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PREMATÜRE KIRIKLARI VE İLİŞKİLİ FAKTÖRLERİN İNCELENMESİ: BİR VAKA-KONTROL ÇALIŞMASI

FRACTURES OF PREMATURITY AND ASSOCIATED FACTORS: A CASE-CONTROL STUDY

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ÖZET

AMAÇ: Preterm yenidoğanların doğumda ve doğumdan sonra yaşadıkları süreçler iskelet büyümesini ve kemik mineralizasyonunu etkileyebilir. Bu çalışmada Yenidoğan Yoğun Bakım Ünitesi'ne kabul edilen prematüre bebeklerde meydana gelen kırıkların değerlendirilmesi ve bazı özelliklerle ilişkisinin araştırılması amaçlanmıştır.

GEREÇ VE YÖNTEM: Bu retrospektif çalışma, 2012 - 2022 yılları arasında Yenidoğan Yoğun Bakım Ünitesine kabul edilen ≤ 36^{+6} gebelik haftasında doğan pretermlerde gerçekleştirilen bir vaka-kontrol çalışmasıdır. Örneklem 78 preterm doğumdan (39 vaka ve 39 kontrol) oluşmaktadır. Doğum kayıtları ve kırıkla ilişkili olabilecek doğum sonrası taburculuk sürecine kadar olan klinik takipleri (laboratuvar sonuçları, konjenital hastalıklar, parenteral beslenme, solunum desteği vb.) analiz edildi.

BULGULAR: Çalışma sonucunda prematürelerde kırık prevalansı %0,94 olarak saptanmıştır. Katılımcıların %26,9'unun (n=21) kırık bölgesi humerus ve kırık gerçekleşme zamanı ortalaması 21,18±23,68 gündür. Bu çalışmada vaka grubundaki pretermlerin kontrol grubuna kıyasla APGAR skorlarının daha düşük, total parenteral beslenme, mekanik ventilasyon ve yatış sürelerinin daha uzun ve aradaki farkın istatistiksel olarak anlamlı olduğu bulunmuştur (p<0,05). Ayrıca pretermlerin bazı laboratuvar sonuç (Fosfor, Parathormon vb) düzeyleri gruplar arasında anlamlı farklılıklar göstermektedir (p<0,05).

SONUÇ: Kırık açısından risk faktörlerinin belirlenmesi ve fark edilmesi, devamında ise uygun tedavi ve bakımın sağlanması prematüre bebeklerde kırık oranlarını azaltacaktır.

ANAHTAR KELİMELER: Kemik hastalıkları, kırık, hemşirelik bakımı, prematüre.

ABSTRACT

OBJECTIVE: The processes experienced by preterm neonates at birth and after birth may affect skeletal growth and bone mineralization. This study aims to evaluate the fractures occurring in premature infants admitted to the Neonatal Intensive Care Unit and to investigate the relationship with some characteristics.

MATERIAL AND METHODS: This retrospective study is a case-control study conducted in preterms born at ≤ 36^{+6} weeks gestational age admitted to the Neonatal Intensive Care Unit between 2012 and 2022. The sample comprised 78 preterm births (39 cases and 39 controls). Birth records and clinical follow-ups (laboratory results, congenital diseases, parenteral nutrition, respiratory support, etc.) until the postnatal discharge process that may be related to fracture were analyzed.

RESULTS: The prevalence of fractures in premature infants was found to be 0.94%. The fracture site of 26.9% (n=21) of the participants was the humerus and the mean time to fracture was 21.18±23.68 days. It was found that preterms in the case group had lower APGAR scores and longer total parenteral nutrition, mechanical ventilation and hospitalization times compared to the control group and the difference was statistically significant (p<0.05). In addition, some laboratory results (Phosphorus, Parathormone, etc.) levels of preterms showed significant differences between the groups (p<0.05). Genetic congenital anomaly, cholestasis and sepsis increased the case status 32.764, 21.782 and 0.051 times, respectively (p<0.05). It appears that the incidence of fractures in premature infants who are breastfed is 0.108 times less than in those who are not breastfed. Total parenteral nutrition duration variable decreases the effect of the presence of breast milk.

CONCLUSIONS: Identifying and recognizing the risk factors for fractures and providing appropriate treatment and care will reduce fracture rates in premature infants.

KEYWORDS: Bone diseases, fracture, nursing care, premature.

