



# Management of Pregnancy-and Lactation-Related Osteoporosis: Case Series

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## ABSTRACT

**AIM:** To share the experience regarding management and follow-up of patients with Pregnancy- and lactation-related osteoporosis (PLRO) who were effectively treated.

**MATERIAL and METHODS:** This case series presented 10 patients diagnosed with PLRO and treated from January 2010 to December 2019. Visual analog scale and laboratory findings were evaluated. Spinal and extremity magnetic resonance imaging was obtained for patients with spinal and extremity pains. Dual energy X-ray absorptiometry was used for the measurement of bone mineral density. Values assessed on dual energy X-ray absorptiometry were L1–L4 T score, L2–L4 T score, and femoral neck T score.

**RESULTS:** In the first-month follow-ups, all patients had meaningful pain relief and symptom resolution. The mean duration of pain control during the treatment period was 2.4 months. Two patients who continued breast-feeding were also the patients whose pain control was achieved at the latest. One patient required vertebroplasty.

**CONCLUSION:** Patients with PLRO should be promptly treated and followed up. Discontinuation of breast-feeding will provide rapid advantage and should be the first step of the management. Early diagnosis and treatment of calcium and vitamin D with conservative procedures with spinal braces are very important for the treatment of PLRO patients. Additionally, bisphosphonates or teriparatide can improve the bone mineral density in patients with PLRO.

**KEYWORDS:** Pregnancy, Osteoporosis, Vertebroplasty, Lactation, Fracture

**ABBREVIATIONS:** PRLO: Pregnancy- and lactation-related osteoporosis, MRI: Magnetic resonance imaging, VAS: Visual analog scale, ALP: Alkaline phosphatase

## INTRODUCTION

Pregnancy- and lactation-related osteoporosis (PLRO) is a rare transient osteoporosis that causes severe low back pain and morbidity in the last trimester of pregnancy and in the postpartum period (11,16). PLRO had an incidence of

0.4 in 100,000 women. However, the number of undiagnosed women with PLRO is even higher (5).

PLRO is usually seen in the third trimester of the first pregnancy, when the mother loses 30 g of calcium, 20 g of phosphorus, and 0.8 g of magnesium (7). Increased intestinal

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absorption in pregnancy could not overcome the loss because of the physiologic hypercalciuria (13). In breast-feeding, mothers keep losing further calcium. Thus, 7% of maternal calcium reserve transfers to the baby during pregnancy and lactation (4). Even though the loss of minerals during pregnancy and lactation is considered as a natural process, PLRO is rarely seen (7). The etiology of PLRO is still unclear. However, low body mass index, poor nutrition, calcium insufficiency, smoking, mechanical and metabolism stress, low prepregnancy bone mineral density, and history of PLRO in the first-degree relatives were reported as risk factors for PLRO (3,6,12).

Patients with PLRO might suffer from severe low back pain and restricted motion. Fragility fractures, particularly in the vertebra, could cause significant morbidity (1,21). Patients' mood could be affected for having such a disabling condition in young adulthood and in the first pregnancy.

Since there is no consensus for its management, PLRO is still a disabling condition. Calcium supplementation in pregnancy and lactation, as well as the discontinuation of breast-feeding, are critical steps for the management for PLRO. Pathological fractures may require surgery in some patients.

The present case series presented 10 patients who were diagnosed with PLRO and treated from January 2010 to December 2019. The aim of the study was to share the experience regarding management and follow-up of patients with PLRO who were treated effectively.

## ■ MATERIAL and METHODS

Consecutive female patients diagnosed with PLRO to our outpatient clinics between January 2010 and December 2019 were retrieved for final analysis. Patients with spinal and extremity pains had to undergo spinal and extremity magnetic resonance imaging (MRI). Since radiographic measurements were limited to MRI and ultrasound during pregnancy, bone mineral densitometry was ordered after delivery. Bone mineral density was measured by dual energy X-ray absorptiometry. Values assessed on dual energy X-ray absorptiometry were L1–L4 T score, L2–L4 T score, and femoral neck T score. Patient charts were reviewed to find demographic, clinical variables, and management strategies of those patients. All study protocol was compliant with declaration of Helsinki and its amendments.

