



Pregnancy Associated Osteoporosis (PAO)

Information on Pregnancy and Lactation-Associated Osteoporosis (PAO) is presented by the PAO Patient Group UK, a network of UK-based PAO diagnosed Mothers & families. www.facebook.com/paogroupuk

What is pregnancy-and-lactation-associated osteoporosis?

- The disease is a severe form of osteoporosis affecting women who are pregnant or postpartum. It is associated with frail bones that break with little or no trauma, particularly in the spine, causing debilitating back or hip pain and related complications, possibly long-term.

How common is PAO?

- Misdiagnosis is common and means that the true incidence of PAO is unclear. It is currently thought to affect between 1 in 50,000 to 1 in 100,000 women during or shortly after childbirth <https://www.ed.ac.uk/centre-genomic-medicine/research-groups/ralston-group/pao-study>

How is PAO diagnosed?

- Diagnosis is usually made through the discovery of multiple low or no impact vertebral compression fractures (VCF) and/or sacral/pelvic/hip or other fractures, confirmed by MRI and/or x-ray. A DEXA scan may show that bone mineral density is in the osteoporotic range.

How does PAO present?

- It usually presents with back pain and height loss due to the occurrence of fractures (broken bones) in the spine, but less commonly can also present with fractures of the hip or other bones.

When do PAO fractures occur?

- Fractures may present at any point in pregnancy or postpartum, but are most common in the last trimester, during childbirth or in the first 12 weeks postpartum.

What causes PAO?

- Causes of the disease are not fully understood yet.
- Large decreases in bone mineral density (BMD) may increase susceptibility to osteoporotic fractures. All women lose BMD during pregnancy and breastfeeding, but this is usually regained naturally after weaning and does not cause issues. Women with PAO may:
 - Experience a greater drop in bone mineral density relative to the average and/or
 - Enter pregnancy with a low baseline BMD, making them more susceptible

What are the known risk factors for development of PAO?

**PAO can occur in women with no apparent risk factors, and women with numerous risk factors do not necessarily develop the disease.*

- Inadequate nutritional intake before or during pregnancy impacting bone health:
 - Hyperemesis
 - Coeliac disease, Crohn's disease or other malabsorption issue
 - Dietary restrictions (i.e. vegan diet without adequate calcium intake, etc.)
 - History of eating disorder or low BMI (<20)
 - Vitamin D deficiency
- Medical history suggestive of bone problems:
 - PAO diagnosed in a previous pregnancy
 - Osteopenia or osteoporosis diagnosed prior to pregnancy
 - History of fractures prior to pregnancy, including in childhood
 - Family history of osteoporosis or fragility fractures
 - Genetic variants leading to bone formation issues
 - Amenorrhea, exercise-induced or otherwise
 - Renal stones/hypercalciuria
- Medical treatments that may negatively impact BMD:
 - Progestogen-only contraception (including Depo-Provera)
 - Anticoagulants before or during pregnancy (including low molecular weight heparin)
 - Thyroid hormone
 - Corticosteroids
 - History of cancer treatment

What are the signs and symptoms of PAO fractures?

Note – these are as reported by PAO Mothers & in medical literature, etc.:

Pain Presentation

- Persistent back or hip pain not fully explained by the birth or c-section recovery process.
- Sudden intense back and/or hip pain ("sensation of an electric pop") with low impact (e.g. putting baby in cot) or no impact, occurring in late pregnancy, during childbirth or in the months after giving birth.
- Severe back or hip pain, with or without difficulty walking, affecting everyday functioning. This can be misdiagnosed as pelvic girdle pain in pregnancy.
- "Getting stuck" and unable to move due to severe pain eg. unable to stand from sitting, etc.
- Note: different vertebral fractures cause different types of pain / impact on individuals, meaning that "general / consistent" pain description is problematic.

Sensation of pain or pain symptoms

- Reporting feeling unable to hold up their own bodyweight due to pain
- Described as crushing or squeezing pain in the chest or back
- Pain radiating from back to the rib cage
- Loss of arm strength or inability to raise arms above shoulder-height without severe pain
- Painful muscle spasms, particularly in the back
- Cracking/popping sounds in spine during certain movements, accompanied by severe pain
- Collapsing with pain

Reduced functioning due to pain

- Significantly affecting daily function (i.e. difficulty with dressing, bathing, walking, moving from sitting to standing position, sleeping, moving in bed, travelling in a car, caring for baby)
- Reduced mobility (i.e. use of walking support when not usually required, house-bound, etc.)
- Difficulty weight bearing on hips
- Difficulty with breastfeeding (i.e. unable to: feed sitting up; support weight of baby in arms)

Progression of pain

- Pain improves for a short period before getting significantly worse, possibly due to further fractures occurring, with a further reduction in functioning
or
- Pain improves as fractures heal but pain may be prolonged and not fully resolve due to changes in biomechanics and joint loading in the spine as well as irritation of the nerves and muscles around the spine (MSK / nerve pain)
- Pain that is reported as electric, shooting, knife-like may indicate nerve pain
- Pain may resolve fully in time

Physical appearance changes

- Loss of height
- Curved or kyphotic posture
- Stomach protruding more than prior to fractures (due to new kyphotic posture)

What treatments are currently available?