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INTRODUCTION

The increasing survival rate of premature infants has increased the morbidities associated with prematurity. Premature birth impairs the incorporation of minerals into the bone matrix since over three-quarters of fetal bone mineralization takes place in the third trimester of pregnancy (1). Mineral incorporation into the bone matrix fails in newborns who do not finish the required amount of time during the intrauterine stage when nutrients are most integrated into the bone matrix. This leads to the partial or total loss of the ideal stage of mineral reserve acquisition (2). Consequently, preterm newborns are born with neonatal problems such as impaired bone mineralization in addition to being metabolically immature (3). Potential complications such as adverse effects during feeding of prematurity, diuretic and steroid use, and infections may also contribute to deficiencies in mineral content (4-6). The cause of fracture in premature infants is often difficult to determine and is often associated with osteopenia of prematurity. In most cases, fractures are incidentally diagnosed on X-rays taken for other reasons and therefore the incidence of early neonatal fractures is unknown. In a few studies in the literature, the incidence of fractures varies between 1.2% and 10.5% (7, 8). The incidence may seem modest because the majority of fractures are asymptomatic and discovered by accident in the early stages. In the newborn stage, birth-related bone fractures are uncommon. However, there are known cases of birth-related long bone fractures (shoulder dystocia-related clavicle fractures) and skull fractures, primarily from the use of forceps or ventouses (7-9). In addition, the risk of bone fractures increases in newborns admitted to the Neonatal Intensive Care Unit (NICU) due to prematurity, low birth weight, malnutrition, and various medical and drug-related reasons (5,9). Few studies on bone fractures may occur due to prematurity and the factors that may cause them in developing countries (9-12). This study aimed to evaluate the fractures in premature infants admitted to the NICU and to characterize them in terms of some characteristics.

MATERIALS AND METHODS

Research Design

This study is a retrospective case-control study.

Participants

Within the scope of the study, the records of premature newborns admitted to the NICU of the university hospital, where high-risk newborns are followed up between January 2012 and January 2022 were retrospectively analyzed. A total of 4.152 patients were admitted to the NICU during the study period.

The population of the study consisted of all preterm infants who were diagnosed with one or more fractures during their hospitalization in the relevant date range (N=42). Inclusion criteria for the case group consisted of premature infants with a gestational age <37 weeks with a fracture diagnosis confirmed by a paediatric radiologist (n=39). Three participants born at term were excluded from the study. The other 39 participants who formed the control group of the study were categorised according to gestational week, birth weight and gender, and the group was formed by paying attention to the similar distribution of these three categories with the case group. In this context, 78 preterm infants (Case: 39, Control: 39) were selected as the study sample **(Figure 1)**. X-rays were scanned from the radiology database using the keyword 'fracture'. Preterm infant was defined as gestational age <37 weeks. The mothers' last menstruation date and the findings of the obstetric evaluation were used to calculate the gestational week at the time of delivery.

The study excluded premature infants, those with insufficient medical information, those receiving medications that may affect bone metabolism (e.g., phenytoin, cortisone), and those with chromosomal abnormalities, congenital anomalies, or known bone diseases. The study's scope included the analysis of data that required orthopedic consultation, including the mechanism of injury, clinical presentation, fracture type, fracture location, and total number.

