Pediatrics. 2023;4(1):24-30. doi: 10.59213/TP.2023.46220.
15. Merzah M, Al-Dayyeni H, Salman K. Role of Serum Alkaline Phosphatase in Osteopenia of Premature Infants. European Journal of Medical and Health Research. 2025;3:34-40. doi: 10.59324/ejmhr.2025.3(4).06.
16. Tabatabaei RS, Mirjalili SR, Ashrafi A, Shamsi F. The relationship between maternal vitamin D levels and osteopenia development in preterm infants: A cross-sectional study. International Journal of Reproductive BioMedicine (IJRM). 2025;22. doi: 10.18502/ijrm.v22i11.17818.
17. Farias PM, Marcelino G, Santana LF, de Almeida EB, Guimarães RCA, Pott A, et al. Minerals in Pregnancy and Their Impact on Child Growth and Development. Molecules. 2020;25(23). Epub 20201130. doi: 10.3390/molecules25235630.
18. Alda MG, Wood AG, MacDonald T, Charlton JK. Care of neonates following in-utero growth restriction: A prospective cohort study exploring neonatal morbidity. Journal of Perinatology.

2025;45(9):1219-25. doi: 10.1038/s41372-025-02397-9.
19. Debere MK, Haile Mariam D, Ali A, Mekasha A, Chan GJ. Factors associated with small-for-gestational-age births among preterm babies born <2000 g: a multifacility cross-sectional study in Ethiopia. BMJ Open. 2022;12(11):e064936. doi: 10.1136/bmjopen-2022-064936.
20. Chin L, Doan J, Teoh Y, Stewart A, Forrest P, Simm P. Outcomes of standardised approach to metabolic bone disease of prematurity: Metabolic bone disease of prematurity. Journal of Paediatrics and Child Health. 2018;54. doi: 10.1111/jpc.13813.
21. Kumar M, Ali A, Khan MA, Sohail S, Saleem SM, Khan M, et al. Relationship of caffeine regimen with osteopenia of prematurity in preterm neonates: a cohort retrospective study. BMC Pediatrics. 2022;22(1):437. doi: 10.1186/s12887-022-03493-x.
22. Angelika D, Ugrasena IDG, Etika R, Rahardjo P, Bos AF, Sauer PJJ. The incidence of osteopenia of prematurity in preterm infants without phosphate supplementation: A prospective, observational study. Medicine (Baltimore). 2021;100(18):e25758. doi: 10.1097/md.0000000000025758.
23. Watrobska-Swietlikowska D. Compatibility of Maximum Inorganic and Organic Calcium and Phosphate Content in Neonatal Parenteral Solutions. Scientific Reports. 2019;9(1):10525. doi: 10.1038/s41598-019-46987-y.
24. Hossain Z, Qasem WA, Friel JK, Omri A. Effects of Total Enteral Nutrition on Early Growth, Immunity, and Neuronal Development of Preterm Infants. Nutrients. 2021;13(8):2755. doi: 10.3390/nu13082755.
25. Cromwell L, Breznak K, Young M, Kasangottu A, Leonardo S, Markel C, et al. Reducing Osteopenia of Prematurity-related Fractures in a Level IV NICU: A Quality Improvement Initiative. Pediatric Quality & Safety. 2024;9(2):e723. doi: 10.1097/pq9.0000000000000723.
26. Chover Martínez C, Portolés Morales M, Sáenz González P, Solaz García Á. The paradox of MBD, we know how to treat it but we don't know how to diagnose it. Anales de Pediatría (English Edition). 2025;102(5):503801. doi: https://doi.org/10.1016/j.anpede.2025.503801.
27. Raju S, Saxena R. Hyperphosphatemia in Kidney Failure: Pathophysiology, Challenges, and Critical Role of Phosphorus Management. Nutrients. 2025;17(9):1587. doi: 10.3390/nu17091587.
28. Rayannavar A, Calabria AC. Screening for Metabolic Bone Disease of prematurity. Seminars in Fetal and Neonatal Medicine. 2020;25(1):101086. doi: https://doi.org/10.1016/j.siny.2020.101086.
29. Batsry L, Matatyahu N, Avnet H, Weisz B, Lipitz S, Mazaki-Tovi S, et al. Perinatal outcome of monochorionic diamniotic twin pregnancy complicated by selective intrauterine growth restriction according to umbilical artery Doppler flow pattern: single-center study using strict fetal surveillance protocol. Ultrasound in Obstetrics & Gynecology. 2021;57(5):748-55. doi: https://doi.org/10.1002/uog.22128.
30. Seetho S, Kongwattanakul K, Saksiriwuttho P, Thepsuthammarat K. Epidemiology and factors associated with preterm births in multiple pregnancy: a retrospective cohort study. BMC Pregnancy and Childbirth. 2023;23(1):872. doi: 10.1186/s12884-023-06186-0.