- There is no standard treatment protocol so far. In addition to rest, movement modification, treatments to ease pain and nutritional support, appropriate specialist care may be required and could include:
 - GP: coordination of specialists, assessment of nutrient deficiencies through blood tests, elimination of other causes of low BMD and fracture (e.g. myeloma/bone cancer)
 - Rheumatologist: medical management of osteoporosis, including medications
 - Endocrinologist: medical management of osteoporosis and/or hormonal conditions impacting bone health
 - Pain Clinics / Specialists – specialist advice coping with fracture pain & associated MSK & also possible associated nerve pain
 - Breast-feeding Specialists – PAO Mothers at diagnosis are usually advised to immediately stop breastfeeding
 - Neurosurgeon: assessment of spinal fragility and guidance on rehabilitation
 - Orthopaedic Spinal Surgeons eg. In selective cases, treatment may sometimes include vertebroplasty, the injection of medical grade cement into the vertebra to help diminish pain and restabilise the spine, although this is controversial and can also result in further spinal fractures. eg, Depending on individual cases, surgeons can carry out interventional surgical procedures to assist with reducing pain & recovery
 - Nutritionist: guidance regarding dietary changes to support bone health
 - Osteoporosis physiotherapists: enable safe return to movement & strength-building
- In the UK, doctors with specialist experience in PAO will assess and determine whether to allow women's bones to heal naturally or to prescribe medicines like teriparatide or bisphosphonates.

What is the prognosis?

- Doctors do not fully understand the disease trajectory.
- Some women recover, either naturally or with medical assistance, but their ongoing quality of life is currently being researched <https://www.ed.ac.uk/centre-genomic-medicine/research-groups/ralston-group/pao-study>
- Other women may require ongoing treatment of osteoporosis and/or for secondary impact of fractures (i.e. chronic pain) for a prolonged period (years or decades).
- Some women fracture again in subsequent pregnancies.

Pregnancy Associated Osteoporosis is an unknown, rare disease:

- There is new UK research, funded by ROS, being undertaken in 2023, which might provide new information and answers:
 - <https://www.ed.ac.uk/centre-genomic-medicine/research-groups/ralston-group/pao-study>

What can be done to prevent PAO injuries and support early diagnosis?

Prevention:

- Build awareness of PAO and the importance of being proactive about bone health with:
 - **Medical community** including midwives, nurses, health visitors, obstetricians, gynaecologists, GPs, physiotherapists, osteopaths, chiropractors and others supporting pre/postnatal women
 - Consider instituting a PAO risk factor checklist for use by clinicians with women who are pregnant or trying to become pregnant:
 - Consider specialist exploration for high-risk cases (e.g. pre-pregnancy DEXA)
 - Doctors to assess suitability of other treatments given PAO risk (e.g. modified use of blood thinners, etc., where indicated)
 - **Women** of child-bearing age, including pregnant women:
 - Discuss importance of vitamin D & calcium for bone health (i.e. ideally at 1st midwife booking apt)
 - Discuss effect of breastfeeding on bone health and the need, if required, to ensure proper supplementation, especially vitamin D & calcium (i.e. 1st midwife visit postpartum)
 - Vitamin D supplements consider supplying for those on income support, etc.
 - Calcium intake form completed at first midwife booking appointment

Support an early diagnosis of PAO:

- Take self-reports of debilitating pain seriously and investigate.
- Women with PAO have repeatedly reported that their pain was dismissed or misdiagnosed.
 - This has resulted in further injury to both mothers and babies – PAO mothers have reported dropping their babies, with severe back pain (presumably from spinal fractures) trying to pick up their babies.
- Refer for x-ray or MRI if pain has a significant effect on a woman's Activities of Daily Living (ADLs), capacity to care for their baby, and/or they are high risk for PAO
- Physiotherapists, osteopaths or chiropractors should consider referring pregnant or postpartum women to their GP for further assessment (i.e. MRI/x-ray) **before** treating them if they present with signs and symptoms suggestive of PAO fractures (with or without the risk factors).
- Urgently refer for DEXA scan once fractures are identified; PAO evaluation requires a DEXA.
- Medical tests should rule out other underlying fracture causes, as some may be treatable.
- Low or no impact fractures occurring in pregnancy or the post-partum period are considered a PAO presentation even if an underlying cause (steroid use, Crohn's, Celiac Disease, etc.) is identified.