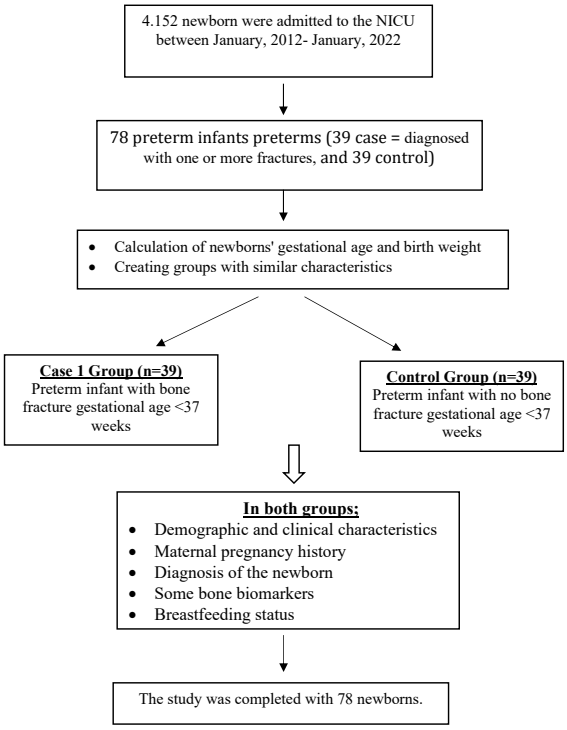

Figure 1: Flow chart of the study

Variables

Clinical data on the mother and newborn were collected by examining the medical records of the mother and using the Infant Follow-up Form. This form includes the mothers' pregnancy-related history, data on the newborn at birth, and data on the newborn's NICU hospitalization. All clinical and nutritional variables were evaluated through daily follow-up, diagnostic updates and feeding protocols from birth until discharge. In the NICU, preterm infant care, feeding, diagnosis and management of diseases, early and late neonatal sepsis are performed by the guidelines of the Turkish Neonatology Society (TND) (13,14). Patients with proven infection by showing growth in blood culture were evaluated as sepsis. Biochemical analyses (Blood Urea Nitrogen (BUN), Creatine, Direct Bilirubin, Magnesium (Mg), Calcium (Ca), Phosphorus (P), Alkaline phosphatase (ALP), Vitamin D, etc.) that may be related to fracture were examined in the hospital laboratory on the day the premature infant was diagnosed with a fracture. All laboratory values were evaluated by considering the reference values of the hospital in the relevant analyses. In the NICU, premature infants are fed by the recommendations of the TND guidelines. Total Parenteral Nutrition (TPN) support is started from the first hour in the hospital, especially in all premature infants younger than 32 weeks or with limited enteral intake. Zinc (1-2 mg/kg/day) is added to TPN from the first day. In addition, 60-80 mg/kg elemental Ca and 45-60 mg/kg P are added daily. To prevent precipitation, P is added to the solution first, then Ca. The recommended doses of neonatal-specific solutions containing fat- and water-soluble vitamins are calculated for all infants receiving TPN from the second day onwards (14-15). TPN support is continued until 75% of the total protein and energy requirement of the preterm infant is met with enteral nutrition. Vitamin D is supported at the daily dose recommended in TPN (160 IU/kg/day) and started when the infant achieved full feeding (400 IU/day with an upper level of 1000 IU/day).

Ethical Committee

The parents or guardians of the children provided informed consent, and the local Ethics Committee of Kahramanmaraş Sütçü İmam University Training and Research Hospital approved the study (02.11.2022/02) and institutional permission was obtained. The study adhered to the ethical principles outlined in the Declaration of Helsinki.

Statistical Analysis

In the research, the data of 78 participants were assessed and transferred to the IBM SPSS Statistics 23 program in the computer environment. The analysis of the participants' descriptive characteristics was carried out by utilizing frequency (n, %) for categorical variables and mean and standard deviation for continuous variables. The independent sample t-test was performed for the purpose of investigating the difference between two-group discontinuous variables. Bivariate logistic regression and the Chi-square test were utilized to evaluate the variables, and logistic regression and the backward stepwise approach were employed in the multivariate analysis to look into the factors linked to the disease's incidence. The TPN duration variable, which was significant in the t-test, was kept as an adjustment factor for the other factors because of the strong correlation between osteopenia of prematurity and mineral deficiency in the etiology of the disease. The odds ratio and corresponding 95% CI for each variable were computed to determine the size of the effect.

RESULTS

A total of 4.152 patients were admitted to the NICU during the study period. Of these, 39 premature infants were diagnosed with bone fractures, corresponding to a prevalence of 0.94%. Fracture sites were observed in 6.4% (n=5) of the participants in the clavicle, 14.1% (n=11) in the femur, 26.9% (n=21) in the humerus, and 2.6% (n=2) in other extremities (toe or finger). The characteristics of the patients are shown in Table 1. Accordingly, 57.7% (n=45) of the participants were female and 92.3% (n=72) were born by cesarean section. The mean gestational age of the participants was 31.36±4.21 years and the mean birth weight was 1564.87±760.80. The fracture site of 26.9% (n=21) of the participants was humerus and the meantime of fracture was 21.18±23.68. Also, the number of newborns with a history of low APGAR score (p=0.001), TPN (p=0.004), mechanical ventilation (p=0.000), and prolonged hospitalization (p=0.000), as well as those born to mothers with a history of gestational diabetes (p=0.033), was found to be significantly higher compared to the control group **(Table 1)**.

Table1: Birth and clinical characteristics of participants in the case and control groups (N=78)

Variable		Case (n=39) Mean±SD	Control (n=39) Mean±SD	Test [a]	p
Gestational age (weeks)		30.82±4.47	31.89±3.93	-1.119	*0.267*
Apgar score 1 minute		4.94±1.57	5.58±1.29	-1.967	*0.053*
Apgar score 5 minutes		5.84±1.72	7.05±1.37	-3.411	***0.001****
Birth weight (grams)		1424.74±806.10	1705.00±694.81	-1.645	*0.104*
Output weight (grams)		2118.71±647.53	2206.15±382.51	-.726	*0.470*
Length at birth (cm)		49.43±3.49	49.83±2.04	-0.627	*0.533*
Total parenteral nutrition duration (days)		18.87±21.23	7.84±9.45	2.962	***0.004****
Duration of oxygen support (days)		12.58±13.21	10.10±6.67	1.049	*0.298*
Duration of non-invasive ventilation (days)		8.15±10.38	8.10±6.88	.026	*0.980*
Duration of mechanical ventilation (days)		27.79±34.30	4.10±8.02	4.199	***0.000****
Length of Hospitalization (days)		63.10±42.52	32.00±20.63	4.109	***0.000****
		n %	n %	Test[b]	p
Gender	Male	17 51.5	16 48.5	0.053	*0.819*
	Female	22 48.9	23 51.1		
Type of delivery	Cesarean birth	35 48.6	37 51.4	0.722	*0.395*
	Vaginal	4 66.7	2 33.3		
Pregnancy history					
Preeclampsia	Yes	22 61.1	14 38.9	3.302	*0.069*
	No	17 40.5	25 59.5		
Gestational Diabetes	Yes	10 76.9	3 23.1	4.523	***0.033****
	No	29 44.6	36 55.4		

