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Title: Obstructive sleep apnea is associated with alterations in markers of feto-placental wellbeing

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Body: Background: Sleep disordered breathing (SDB) has been associated with adverse pregnancy and fetal outcomes. As the placenta plays a central role in mediating many of these outcomes, we hypothesized that markers of feto-placental wellbeing are altered in women with obstructive sleep apnea (OSA). Methods: A retrospective case-control study was performed. Cases were identified by ICD-9 codes. Controls were identified from a sample of women screened for symptoms of SDB by using questions from the multivariable apnea prediction index. Women who scored zero (never) on snoring, gasping and apneas were selected as controls. Women with available feto-placental screening markers (estriol (uE3) and alpha-fetoprotein (AFP)) were then selected. Standard statistical analyses were used. Results: Twenty six OSA cases and 165 controls were identified. Median age and body mass index (BMI) were 27.0 and 28.5, $p=0.5$, and 37.7 and 22.9, $p<0.0001$ in cases and controls, respectively. Marker values were adjusted for gestational age and race and reported as multiples of median. Median uE3 was significantly lower in OSA cases compared to controls, even after adjusting for confounders such as BMI, preeclampsia and gestational diabetes (0.85 +0.31 vs. 1.06 +0.35, $p=0.03$). Median AFP was lower in cases than controls (0.84 + 0.35 vs. 1.02 + 4.16, $p=0.04$) but were no longer significant after adjusting for confounders. In OSA group with polysomnograms, AFP and uE3 negatively correlated with nadir oxygen saturation and the apnea hypopnea index, respectively. Conclusion: OSA is associated with alterations in markers of feto-placental wellbeing. Prospective studies need to elucidate this association further.