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Bone remodeling during pregnancy and post-partum assessed by metal lead levels and isotopic concentrations☆

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ABSTRACT

Bone remodeling is normally evaluated using bone turnover markers/indices as indicators of bone resorption and formation. However, during pregnancy and post-partum, there have been inconsistent results between and within biomarkers for bone formation and resorption. These differences may relate to pregnancy-related changes in metabolism and/or hemodilution altering measured marker levels. An alternative approach to evaluating bone remodeling is to use the metal lead (Pb) concentrations and Pb isotopic compositions in blood. These measurements can also provide information on the amount of Pb that is mobilized from the maternal skeleton. Despite some similarities with accepted bone turnover markers, the Pb data demonstrate increased bone resorption throughout pregnancy that further continues post-partum independent of length of breast-feeding, dietary intake and resumption of menses. Furthermore the isotopic measurements are not affected by hemodilution. These data confirm calcium balance studies that indicate increased bone resorption throughout pregnancy and lactation. They also indicate potentially major public health implications of the transfer of maternal Pb burden to the fetus and new born.

1. Introduction

The entire adult skeleton, comprised of about two-thirds mineral and one-third osteoid, is replaced about every 10 years with approximately 10% of the skeleton being involved in bone remodeling at any one time. The remodeling process begins when an area of bone is resorbed by osteoclasts, forming a discrete pit. Osteoblasts then deposit organic matrix, or osteoid, into the pit, and the osteoid then becomes mineralized or calcifies. The entire process occurs over about 3 months at any single site [1]. Bone resorption and formation are usually coupled with an increase in bone resorption followed by increased bone formation within approximately 6–8 weeks. This bone remodeling is commonly evaluated by biochemical markers and, because bone resorption and bone formation are tightly coupled, a marker from either group usually reflects bone turnover rate [1], [2,3], [4].

Pregnancy and lactation are characterized by major changes in maternal calcium homeostasis and bone metabolism in order to satisfy the needs of the fetus and the newborn infant for calcium during skeletal growth and mineralization [2,5]. The potential calcium sources are: increased intestinal absorption, decreased renal excretion, and increased resorption from the maternal skeleton. Calcium balance studies suggest that increased dietary intake and intestinal absorption are not sufficient to provide the calcium required by the fetus and the maternal skeleton is used as a source of calcium for the fetus [6] and particularly for the newborn infant during breast feeding. During pregnancy there is increased bone resorption despite high estradiol levels that could be expected to suppress bone resorption and even promote bone formation [7].

Biochemical markers used for analysis of bone formation and resorption have given divergent results and lead to alternative suggestions for markers (Table 1). The changes in Table 3 for post-partum are relative to values in trimester 3. Thus some studies observed increased bone resorption from early pregnancy [8,9] but others only during late pregnancy [10,11]. Likewise, bone formation markers in early pregnancy have been reported to be unchanged [11] or decreased [9] [12,13,10]. During lactation most studies have reported an increase in bone turnover [9–14]. As 1,25-dihydroxyvitamin D levels decrease following delivery resulting in normalization of the intestinal calcium absorption

☆ This paper is dedicated to Dr Paul Mushak who sadly did not wake up on February 3, 2016. Paul provided continual encouragement to the first author and without his perspicacity and encouragement it is highly unlikely that the use of lead isotopic tracing in environmental health would have reached its current status.

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Table 1
Summary of studies employing biochemical markers to evaluate bone remodeling.

Bone Formation Markers (measured in serum)

Marker	No. of subjects	Trimester 1	Trimester 2	Trimester 3	Postpartum	Reference	Changes over pregnancy & postpartum (PP) and comment
Osteocalcin (OC)							
	10	X (No change)	X	X	↑	Gallacher (1994)	Longitudinal study; abstract only available. Increase PP.
	40	↓	↓	↑	↑	Ardawi (1997)	Compared with non pregnant controls. Increase trimester 3 & PP.
	16	↓	X	↓	↑	Naylor (2000)	Compared with baseline. OC considered to be unreliable marker.
	22	X	↓	X	↑	Yoon (2000)	Compared with non↓pregnant controls. No change trimester 1 &3; decrease trimester 2.
	962	X	↓	X	-	Sowers (2001)	No background or controls. Decreased trimester 1 to 2, then unchanged.
	14	X	↓	X	↑	Umera (2002)	No controls. Low values. Decrease trimester 2, no change till PP.
	20	-	X	↑	↑	More (2003)	Compared with baseline. All indices increased during pregnancy but didn't reach baseline even after 12 months PP.
							Some results different to other studies.
	15	↓	X	↑	↑	Ulrich (2003)	Compared with baseline & non pregnant controls. Decrease baseline to trimester 2; baseline again trimester 3.
	95	X	↓	↓	-	Ainy (2006)	Compared with non pregnant controls. Higher trimester 1 compared with trimesters 2 & 3. Significant difference between trimesters 2 & 3.
	78+	↑	↓	X	-	Dorota (2012)	Cross-sectional study. Comparison with nonpregnant subjects. Highest values trimester 1, decreases in trimesters 2 & 3.
	92	↓	↓	X	↑	Möller (2013)	Compared with baseline & non pregnant controls. Decreases trimester 1 & 2.