[a]*Student t Test* [b] *Continuity Correction Test* ** p<0.05* ***p<0.001*

As shown in Table 2, the number of newborns with at least one fracture was found to be statistically significantly higher in cases diagnosed with genetic congenital anomaly (p=0.000), metabolic bone disease (p=0.001), cholestasis (p=0.036), pneumothorax (p=0.008), intraventricular hemorrhage (p=0.011), hypoglycemia (p=0.042), and sepsis (p=0.000), compared to the control group **(Table 2)**.

Table 2: Diagnosis of the newborn in the case and control groups (N=78)

		n	%	n	%	Test[b]	p
Diagnosis of the newborn							
Genetic congenital anomaly	Yes	23	92.0	2	8.0	23.961	***0.000****
	No	16	30.2	37	69.8		
Metabolic bone disease	Yes	30	43.5	39	56.5	10.174	***0.001****
	No	9	100	0	0.0		
Cholestasis	Yes	10	33.3	20	66.7	4.387	***0.036****
	No	29	60.4	19	39.6		
Patent ductus arteriosus	Yes	27	55.1	22	44.9	1.372	*0.241*
	No	12	41.4	17	58.6		
Pneumothorax	Yes	19	73.1	7	26.9	6.981	***0.008****
	No	20	38.5	32	61.5		
Necrotizing enterocolitis	Yes	11	57.9	8	42.1	.278	*0.598*
	No	28	47.5	31	52.5		
Intraventricular hemorrhage	Yes	16	76.2	5	23.8	6.516	***0.011****
	No	23	40.4	34	59.6		
Hypoglycemia	Yes	8	80.0	2	20.0	4.129	***0.042****
	No	31	45.6	37	54.4		
Sepsis	Yes	33	67.3	16	32.7	14.052	***0.000***
	No	6	20.7	23	79.3		

[a]*Student t Test* [b] *Continuity Correction Test* ** p<0.05 **p<0.001*

When some bone-related laboratory results are compared between the groups in Table 3, it is seen that Calcium (Ca), Phosphorus (P), Alkaline phosphatase (ALP), Thyroid-Stimulating Hormone (TSH), Parathormone (PTH) and Vitamin D levels were significantly different between the groups **(Figure 2 and Figure 3)**.

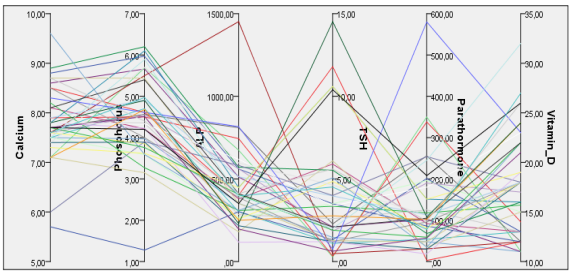

Figure 2: Distribution of Case Group' Biochemical Markers

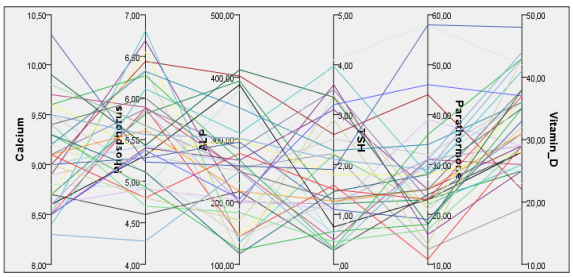

Figure 3: Distribution of Control Group' Biochemical Markers

According to biochemical tests, on the day of fracture diagnosis, Ca, P and Vitamin D levels were significantly lower in the case group compared to the control group (1.28 mg/dl, 1.01 mg/dl, 15.00 mg/mL, respectively) (p=0.000); mean serum values of ALP, TSH and PTH were significantly higher (198.30 IU/L, 2.04 mUI/mL, 106.03 mg/dL, respectively) (p= 0.000, 0.001, 0.000 respectively). No statistically significant difference was found between the groups in terms of diuretic treatment, postnatal steroid use and antiepileptic drug use. In addition, there was no statistically significant difference between formula intake and fracture occurrence, whereas there was a statistically significant difference between breast milk intake and the presence of fracture in premature infants (p=0.004). Accordingly, the occurrence of fracture was significantly less in infants receiving breast milk **(Table 3)**.