### Case Series

All total 10 patients were diagnosed with PLRO between January 2010 and December 2019 using our retrospectively collected database. All the patients were young (mean age:  $29.75 \pm 3.24$  years, median: 30 years) and giving birth for the first time. None of them had a history of metabolic bone disease and family history. MRI results of all patients revealed no other differential diagnostic diseases including multiple myeloma or osteogenesis imperfecta, etc. These patients had regular prenatal follow-ups and had received vitamins and calcium supplements during their pregnancies. Only one patient (Patient 4) gave birth to twins. Four patients (Patients 5, 6, 8, and 10) had history of smoking (Table I).

All patients were referred to our outpatient clinics with symptoms occurred within postpartum 2–24 weeks (mean:  $7 \pm 7.15$  weeks, median 4 weeks). Fifty percent of our patients ( $n=5$ ) had back pain and low back pain, 20% ( $n=2$ ) had hip and low back pain, 10% ( $n=1$ ) had hip and ankle pain, 10% ( $n=1$ ) had hip and right-sided inguinal pain, and 10% ( $n=1$ ) had only low back pain. Low back pain was detected in 80% of these patients. The mean visual analog scale (VAS) score for spinal pain was  $7.9 \pm 0.8$ . Patients were diagnosed with PLRO following detailed history taking, physical examination, laboratory work-up (serum levels of calcium, magnesium, alkaline phosphatase, parathormone, 25-(OH)-D<sub>3</sub>), urine work-up, imaging techniques, bone mineral density measurement, as well as multidisciplinary consultation (Table II). MRI revealed spinal involvement in seven patients, sacroiliac joint involvement in one patient (Figure 1), and bilateral femoral neck involvement in one patient (Figure 2). Other etiological factors that could cause bone involvement were excluded and osteoporosis was detected and the absence of trauma history enabled them to be diagnosed with PLRO. A patient suffering from low back pain also had severe pain and limited range of motion in her ankle. Her diagnostic tests revealed edema and stress fracture in the talus (Figure 3). Her laboratory work-up showed mild hypercalcemia and mild elevation of alkaline phosphatase (ALP). In bone mineral density measurements of all patients, the mean L1–L4 T score was  $-2.91 \pm 0.39$ , the mean L2–L4 T score was  $-2.85 \pm 0.38$ , and the mean femoral neck T score was  $-2.19 \pm 0.50$ .

### Management

Immediately after our patients were diagnosed with PLRO, our first step was the discontinuation of breast-feeding. Two patients (patient 8 and 10) did not discontinue breast-feeding. Then, all patients received vitamin D 1000 IU orally and calcium carbonate (1000 mg calcium ion) 250 mg orally daily, diclofenac potassium 50 mg orally twice a day, and paracetamol 500 mg orally thrice a day. Four patients (patients 1, 3, 6, and 7) received bisphosphonates. Patients with spinal symptoms wore spinal braces 16 hours a day for first 4 weeks. Patients were recommended to have bed rest and abstain from strenuous physical activities including weight bearing and forward bending.

One patient with severe back pain (patient number 4) and compression fractures at T6, T10, and T11 vertebrae on MRI underwent vertebroplasty (Figure 4 and 5). She had a significant pain relief after the vertebroplasty (VAS score: 1). Her peri- and postoperative periods were uneventful.

All patients had meaningful pain relief and symptom resolution in the first-month follow-ups. The mean duration of pain control during the treatment period was 2.4 months. Two patients who continued breast-feeding were also the patients whose pain control was achieved at the latest (patient 8 of 3.5 months and patient 10 with 4 months) (Table II). No significant difference was found between those who used bisphosphonates in the follow-up of all patients, but we would like to remind that our data number is small. All the patients were referred to the outpatient clinics of physical medicine and rehabilitation for the treatment of osteoporosis.

