Dr. Adi Cohen

Pregnancy and lactation associated osteoporosis (PLO) is a severe early presentation of osteoporosis in which young women experience low trauma or spontaneous fractures, most commonly vertebral fractures, during late pregnancy or lactation. Information on characteristics and management is derived only from case reports and small series. Before therapies for PLO can be developed, it is necessary to address several key gaps in our knowledge about this disorder. Currently, there is little information available on the natural history of and risk factors for PLO, the pathophysiological mechanisms of this acute fracturing syndrome, any biomarkers of severity, and risk of fracture with subsequent pregnancies. In our studies of the pathogenesis (AR49896) and treatment (FD003902; FD005114)of premenopausal idiopathic osteoporosis (IOP), 10 of 66 women had PLO. We detected several important differences between women with PLO and those with IOP unrelated to pregnancy or lactation; those with PLO had more fractures, more vertebral fractures, more profound cortical bone deficits, and lower bone remodeling than those with IOP. **These data lead us to hypothesize that the pathophysiology of PLO is distinct from other forms of IOP and may involve persistent deficits in bone formation and structure, hypotheses with important implications for the development of effective therapies.** The goals of this study are to define the natural history of PLO and its phenotype, including clinical features, hormonal characteristics, skeletal structure and remodeling, and predictors of disease severity. We will also investigate potential genetic etiologies of PLO. We will recruit premenopausal women who experience osteoporotic fracture(s), associated with no trauma or low trauma, during or within 6 months of pregnancy or lactation. We will categorize participants according to time of evaluation relative to time of presentation: Recent PLO subjects evaluated <6 months of their initial fracture(s) and Distant PLO subjects evaluated >6 months after their initial fracture(s). Inclusion of both groups will allow us to compare patients who are at different stages of disease evolution. In Aim 1, we will conduct an online survey to obtain information on clinical characteristics and natural history of PLO, capitalizing on our long-term relationship with a large (>135 women), international Facebook PLO support group. In Aims 2 and 3, we will recruit 50 women with PLO, the largest cohort to date. Participants will undergo detailed phenotyping at Columbia University in terms of historical, biochemical, imaging and transiliac biopsy characteristics, and genotyping by whole exome sequencing. All indices will be investigated as potential biomarkers of disease severity. This study will provide the first comprehensive characterization of PLO, an essential step towards the design of future studies of targeted treatment strategies to improve skeletal recovery and bone quality.