Table 3: Some bone biomarkers of participants in the case and control groups

Variable		Case (n=39)		Control (n=39)		Test [a]	p
		Mean±SD		Mean±SD			
Blood Urea Nitrogen (BUN) (mg/dL)		10.03± 8.23		8.05± .99		1.487	*0.141*
Creatinine (mg/dL)		0.38± 0.33		0.50±0.12		-1.960	*0.054*
Direct Bilirubin (mg/ dL)		0.73± 1.60		0.27±0.08		1.797	*0.076*
Magnesium (mg/dL)		1.98±.49		2.07±.30		-1.010	*0.316*
Calcium (mg/dL)		7.79±0.71		9.07±0.47		-9.308	***0.000***
Phosphorus (mg/dL)		4.52±0.96		5.54±.60		-5.514	***0.000***
Alkaline Phosphatase (IU/L)		445.64±237.30		247.33±82.13		4.932	***0.000***
Thyroid-stimulating hormone (TSH) (mUI/mL)		3.86±3.46		1.81±1.13		3.509	***0.001***
Parathormone (mg/dL)		133.39±111.76		27.35±10.52		5.899	***0.000***
Vitamin D (25(OH)D3; mg/mL)		17.88±5.19		32.89±6.89		-10.856	***0.000***
CRP (C-reaktif Protein) 4. gün		1.69±0.46		1.58±0.49		.937	*0.352*
		n	%	n	%	Test [b]	p
Diuretic Treatment Status	Yes	21	51.2	20	48.8	0.000	*1.000*
	No	18	48.6	19	51.4		
Postnatal steroid use	Yes	23	53.5	20	46.5	0.466	*0.495*
	No	16	45.7	19	54.3		
Antiepileptic Drug Use	Yes	13	40.6	19	59.4	1.325	*0.250*
	No	26	56.5	20	43.5		
Breastfeeding status	Yes	26	41.3	37	58.7	8.254	***0.004***
	No	13	86.7	2	13.3		
Formula formula intake status	Yes	26	57.8	19	42.2	1.891	*0.169*
	No	13	39.4	20	60.6		

*[a] Student t Test [b] Continuity Correction Test * p<0.05 **p<0.001*

The results of logistic regression analysis are given in Table 4. When the table is examined, it is seen that mechanical ventilation and hospitalization duration, presence of pneumothorax / intraventricular hemorrhage / hypoglycemia do not have a statistically significant effect on fracture incidence, while presence of genetic congenital anomaly, presence of cholestasis and presence of sepsis have a statistically significant effect on fracture incidence. Genetic congenital anomaly, cholestasis and sepsis increased the incidence of fracture 26.648, 26.566 and 0.059 times, respectively. When the total parenteral nutrition duration variable was used as an adjustment variable in the model, it was observed that the presence of genetic congenital anomaly, the presence of cholestasis and the presence of sepsis had a statistically significant effect on fracture incidence. Genetic congenital anomaly, cholestasis and sepsis increased the case status 32.764, 21.782 and 0.051 times, respectively (p= 0.003, 0.007, 0.015 respectively). Total parenteral nutrition duration variable increased the effect of genetic congenital anomaly status, but decreased the effect of cholestasis and sepsis status. In addition, the presence of breast milk has a statistically significant effect on the incidence of fractures. It appears that the incidence of fractures in premature infants who are breastfed is 0.108 times less than in those who are not breastfed (p= 0.006). When the total duration of parenteral nutrition is used as an adjustment variable in the model, it is seen that the presence of breast milk has a statistically significant effect on the incidence of fracture. It is observed that the incidence of fracture cases is 0.082 times lower in breast milk recipients compared to non-breast milk recipients (p= 0.003). The total parenteral nutrition duration variable decreases the effect of the presence of breast milk **(Table 4)**.

Table 4: Final model of multivariate logistic regression of factors associated with fracture of prematurity

		Not-Adjusted Model OR (95% CI)	p	Adjusted Model OR (95% CI)	p
Demographic and birth characteristics of the participants					
Duration of mechanical ventilation (days)		1.003	0.921	0.973	0.444
Length of Hospitalization (days)		0.985	0.431	0.971	0.196
Genetic congenital anomaly	Yes	26.648	**0.004****	32.764	**0.003****
	No				
Cholestasis	Yes	26.566	**0.003****	21.782	**0.007****
	No				
Pneumothorax	Yes	0.484	0.492	0.438	0.459
	No				
Intraventricular hemorrhage	Yes	1.533	0.695	0.827	0.868
	No				
Hypoglycemia	Yes	0.275	0.292	0.278	0.298
	No				
Sepsis	Yes	0.059	**0.013***	0.051	**0.015***
	No				
Breastfeeding Status	Yes	0.108	**0.006****	0.082	**0.003****
	No				