Support with management of the disease:

- Urgent referral to the local osteoporosis service and/or pain service (as indicated).
- Consult with or refer to national expert services at UK rare disease Clinical Centres of Excellence, with existing clinical caseloads and knowledge of PAO, to determine best practice treatment. This is particularly important if local healthcare is inexperienced re. PAO.
 - There is currently a UK rare disease action plan being implemented, which should be followed regarding PAO patients.
 - <https://www.gov.uk/government/publications/england-rare-diseases-action-plan-2023>
- Should medication be indicated, it should commence immediately to prevent further fractures, further harm to mothers and babies and associated disability; Teriparatide should be considered as a first line treatment should the treating clinician deem it to be necessary.
- Assess mental health and refer to specialist services as indicated; PAO and associated loss of functioning due to fractures can significantly impact on mental health.

- The RNOH is currently in 2023 researching the mental health impact and quality of life impact of PAO on both mothers and fathers, with interviews and new qualitative research – rnoh.ploresearch@nhs.net
- The University of Edinburgh 2022-2023 research also reviews quality of life impact <https://www.ed.ac.uk/centre-genomic-medicine/research-groups/ralston-group/pao-study>
- Provide women with information about the PAO Patient Network Group UK www.facebook.com/paogroupuk & email paopatientgroup@gmail.com & the international support group (Pregnancy and Lactation Induced Osteoporosis (PLO) private Facebook group; <https://www.facebook.com/groups/594723037694535/?ref=share>).
- Refer to occupational therapy / social services, etc. for assistance and advice on daily activities and baby care as indicated.
- Women who have lost height as a result of compression fractures should have future BMI calculated to take account of height prior to compression fractures.

For further information

- **Useful Organisations:**
 - The Royal Osteoporosis Society [https://theros.org.uk/information-and-support/osteoporosis/pregnancy-associated-osteoporosis/#:~:text=Pregnancy%2Dassociated%20osteoporosis%20\(PAO\),hip%2C%20causing%20pain%20and%20disability.](https://theros.org.uk/information-and-support/osteoporosis/pregnancy-associated-osteoporosis/#:~:text=Pregnancy%2Dassociated%20osteoporosis%20(PAO),hip%2C%20causing%20pain%20and%20disability.)
 - The University of Edinburgh research study <https://www.ed.ac.uk/centre-genomic-medicine/research-groups/ralston-group/pao-study>
 - The PAO Patient Group UK www.facebook.com/paogroupuk
 - Early-onset Osteoporosis Center, Colombia University USA <http://www.eoc.columbiamedicine.org/index.html>
- **Research Papers:**
 - Pregnancy and Lactation Associated Osteoporosis, Sarah A. Hardcastle, Calcified Tissue International 2022, 110:531-545, <https://doi.org/10.1007/s00223-021-00815-6>
 - The experience of pregnancy associated osteoporosis: An international survey with implications for Midwifery Care, S.B.Condon, M, Veitch, Midwifery, 2022, 115: 103468
 - Women with pregnancy & lactation associated osteoporosis (PLO) have low bone remodelling, Cohen, M, Kamanda-Kosseh, D>W. Dempster, D, et. al. J Bone Miner. Res., 34, 2019, 34 (9) 1552-1561 <https://asbmr.onlinelibrary.wiley.com/doi/full/10.1002/jbmr.3750>
 - Associations of parity, breastfeeding and fractures in the Women’s Health Observational Study, Crandall, C.J., Liu, J., Cauley, J. et. al. 2017 Obstet.Gynecol. 130 (1), 171.
 - Comparison of efficacy of pharmacologic treatments in pregnancy and lactation associated osteoporosis, Hong, N., Rhee, Y. 2019 Clin. Rev. Bone Research Miner.Metab, 17 (2), 86-93
 - Long-term outcome of patients with Patients with pregnancy and lactation associated osteoporosis (PLO) with a particular focus on quality of life, Gehlen, M., Lazarescu, A.D, Hinz, C. et. al. 2019 Clin.Rheumatol. 38 (12), 3575-3583
 - Effect of Teriparatide on Bone Remodeling and Density in Premenopausal Idiopathic Osteoporosis: A Phase II Trial, 2020, Cohen, A. et. al. Published by Oxford University Press on behalf of the Endocrine Society 2020 ISSN online 1945-7197 ISSN Print 0021-972X
 - Subsequent fracture risk of women with pregnancy and lactation-associated osteoporosis after a median of 6 years of follow-up, Kybernitakis, I., Hadji, P., et. al, 2018, Osteoporos Int. 29@ 135-142
 - Pregnancy-associated osteoporosis: Does the skeleton recover? Phillips, A.J., Ostlere, S.J., & Smith, R. 2000. Osteoporosis International 11: 449-454
 - Presentation and management of osteoporosis presenting in association with pregnancy or lactation, Kovacs, C.S. Ralston, S.R. 2015, Osteoporos Int, DOI 10.1007/s00198-015-3149-3
 - The skeleton is a Storehouse of Mineral that is Plundered during Lactation and (Fully?) Replenished Afterwards, Kovacs, C.S. Journal of Bone and Mineral Research, JBMR, 2017, Vol. 32, No. 4: 676-680
 - Pregnancy-associated osteoporosis: a case-control study, Hadji, P. et. al, Osteoporos Int (2017) 28: 1393-1399

