European Journal of Obstetrics & Gynecology and Reproductive Biology 210 (2017) 166–172

Contents lists available at ScienceDirect

European Journal of Obstetrics & Gynecology and Reproductive Biology

journal homepage: www.elsevier.com/locate/ejogrb

Full length article

Association of obstructive sleep apnea with adverse pregnancy-related outcomes in military hospitals

Dennis L. Spence[a,b,*], Rhonda C. Allen[b], Monica A. Lutgendorf[c], Virginia R. Gary[b], John D. Richard[c], Sara C. Gonzalez[a]

[a] Department of Anesthesiology, Naval Medical Center San Diego, San Diego, CA, United States
[b] Clinical Investigation Department, Naval Medical Center San Diego, San Diego, CA, United States
[c] Department of Obstetrics and Gynecology, Division of Maternal Fetal Medicine, Naval Medical Center San Diego, San Diego, CA, United States

ARTICLE INFO

Article history:
Received 25 July 2016
Received in revised form 1 December 2016
Accepted 12 December 2016

Keywords:
DoD: Department of Defense
OSA: Obstructive sleep apnea
Pregnancy complications
Fetal-infant outcomes

ABSTRACT

Background: Obstructive sleep apnea (OSA) is associated with significant morbidity and mortality in non-obstetrical and obstetrical patients.
Objectives: To estimate the prevalence of OSA and its relationship with pregnancy-related complications in a general obstetric population of Department of Defense beneficiaries receiving direct-care at military treatment facilities.
Study design: A retrospective cohort study of all women (N = 305,001) who gave birth at a military treatment facility from 2008 to 2014. OSA cases were randomly selected and matched on age (3:1 ratio) to non OSA cases. Multivariable logistic regression was used to examine the risks of adverse pregnancy outcomes (cesarean delivery, gestational diabetes, gestational hypertension, preeclampsia, postoperative wound complications, hospital stay greater than five days, acute renal failure, pulmonary edema, preterm delivery, poor fetal growth, and stillbirth) between pregnant women with and without a diagnosis of OSA. Cases were identified using ICD-9 codes, while controlling for demographics, obesity, and medical comorbidities associated with OSA and the outcomes of interest.
Results: We identified 266 cases of OSA (OSA rate = 8.7 per 10,000; increased from 6.4 to 9.9 per 10,000 from 2009 to 2013). OSA was associated with a higher odds of cesarean delivery (AOR,1.60; 95% CI, 1.06–2.40), gestational hypertension, (AOR, 2.46; 95% CI, 1.30–4.68), preeclampsia (AOR, 2.42; 95% CI, 1.43–4.09), and preterm delivery (AOR, 1.90; 95% CI, 1.09–3.30).
Conclusions: Obstructive sleep apnea is associated with adverse maternal and fetal outcomes.
Published by Elsevier Ireland Ltd.

Introduction

Obstructive sleep apnea (OSA) is associated with significant morbidity and mortality in non-obstetrical [1,2–5] and obstetrical patients [6–10]. It is hypothesized that the sleep fragmentation and frequent hypoxia-re-oxygenation that occurs with OSA may lead to increased sympathetic activity, oxidative stress,[11] and inflammation, which may contribute to adverse pregnancy-related and fetal-infant outcomes [9,12]. In a pregnant population, Louis et al [10] reported that after controlling for obesity and other confounders, OSA was associated with increased rates of cesarean delivery (OR, 1.12, 95% CI, 1.01–1.23), preeclampsia (OR, 2.5; 95% CI, 2.2–2.9), eclampsia (OR, 5.4; 95% CI, 3.3–8.9), cardiomyopathy (OR, 9.0; 95% CI, 7.5–10.9), pulmonary embolism (OR, 4.5; 95% CI, 2.3–8.9), and in-hospital mortality (OR, 5.28; 95% CI, 2.42–11.53). A summary of studies examining the association between OSA and adverse pregnancy outcomes is provided in Table 1 [8,10,13–20].

An estimated five percent of the female population is thought to have OSA as defined by an apnea-hypopnea index (AHI) ≥5 plus daytime sleepiness [21]. The AHI is defined as an index used to indicate the severity of sleep apnea. The index is calculated from the number of apnea (pauses in breathing) and hypopnea (complete cessation of breathing) events per hour of sleep. The apnea must last for at least 10 s and also be associated with a decrease in blood oxygenation. Unfortunately, 93% of women with moderate-to-severe OSA has never been diagnosed with the condition [22]. The frequency of this condition is rising, with an increase in the prevalence of OSA in pregnancy from 0.7 per 10,000 in 1998 to 7.3 per 10,000 in 2009 [10]. However, these rates are determined from diagnosed cases of OSA, which likely

* Corresponding author at: Department of Anesthesiology, Naval Medical Center, San Diego, 34800 Bob Wilson Drive, San Diego, CA, United States.
E-mail addresses: dennis.l.spence.mil@mail.mil, elisea.e.avalos-reyes.civ@mail.mil (D.L. Spence).

http://dx.doi.org/10.1016/j.ejogrb.2016.12.013
0301-2115/Published by Elsevier Ireland Ltd.

Table 1
Studies Examining Association Between OSA and Adverse Pregnancy Outcomes.