OR not-adjusted: Bivariate analysis; OR adjusted: Adjustment by Total Parenteral Nutrition Time
** p<0.05 **p<0.001*

DISCUSSION

In recent years, the prolonged life expectancy of premature infants and the parallel increase in fracture cases have increased the clinical interest in premature infants with bone deformities. It has been reported in the literature that fractures and rickets may occur early in life due to osteopenia of prematurity (16) and may lead to future losses in posture, mobility and muscle strength, short stature, and suboptimal peak bone mass in these children (17-19). All these results may lead to lower school performance, behavioral disorders and low self-esteem in adulthood (17). In this study, which was conducted to determine the incidence of fractures in preterm neonates treated in an NICU and to characterize some features that may be associated with fractures, the prevalence of fractures in preterm infants was determined as 0.94%. However, it was observed that 26.9% of fractures occurred in the humerus, followed by femur and clavicle fractures. When evaluated in terms of fracture sites and locations, the fractures were observed in the long bones in 12 premature infants and only two of these deliveries were vaginal. The risk of fracture in long bones may increase in newborns treated in the NICU due to vaginal delivery, prematurity, low birth weight and administration of some pharmacologic agents (20). In the literature, the incidence of bone fractures in the NICU is reported to vary between 1.1% and 10.5% (7, 9, 12, 21). According to Pektas et al. (2019), there were 0.16 femur fractures per 1000 live births as a result of birth trauma, and 1.08 femur fractures per 1000 live births as a result of osteopenia of prematurity (20). Both vaginal and cesarean deliveries can result in birth trauma, and it appears that choosing a caesarean section over a vaginal delivery does not completely remove the risk. Our study's results (0.94%) are significant for updating this data and demonstrate the need for care healthcare providers to treat and care for patients using a multidisciplinary strategy in order to prevent fractures that are either birth-induced or not.

This study shows that the preterms' APGAR score, duration of TPN, duration of mechanical ventilation and hospitalization, and some maternal and infant disease histories (gestational diabetes, genetic congenital anomaly, metabolic bone disease, etc.) are among the important factors to be considered in premature fractures. Long-term use of parenteral feeding as the only or primary source of nutrition is highlighted as a significant risk factor (3,22). Failures to ensure adequate mineral supply are often encountered in this vulnerable population due to several factors, including variability of the parenteral nutrition formulation, low mineral solubility, lack of appropriate mineral formulations, and nutrient antagonistic relationships, the effect of pH, and the ability to administer intravenous therapy within certain limits (22, 23). Therefore, early enteral nutrition is recommended in addition to parenteral nutrition (20). Within the scope of the study, it was observed that the number of fractures was less in infants who received breast milk compared to those who did not. It was also observed that the duration of TPN decreased the effect of the presence of breast milk. It is known that mothers with premature infants are not considered sufficient even though breast milk is rich in Ca and P (24). Although formula milk appears to be richer in Ca and P than breast milk, the bioavailability of these minerals is low. Therefore, breast milk intake should be encouraged in infant nutrition and enrichment of breast milk content may be recommended. The use of sedatives and respiratory support during hospitalization of premature infants increases the duration of immobilization in the NICU. This contributes to increased bone resorption and demineralization and may increase the rate of bone fractures (22, 25). Movement promotes bone formation, reduces natural postpartum bone loss and helps to ensure adequate bone mineral content and muscle development (22, 23, 25). Nurses working in the NICU can support preterm' movement, increase comfort and minimize the risk of fracture formation by giving therapeutic positions specific to the premature infant in line with their nursing roles (26, 27). When the laboratory results of premature infants were analyzed, it was observed that the preterms in the case group had significantly lower Ca, P and Vitamin D levels compared to the control group, while the mean serum values of ALP, TSH and PTH were significantly higher. Although risk factors for bone fractures are wi-