**Table I:** Demographic Data of Our Patients

Patients	Age (years)	Risk factors for osteoporosis	Symptoms	Time of diagnosis (week)	L1-4 T score	L2-4 T score	Femoral neck T score	Management protocol
1	31	N/A	Back and low back pain (VAS 9)	Postpartum 24	-2.9	-2.9	-2.7	Discontinuation of breastfeeding, Supplementation of Vitamin D and Calcium, Bisphosphonate
2	33	N/A	Back and low back pain (VAS 8)	Postpartum 4	-3.0	-3.0	-2.2	Discontinuation of breastfeeding, Supplementation of Vitamin D and Calcium
3	27	N/A	Hip and ankle pain, difficulty in walking (VAS 7)	Postpartum 2	-2.5	-2.6	-1.5	Supplementation of Vitamin D and Calcium, Bisphosphonate
4 Twin pregnancy	29	N/A	Back and low back pain (VAS 9)	Postpartum 8	-3.2	-3.0	-2.0	Vertebroplasty (T6, T10 and T11) Discontinuation of breastfeeding, Supplementation of Vitamin D and Calcium
5	24	Smoking	Low back pain (VAS 7)	Postpartum 7	-2.7	-2.4	-1.0	Discontinuation of breastfeeding, Supplementation of Vitamin D and Calcium,
6	31	Smoking	Hip and low back pain VAS 7)	Postpartum 4	-2.6	-2.5	-2.0	Discontinuation of breastfeeding, Supplementation of Vitamin D and Calcium, Bisphosphonate
7	29	N/A	Hip and low back pain VAS 7)	Postpartum 3	-2.7	-2.9	-2.4	Discontinuation of breastfeeding, Supplementation of Vitamin D and Calcium, Bisphosphonate
8	34	Smoking	Back and low back pain (VAS 9)	Postpartum 3	-3.7	-3.6	-2.2	Supplementation of Vitamin D and Calcium, <b>Keep on breastfeeding</b>
9	31	N/A	Hip and inguinal pain (right sided) (VAS 7)	Postpartum 2	-2.9	-3.1	-2.6	Discontinuation of breastfeeding, Supplementation of Vitamin D and Calcium
10	30	Smoking	Back and low back pain (VAS 9)	Postpartum 4	-3.5	-3.5	-3.3	Supplementation of Vitamin D and Calcium, <b>Keep on breastfeeding</b>

