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Original Article

Hyperemesis gravidarum is not a negative contributing factor for postpartum bone mineral density

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Abstract

Background: Hyperemesis gravidarum (HG), related to protracted vomiting and nausea, is a common cause of hospitalization during the first trimester of pregnancy. It can be accompanied by ketonuria, dehydration, and weight loss. Our aim was to investigate bone loss in patients with HG.
Methods: In our study, we investigated decreased bone mineral density (BMD)in a total of 79 patients (40 HG and 39 control) by means of dual energy X-ray absorptiometry (DEXA) measurements and laboratory parameters related to HG. All patients received DEXA measurement during the early postpartum period (usually two days after delivery, prior to discharge).This study was registered in the database via the Protocol Registration and Results System (PRS) (NCT03127293).
Results: There was no significant difference in DEXA results (lumbar spine and total hip) and laboratory parameters between case and control groups, although a significant difference in vitamin intake was identified between cases and controls (65% vs. 92%, respectively, $p = 0.003$). Except for low serum levels of vitamin D, other laboratory parameters were in normal range in both groups.
Conclusion: Pregnancies complicated by HG did not have decreased bone mineral density compared to those without HG. There is no evidence to relate HG to future osteoporosis.

Keywords: Decreased bone mineral density; DEXA; Hyperemesis gravidarum; Vitamin D

1. Introduction

Hyperemesis gravidarum (HG) is a disorder that is characterized by severe nausea and vomiting in the early period of pregnancy. Definition of HG includes protracted vomiting and nausea accompanied by weight loss, ketonuria, and disturbance of electrolyte balance due to dehydration. Most cases require hospitalization during pregnancy.[1] The prevalence of HG is about 0.3−2% of pregnancies.[1] However, the etiology is not well understood, and data about maternal outcomes of HG in literature are limited.[1] HG may be a heterogeneous medical condition and is mainly thought to have a genetic basis.[2]

As mentioned above, HG can cause severe electrolyte disturbances and malnutrition or even weight loss during pregnancy in some patients.[3] Mineral metabolism also changes during pregnancy, such that both excretion of urinary calcium and absorption of intestinal calcium tend to increase gradually.[4]

Conflicts of interest: The authors declare that they have no conflicts of interest related to the subject matter or materials discussed in this article.

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Elevated absorption of intestinal calcium increases when the first trimester ends. It is reported that calcium storage in the maternal skeleton accelerates during the first trimester.[4] As a consequence of prolonged fasting in HG, physical activity decreases, and the levels of hormones also change.[5] Therefore, all these metabolic fluctuations may lead to decreased BMD, which is a systemic skeletal disease characterized by low bone mass with deterioration of microarchitectural bone tissue.[4,6] On the other hand, pregnancy is a physiological event that almost every woman will experience during her life. About 50−80% of pregnant women have daily nausea and occasional vomiting in the first half of gestation.[7] The question is whether hyperemesis gravidarum is really a risk factor for decreased BMD in young adults. Although HG is a very short-term condition, might it cause decreased BMD during pregnancy? Unfortunately, an exact definition and cut-offs for intervention in decreased BMD for young adults do not yet exist.[8]

Since HG may induce alterations in bone-mineral metabolism and maternal serum hormone levels, the outcome of HG on bone mineral metabolism was investigated in this study. As HG is common and there has not been any research on its association with decreased BMD, we have concentrated on this issue. This is the first study about this topic in the literature.

2. Methods

Fourty pregnant women with a history of severe HG and 40 gestational-age-matched healthy pregnant women were enrolled in this study between June and December 2015 in Kayseri Education and Research Hospital, a tertiary teaching hospital in Kayseri, Turkey. Ethics approval for the study was obtained from Erciyes School of Medicine. All procedures involving human participants were performed in accordance with the ethical standards of the institutional and/or national research committees and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Written informed consent was obtained from all subjects. This study was registered in the database via the Protocol Registration and Results System (PRS) (NCT03127293).

2.1. Patient selection

A total of 40 consecutive primigravid patients aged over 18 years with singleton pregnancy diagnosed with severe hyperemesis gravidarum were included in our study as the HG Group. Considering a power of 90% and Altman monogram, a minimum of 21 subjects per group sample size was determined for the study. Severe HG was defined if the following symptoms were present: admission to the hospital one or more times mostly before 20 completed weeks of gestation because of protracted vomiting and nausea accompanied by weight loss, disturbance of electrolyte balance, ketonuria, or dehydration. Because of one missed laboratory analysis, the control group comprised 39 primigravid singleton gestational-age-matched healthy pregnant women.

Patients with diagnostic confounders such as overt hyperthyroidism, stomach disease, cholelithiasis, or gastroenteritis; patients with chronic illness; patients with history of thyroid surgery, calcium and/or hormone producing tumors, systemic lupus erythematosus; and patients with eating disorders were excluded from the study. Patients with usage of steroids (including for fetal lung maturation),antiepileptic drugs, and/or low molecular weight heparin (a long-term medication known to affect bone metabolism); patients with history of osteoporosis, bone fracture at young ages in the family, and multi gestational pregnancies were also excluded from study.

2.2. Study design

All patients gave birth between 37 and 40 gestational weeks. Data regarding demographic variables including age, body mass index (BMI), parity, gravida, abortions, and vitamin usage in pregnancy were asked and recorded.

All patients underwent Standard dual energy X-ray absorptiometry (DEXA, Hologic Discovery Wi S/N 80848) during the early postpartum period (frequently within two days after birth, prior to discharge) by a single technician. Results for bone area, bone mineral density (BMD), bone mineral content (BMC), T and Z scores for lumbar spine (antero posterior projection at L1−L4) and right hip were recorded. The radiation dose for all of the scans for lumbar spine and right hip were 4.3 μSv and 4.9 μSv, respectively. According to the World Health Organization (WHO) classification system,[9] a T-score ≤ -2.5 is classified as osteoporosis and a T-score between -2.5 and -1 is classified as osteopenia. Z score is the number of standard deviations above or below the mean for patient's age, sex, and ethnicity, while T score is the number of standard deviations above or below the mean for a healthy 30-year-old adult of the same sex and ethnicity.[9]

2.3. Biochemical analysis

Blood samples (10 mL) were drawn at the time of DEXA scans in early postpartum period and collected into ethylenediaminetetraaceticacid (EDTA)-containing sterile tubes and serum separator tubes (SSTs). Samples were centrifuged at 3000 g for 10 min at room temperature. A single technician separated the serum and plasma of samples, and samples were stored at −80 °C until the assay. Serum phosphorus (P) and calcium (Ca) were measured by ionselective electrode (ISE), and alkaline phosphatase (ALP) activity was measured by kinetic enzymatic method with reagents from Beckman Coulter on an auto-analyzer (Olympus AU5400, Beckman Coulter, Inc., U.S.A.). Serum intact parathyroid hormone (PTH) was analyzed by two-site immune enzymatic method, and 25-hydroxy D level was analyzed by competitive immune enzymatic method on a UniCel DxI 800 Immunoassay System (Beckman Coulter, Inc., U.S.A.).

2.4. Statistical analysis

All statistical analyses were performed using PASW Statistics for Windows, Version 18, SPSS, Inc. Chicago, IL, USA. Descriptive statistics of all variables were calculated.

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