- Risk Factors, fractures and management of pregnancy-associated osteoporosis: a retrospective study of 14 Turkish patients, *Gynecol Endocrinol.* 202 March; 36 (3) : 238-242
- Pregnancy-related fractures: a retrospective study of a French cohort of 52 patients and review of the literature, Laroche, M. et. al. 2017, *Osteoporos Int.* 2017, Nov 28 (11): 3135-3142
- Pregnancy and lactation associated osteoporosis with vertebral fractures: a systematic review, Ying Qian, et. al, 2021, *BMC Musculoskelet Disord* 2021; 22: 926
- Relevant genetic variants are common in women with pregnancy and lactation-associated osteoporosis (PLO) and predispose to more severe clinical manifestations, Butscheidt, S. et al, *Bone*, 2021 June: 147: 115911 PMID 33716164, DOI: 10.1016/j.bone.2021.115911
- Effect of Teriparatide on Subsequent Fracture and Bone Mineral Density in 47 women with Pregnancy and Lactation-Associated Osteoporosis & Vertebral Fractures. Hadji, P. 2022 <https://www.thieme-connect.com/products/ejournals/pdf/10.1055/a-1816-6700.pdf>
- Bone Turnover in pregnancy, measured by urinary CTX, is influenced by Vitamin D Supplementation and is associated with maternal bone health Osteoporosis Study (MAVIDOS) trial, Curtis, E. et al. *The American Journal of Clinical Nutrition*, November 2021, Vol 114, Issue 5: 1600-1611
- Femoral Analysis, Mechanical Testing and Immunolocalization of Bone Proteins in a Model of Pregnancy and Lactation-Associated Osteoporosis, Tomaszewska, E. et al, *J. Clin. Med* 2021, 10(21), 4808 <https://www.mdpi.com/2077-0383/10/21/4808>
- Effect of Teriparatide on Bone Remodelling and Density in Premenopausal Idiopathic Osteoporosis: a Phase II Trial, Cohen, A. et al, *The Journal of Clinical Endocrinology and Metabolism*, Volume 105, Issue 10, October 2020, pages e3540-3556 <https://academic.oup.com/jcem/article/105/10/e3540/5900497>
- Review of Current Real-World Experience with Teriparatide as Treatment of Osteoporosis in Different Patient Groups, Hauser, B. etc. at. *J. Clin. Med*, 2021, 10 (7), 1403 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8037129/>
- Denosumab after Teriparatide in Premenopausal Women with Idiopathic Osteoporosis, Shane, E. Cohen, A. et al, *The Journal of Clinical Endocrinology & Metabolism*, April 2022, Volume 107, Issue 4, Pages e1528-1540 <https://academic.oup.com/jcem/article/107/4/e1528/6437931?login=false>
- Also:
 - <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5313358/>
 - <https://pubmed.ncbi.nlm.nih.gov/30671611/>

The following NICE Guidelines may be relevant to the clinical care of PAO patients, but this list is not exclusive and other Guidelines may also apply:

- Antenatal Care <https://www.nice.org.uk/guidance/ng201>
- Postnatal Care <https://www.nice.org.uk/guidance/qs37>
- Caesarean Birth <https://www.nice.org.uk/guidance/ng192>
- Maternal and child nutrition <https://www.nice.org.uk/guidance/ph11>
- Weight management before, during and after pregnancy <https://www.nice.org.uk/guidance/ph27>
- Antenatal and postnatal mental health <https://www.nice.org.uk/guidance/qs115>
- Abortion Care <https://www.nice.org.uk/guidance/qs199>
- Osteoporosis <https://www.nice.org.uk/guidance/indevelopment/gid-ng10216>
- Osteoporosis <https://www.nice.org.uk/guidance/qs149>
- Chronic Pain <https://www.nice.org.uk/guidance/ng193>

Useful Publication:

- Pregnancy and Lactation-Associated Osteoporosis (PAO/PLO) – Exercising Safely & Effectively with PAO and Vertebral Fractures, Lynn Hammond, Chartered Physiotherapist HCPC Registered & Fully Certified APPI Pilates Instructor, February 2023 – Booklet first launched at a presentation to the NOS Pregnancy Associated Osteoporosis Meeting, Nuffield Orthopaedic Centre, 2016 obtain via paopatientgroup@gmail.com