**Table II:** VAS Scores And Laboratory Findings Of Our Patients In First Six-Months' Follow-Up

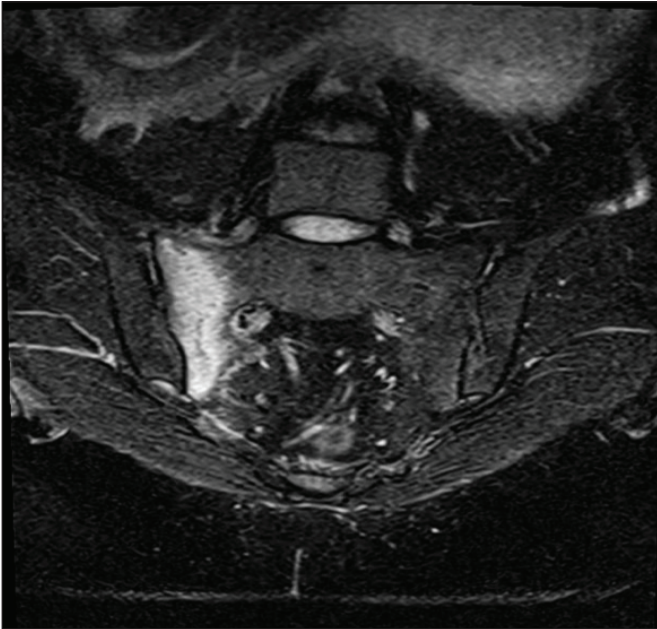
Case	Time	VAS	Ca (mg/dL)	Mg (mg/dL)	Vit D (IU)	ALP (U/L)	PTH (pg/mL)	Other specific findings
1	Baseline	9	8.9	4.1	46	N/A	N/A	High weight gain of 26kg
	1 <sup>st</sup> month	5	8.6	3.9	39	48	27	
	3 <sup>rd</sup> month	1	8.3	4.0	47	N/A	N/A	
	6 <sup>th</sup> month	0	9.1	3.7	37	42	N/A	
2	Baseline	8	8.9	4.0	31.3	102	N/A	
	1 <sup>st</sup> month	2	9.2	3.6	44	N/A	19	
	3 <sup>rd</sup> month	2	9.0	3.7	36	96	24	
	6 <sup>th</sup> month	1	8.6	4.1	N/A	63	31	
3	Baseline	7	11.4↑	N/A	36.7	126↑	N/A	edema and stress fracture in the talus
	1 <sup>st</sup> month	1	9.1	3.9	62	N/A	N/A	
	3 <sup>rd</sup> month	2	8.7	N/A	54	67	21	
	6 <sup>th</sup> month	0	8.9	N/A	39.7	43	32	
4	Baseline	9	10.1	4.9	21.9	69	23	Twins! vertebroplasty procedure for T6, T10 and T11
	1 <sup>st</sup> month	1	7.8	4.2	28	42	35	
	3 <sup>rd</sup> month	1	9.2	3.7	N/A	N/A	N/A	
	6 <sup>th</sup> month	0	8.9	4.1	N/A	N/A	N/A	
5	Baseline	7	9.8	4.7	41.8	87	36	
	1 <sup>st</sup> month	3	8.4	4.0	39	72	28	
	3 <sup>rd</sup> month	2	8.9	4.1	51	48	24	
	6 <sup>th</sup> month	0	N/A	N/A	N/A	N/A	N/A	
6	Baseline	7	7.9↓	3.8	26.4	123↑	N/A	bilateral femoral neck involvement
	1 <sup>st</sup> month	4	8.7	4.1	19	92	26	
	3 <sup>rd</sup> month	1	9.0	4.0	34	96	29	
	6 <sup>th</sup> month	0	8.8	3.8	35	52	34	
7	Baseline	7	9.1	3.9	27.2	99	43	
	1 <sup>st</sup> month	2	N/A	N/A	N/A	N/A	N/A	
	3 <sup>rd</sup> month	2	9.4	4.2	41	38	44	
	6 <sup>th</sup> month	0	N/A	N/A	N/A	N/A	N/A	
8	Baseline	9	9.2	4.1	22.2↓	88	6.2↓	T9, T10, T12 acute compressions <b>Keep on breastfeeding</b>
	1 <sup>st</sup> month	6	N/A	N/A	N/A	N/A	N/A	
	3 <sup>rd</sup> month	3	N/A	N/A	N/A	N/A	N/A	
	6 <sup>th</sup> month	1	9.0	3.9	44	56	41	
9	Baseline	7	8.9	4.3	24.5	101	51	Sacroiliac joint involvement
	1 <sup>st</sup> month	4	9.1	3.7	26	95	33	
	3 <sup>rd</sup> month	3	8.8	4.1	39	74	31	
	6 <sup>th</sup> month	1	9.2	4.4	33	78	52	
10	Baseline	9	8.3↓	5.3↑	20.6↓	104	N/A	T12, L1, L2, L4 acute compressions <b>Keep on breastfeeding</b>
	1 <sup>st</sup> month	5	8.2↓	4.3	28	84	N/A	
	3 <sup>rd</sup> month	3	8.7	3.9	40	101	61	
	6 <sup>th</sup> month	1	8.9	4.0	38	99	47	

**DISCUSSION**

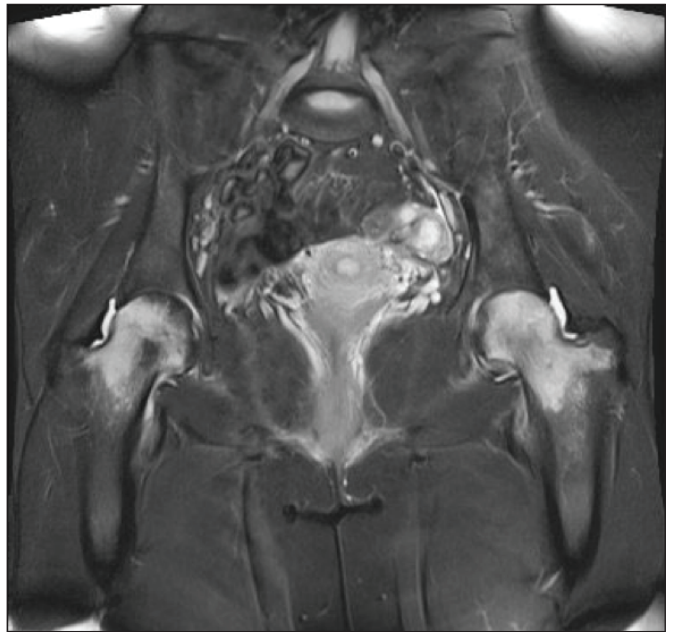
This case series presented 10 patients who were diagnosed with PLRO and treated from January 2010 to December 2019. The aim of the study was to share our experience regarding management and follow-up of patients with PLRO who were treated effectively.