dely recognized, there is still no unified approach to diagnosis. In the human body, thyroid hormones contain important factors that regulate metabolism and cell differentiation, and their increases/decreases have an effect on the whole body. This important effect is often associated with changes in bone metabolism leading to a decrease in bone mineral density, so-called osteoporosis. These effects on bone tissue are well documented in the case of hyperthyroidism. On the other hand, there is no consensus in the case of hypothyroidism (28). When the literature was examined, two studies were found that examined the incidence of fracture risk in adults with hypothyroidism with 92.341 and 16.249 patients and showed that the incidence was higher. We think that our study will contribute to the field in this regard (29, 30). ALP and P are widely used in the investigation of osteopenia in health care (22, 31). There are different findings on the subject in the literature. One of the most prominent etiologic factors of osteopenia is Ca and P deficiency (18, 22). Therefore, adequate mineral, Ca and P supplementation has been recommended for newborns at risk in order to ensure growth and development in the postnatal nutritional support similar to that in the intrauterine environment (32). In the present study, although both groups had adequate mineral intake, lower Ca and P levels were observed in the case group. This finding shows similar results with the literature (6, 22, 33). However, although P levels were found to be higher in the study by Pinto et al. (22), unlike our study, it may reveal the need for reevaluation and discussion of current recommendations regarding mineral supplementation in premature infants in the postnatal period, as emphasized by Avila-Alvarez et al. (33), on the other hand, the importance of considering the bioavailability of supplemented minerals has already been reported (6, 22). Therefore, even if supplemental minerals are given in quantitatively adequate amounts, these minerals may not be effectively absorbed or utilized by the premature infant.

This study has some limitations. Limitations include the inadequacy in the detection of prenatal or intrapartum risk factors due to the retrospective nature of the study and the presence of cases that were diagnosed but not included in the study due to lack of records. In addition, the number of cases is limited. It is recommended that the study be conducted in groups with more participants.

In order to prevent fractures, it is extremely important to prevent trauma and to know the baby's predisposition to fractures due to prematurity. It is not known how many babies are at risk of osteopenia and bone fractures, or how many newborns are already predisposed to this risk. Premature infants are deprived of essential minerals by not being able to spend the last period of pregnancy in the womb, and they also face some restrictions in mineral intake required for bone development after birth. The best approach to premature osteopenia is interventions aimed at prevention. Therefore, although monitoring frequency varies according to mineral levels and risk factors, in premature and low birth weight babies; serum calcium, phosphorus and alkaline phosphatase levels should be measured at regular intervals during the period when they receive TPN and enteral feeding until their postconceptional age reaches at least 40 weeks or their weight reaches 2500 g, and precautions should be taken when necessary. In addition, examination of urinary calcium and phosphorus excretion can also provide important information about serum mineral levels. However, long-term studies are needed regarding the mineral supplement recommended today. Nurses are in a key position to make a significant difference in the quality of life of infants who may face life-threatening fractures, disabilities and early death. The incidence of postnatal bone fractures can be reduced by improving the quality of care in the NICU. It is thought that fractures that may develop in the premature population can be significantly prevented with an interdisciplinary team approach and effective nursing care within the framework of individualized developmental care principles. All infants deserve to be protected from the often preventable risks of fractures in order to live their lives with the quality of life they desire. Also, prospective studies are recommended to compare the characteristics of prematurity-related fractures with those of a term but fractured control group to identify problems specific to this group.

REFERENCES

1. Cooper C, Westlake S, Harvey N, et al. Review: Developmental origins of osteoporotic fracture. Osteoporos Int 2006;17:337–47.

2. Meneghelli M, Peruzzo A, Priante E et al. Bone status and early nutrition in preterm newborns with and without intrauterine growth restriction. Nutrients 2023;15(22):4753.

3. Dombrovski FMOS, Méndez CKI, Vargas DM. Ocorrência de doença metabólica óssea em prematuros de muito baixo peso internados em uti neonatal. Arquivos Catarinenses de Medicina 2009;2(48):12–20.

4. Rehman MU, Narchi H. Metabolic bone disease in the preterm infant: Current state and future directions. World J Methodol 2005;5(3):115-21.

5. Rigo J, Pieltain C, Salle B et al. Enteral calcium, phosphate and vitamin D requirements and bone mineralization in preterm infants. Acta Paediatr 2007;96(7):969–74.

6. Hovi P, Andersson S, Jarvenpaal A-L. Decreased bone mineral density in adults born with very low birth weight: a cohort study. PLoS Med 2009;6(8):e1000135.

7. Wei C, Stevens J, Harrison S et al. Fractures in a tertiary neonatal intensive care unit in Wales. Acta Paediatr 2012;101(6):587-90.

8. Gomella TL, Cunningham MD, Eyal FG. Neonatology: management, procedures, on-call problems, diseases, and drugs. 6th ed. Philadelphia: McGraw-Hill Companies, 2009.

9. Tong L, Pooranawattanakul S, Gopal-Kothandapani JS et al. Comparison of prevalence and characteristics of fractures in term and preterm infants in the first 3 years of life. Pediatric radiology. 2021;51(1):86-93.

10. Hekimoğlu BS. Risk factors and clinical features of osteopenia of prematurity: Single-center experience. Trends in Pediatrics. 2023;4(1):24-30.