PLRO is a relatively rare condition that affects young women. It could present with severe vertebral compression fractures

and disabling back pain (11). Pregnancy-related low back pain was reported in 53.9% of the women, mostly in the third trimester. History of previous low back pain and pregnancy-related low back pain in prior pregnancies are considered as the risk factors for low back pain during new pregnancies (15). Therefore, it is essential to prevent low back pain before, during, and following pregnancy to improve the quality of life in future pregnancies.



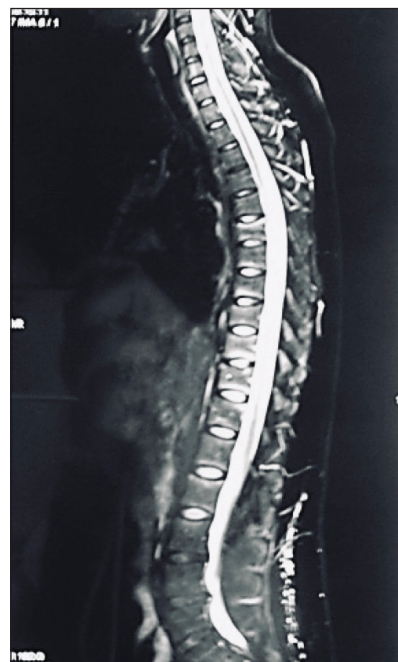
**Figure 1:** Right-sided sacroiliac joint involvement of patient no 9.



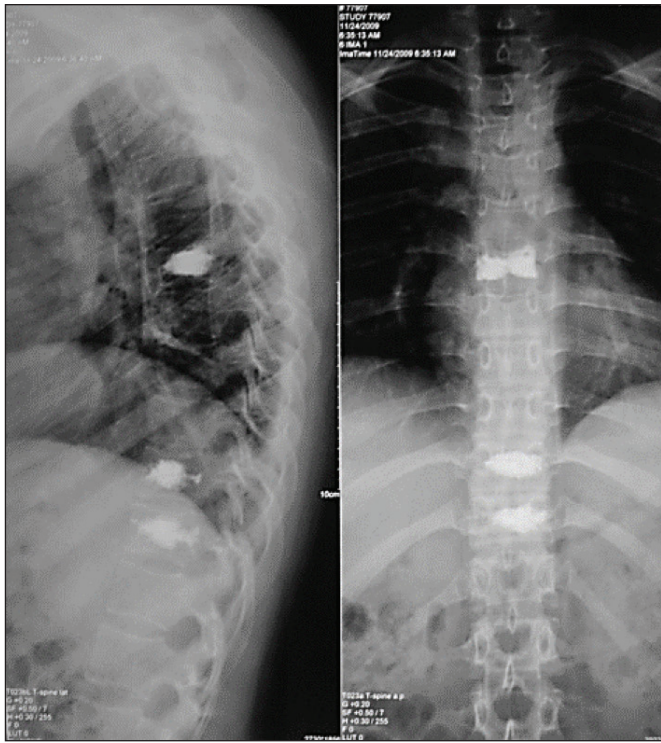
**Figure 2:** Bilateral femoral neck involvement of patient no 6.



**Figure 3:** Edema and stress fracture in the talus of patient no 3.



**Figure 4:** Sagittal MRI image of patient before the vertebroplasty procedure (patient no 4).



**Figure 5:** Postoperative X-ray image after vertebroplasty (patient no 4).

Osteoporosis is a progressive loss of bone mineral density in patients older than 50 years, and PLRO is a rare transient osteoporotic disease in young women, which improves upon appropriate management (23). Radiographic measurements are limited to MRI and ultrasound during pregnancy (16). Measurements of bone mineral density are required after delivery, and the bone density before pregnancy is rarely known.