11. Armangil D, Gürsoy T, Korkmaz A et al. Decreased bone ultrasound velocity in premature infants conceived with assisted reproduction. Turkish Journal of Pediatrics. 2015;57(1):17-25.

12. Pektaş MK, Koyuncu H, Kundak AA. Long bone fractures in neonatal intensive care units of Afyonkarahisar: Five-year's experience. Turkish Journal of Obstetrics and Gynecology. 2019;16(4):219-23.

13. Satar M, Arısoy AE, Çelik İH. Turkish Neonatal Society guideline on neonatal infections- diagnosis and treatment. Turkish Archives of Pediatrics 2018;53(1): 88-100.

14. Türkyılmaz C, Bilgen H, Kültürsay N. Turkish Neonatal Society guideline on the parenteral nutrition in preterm infants. Turkish Archives of Pediatrics 2018;53:119-27.

15. Kültürsay N, Bilgen H, Türkyılmaz C. Türk Neonatoloji Derneği Prematüre ve Hasta Term Bebeğin Beslenmesi Rehberi 2018 Güncellemesi. Ankara, Türk Neonatoloji Derneği. [cited 2025 Aug 27]. Available from: https://www.neonatology.org.tr/wp-content/uploads/2020/04/premature_rehber_2018.pdf

16. Nallagonda S, Nallagonda M, Deorukhkar A. Metabolic bone disease of prematurity – an overview. Paediatr Child Health. 2017;27(1):14–7.

17. Rugolo LMSS. Crescimento e desenvolvimento a longo prazo do prematuro extremo. J Pediatr. 2005;81(1):101–10.

18. Xie LF, Alos N, Cloutier A et al. The longterm impact of very preterm birth on adult bone mineral density. Bone Rep. 2018;12(10):100189.

19. Demirbaş F, Arısoy AE, Demir H. The long-term effect of very low birth weight and prematurity on bone mineral density in 5–7 years old children. Dicle Med J. 2020;47(2):268–77.

20. Faienza MF, D'Amato E, Natale MP et al. Metabolic bone disease of prematurity: Diagnosis and management. Front Pediatr. 2019;12(7):143.

21. Bülbül A, Okan F, Nuhoğlu A. Yenidoğanın fiziksel doğum travmaları Haseki Tıp Bülteni. 2006; 44:3–5.

22. Pinto MRC, Machado MMT, de Azevedo DV et al. Osteopenia of prematurity and associated nutritional factors: case–control study. BMC pediatrics. 2022; 22(1):1-11.

23. Hanson C, Thoene M, Wagner J et al. Parenteral nutrition additive shortages: the short-term, long-term and potential epigenetic implications in premature and hospitalized infants. Nutrients. 2012;4(12):1977-88.

24. Gupta P, Shah D, Bedi N et al. Indian academy of pediatrics guidelines on screen time and digital wellness in infants, Children and Adolescents. Indian Pediatr. 2022;59(3):235-44.

25. Mo Y, Gu X, Li D et al. Use of narcotics and sedatives among very preterm infants in neonatal intensive care units in China: an observational cohort study. Translational Pediatrics. 2023;12(6):1170-80.

26. Tokan F, Geçkil E. Consept of clustered care in the comprehensive of individualized developmental care in premature infants. Journal of General Health Sciences. 2019;1(1):64-77.

27. Derneği TN, Derneği TO. Türkiye Prematüre Retinopatisi Rehberi 2021 Güncellemesi. (cited 2022 Aug 27). Available from: http://www.neonatology.org.tr/wp-content/uploads/2021/08/Turkiye-Premature-Retinopatisi-2021-Guncellemesi-1.pdf

28. Apostu D, Lucaciu O, Oltean-Dan D, et al. The influence of thyroid pathology on osteoporosis and fracture risk: a review. Diagnostics. 2020;10(3):149.

29. Maccagnano G, Notarnicola A, Pesce V, et al. The prevalence of fragility fractures in a population of a region of southern italy affected by thyroid disorders. BioMed Res. Int. 2016;2016:6017165.

30. Vestergaard P, Mosekilde L. Fractures in patients with hyperthyroidism and hypothyroidism: A nationwide follow-up study in 16,249 patients. Thyroid. 2002;12:411–19.

31. Boskabadi H, Mamoori G, Khatami SF et al. Serum level of vitamin D in preterm infants and its association with premature-related respiratory complications: a case-control study. Electron Physician 2018;10(1):6208-14.

32. Harding JE, Wilson J, Brown J. Calcium and phosphorus supplementation of human milk for preterm infants. Cochrane Database Syst Rev 2017;2(2):CD003310.

33. Avila-Alvarez A, Urisarri A, Fuentes-Carballal J et al. Metabolic bone disease of prematurity: risk factors and associated short-term outcomes. Nutrients. 2020; 12(12):3786.