Management of the underlying factors and osteoporosis provides effective improvement in patients with PLRO. No comprehensive algorithms have been established for the management of PLRO, even though the case reports and case series are available in the literature (9,17). History of PLRO in first-degree relatives, low body mass index, malnutrition, inadequate calcium intake, smoking, and low physical activity are reported as the risk factors for PLRO (2,12,23). Only three patients in the present series had history of smoking. Other patients were free of etiological risk factors for PLRO. Management of underlying factors was recommended following a detailed prepregnancy history. Patients discontinued breast-feeding as soon as they were diagnosed with PLRO. Calcium supplementation during lactation was reported to be pointless; however, the patients were benefited from the discontinuation of breast-feeding (17,23). Patients received diclofenac potassium 50 mg orally twice a day, and paracetamol 500 mg orally thrice a day, calcium 1000 mg orally once a day, vitamin D<sub>3</sub> 880 IU orally once a day. They were asked to wear spinal braces and refrain from strenuous activities, forward bending, and weight lifting. Patients with

PLRO had significant pain relief following conservative management. Patients started to have pain relief within 3 weeks, while the average time elapsed to achieve pain control was 2.4 months. All patients received treatment for PLRO for 6 months and started exercise programs for improving their functionality and condition as soon as their symptoms relieved. Patients were followed up at 1, 3, and 6 months. Bone density was measured annually. Bone mineral density measurements were presented for the first six months' follow-up for all 10 patients in our clinic follow-up period (Table I). Serum calcium levels were reported to be remained within normal limits. Only one patient required three-level vertebroplasty because of symptomatic vertebral compression fractures with intractable pain.

Patients with PLRO commonly received antiresorptive agents against high bone turnover. Bisphosphonates (12,23), teriparatide (8,10,14), and strontium ranelate (19,22) were previously used for the management of PLRO. Tanriover et al., in their letter to the editor in 2015 (20), reported that the bone mineral density did not improve following strontium ranelate in the 7<sup>th</sup> year of follow-up, and it rather deteriorated, and was discontinued. Then, ibandronate (bisphosphonate) was started and improved bone parameters (20). However, long-term outcomes of bisphosphonates in PLRO are lacking, and bisphosphonates could accumulate in the bones crossing the placenta. Bisphosphonates accumulate in the maternal skeleton. Thus, they are recommended to be discontinued a year before the conception to ensure appropriate elimination from the body. Although their direct toxic effects on the mother and fetus during pregnancy have not been demonstrated clearly, the issues and drawbacks associated with their use are obvious (18,23). Laroche et al. reviewed 50 case reports and 3 separate case series of 8, 16, and 34 patients, presenting them along with the 52 cases from his multicenter retrospective study (9). They concluded that bisphosphonates or teriparatide improved the bone mineral density in patients with PLRO. Supplementation of calcium and vitamin D<sub>3</sub> was an essential step in the management of PLRO. Pain management and short-term use of spinal braces were also recommended. Patients should also refrain from strenuous activities, weight lifting, and forward bending.

## ■ CONCLUSION

PLRO is a rare clinical condition in patients with prolonged low back pain and/or hip pain during or after pregnancy. A detailed work-up and the exclusion of other causes for osteoporosis would be helpful in the diagnostic process. Patients with PLRO should be promptly treated and followed up. Discontinuation of breast-feeding will provide rapid advantage and should be the first step of the management. Early diagnosis and treatment of calcium and vitamin D with conservative procedures with spinal braces are very important for the treatment of PLRO patients. Bisphosphonates or teriparatide can improve the bone mineral density in patients with PLRO. Further studies with large sample size are required to develop an algorithm for the management of PLRO.

## ■ AUTHORSHIP CONTRIBUTION

**Study conception and design:** MHA, SO, MSE

**Data collection:** SO, MHA, ECA, EEOE

**Analysis and interpretation of results:** MHA, MSE, EEOE

**Draft manuscript preparation:** MSE, ECA

**Critical revision of the article:** SO, ZSUO

**Other (study supervision, fundings, materials, etc...):** ZSUO, EEOE

All authors (MHA, EEOE, MSE, ECA, ZSUO, SO) reviewed the results and approved the final version of the manuscript.

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