Source	Design/Sample	Results
Xu et al. [13]	Meta-analysis: OSA N = 87 OSA, Controls N = 266 from 3 studies [9,16,20]	Preeclampsia: RR, 2.31; 95% CI, 1.82–3.23
Pamidi et al. [8]	Meta-analysis: OSA N = 663, Controls N = 5127 from 6 studies [14–18,24]	GHTN/Preeclampsia: OR, 2.25; 95% CI, 1.13–4.52
Louis et al. [10]	Retrospective cross-sectional study in United States: N = 55,781,965 pregnancy-related inpatient hospital discharges	OSA prevalence (per 10,000 pregnancy-related discharges) = 1998 OSA rate = 0.7; 2009 OSA rate = 7.3; overall = 3.0 Preeclampsia: AOR, 2.5; 95% CI, 2.2–2.9 Eclampsia: AOR, 5.4; 95% CI, 3.3–8.9 GHTN: AOR, 5.42; 95% CI, 3.29-8.92 GDM: AOR, 1.89; 95% CI, 1.67–2.14 CS: AOR, 1.12; 95% CI, 1.01–1.23 Postoperative Wound: AOR, 1.89; 95% CI, 1.53–2.34 Hospital stay >5 days: AOR, 3.06; 95% CI, 2.75–3.40 ARF: AOR, 2.73; 95% CI, 1.69–4.41 Pulmonary edema: AOR = 7.5; 95% CI, 4.63–12.15 Pulmonary embolism: AOR, 4.5; 95% CI, 2.3–8.9 Congestive Heart Failure: AOR, 8.94; 95% CI, 7.45–10.73 Cardiomyopathy: AOR, 9.0; 95% CI, 7.5–10.9 Stroke: AOR, 2.93; 95% CI, 1.07–8.04 In-hospital mortality: AOR, 5.28; 95% CI, 2.4–11.5 Early-onset delivery: AOR, 1.2; 95% CI, 1.06–1.37 Poor fetal growth: AOR, 1.21; 95% CI, 0.96–1.53 Stillbirth: AOR, 1.01; 95% CI, 0.66–1.53 Stronger associations between OSA and preeclampsia, GDM, GHTN, postoperative wound, congestive heart failure, and cardiomyopathy in obese vs. non-obese women ($P < 0.05$)
Chen et al. [14]	Retrospective cross-sectional study in Taiwan: OSA N = 791, randomly-selected, age-matched controls N = 3955	Preeclampsia/Eclampsia: AOR, 1.60; 95% CI, 2.16–11.26 GHTN: AOR, 3.18; 95% CI, 2.14–4.73 GDM: AOR, 1.63; 95% CI, 1.07–2.48 CS: AOR, 1.74; 95% CI, 1.48–2.04 Preterm birth: AOR, 1.63; 95% CI, 1.77–3.01 LBW: AOR, 1.76; 95% CI, 1.28–2.40 SGA: AOR, 1.34; 95% CI, 1.09–1.66
Facco et al. [15]	Retrospective Cohort study: OSA N = 143	Rate of APOs (pregnancy-related hypertension, gestational diabetes, or preterm birth ≤34 weeks): No OSA = 18.1%; Mild OSA = 23.5%; Moderate/Severe OSA = 38.5% (*P = 0.038*) Obese women (BMI ≥30) with Moderate/Severe OSA rate of APOs = 41.7%
Louis et al. [16]	Retrospective cohort study: OSA N = 57, Obese Controls N = 114, Normal Weight Controls N = 114	Preeclampsia: 19.3% vs. 10.5% vs. 7%; *P = .15* vs. obese; *P = 0.02* vs. normal CS: 57.9% vs. 40.4% vs. 14.9%; *P = 0.04* vs. obese; *P < 0.001* vs. normal P-CS: 26.3% vs. 14.9% vs. 8.8%; *P = .095* vs. obese; *P = 0.01* vs. normal Preterm birth: 29.8% vs. 9.6% vs. 12.3%; *P = 0.002* vs. obese; *P = 0.007* vs. normal SGA: 7% vs. 7.7% vs. 9.6%; *P = 0.99* vs. obese; *P = 0.79* vs. normal NICU admission: 26.3% vs. 10.5% vs. 10.5%; *P = .014* vs. obese; *P = 0.01* vs. normal Preterm birth: AOR, 2.6; 95% CI, 1.0–6.6
Louis et al. [9]	Observational study: N = 175 (OSA N = 27, no OSA N = 148) Inclusion criteria: obesity (prepregnancy BMI ≥ 30)	OSA rate = 15.4% (none = 84.6%, mild = 7.4%, moderate = 5.1%, severe = 2.9%) Prepregnancy BMI = 46.86 ± 12.2 vs. 38.16 ± 7.5; *P = 0.002* CHTN: 57.7% vs. 33.3%, *P = 0.02* GDM = 19% vs. 10.6%, *P = 0.40* Preeclampsia: AOR: 3.54; 95% CI, 1.26–9.92 CS: AOR, 3.04; 95% CI, 1.14–8.1 Preterm birth: AOR, 0.63; 95% CI, 0.18–2.24 Wound complications: AOR, 3.44; 95 CI, 0.7–16.93 NICU admission: AOR, 3.39; 95% CI, 1.23–9.32 Hyperbilirubinemia: AOR, 3.63; 95% CI, 1.35–9.76
Champagne et al. [17]	Case-control study: GHTN N = 17, no GHTN N = 33; matched on gestational age Completed PSG during second or third trimester	OSA (AHI ≥ 15): AOR = 7.5; 95% CI, 3.5–16.2
Reid et al. [18]	Cross-sectional study: GHTN/Preeclampsia N = 32, Healthy Controls N = 26 Completed PSG during third trimester	OSA rate: 53% vs. 12%, *P < 0.001* Pregnancy BMI: 37.4 ± 7.3 vs. 28.7 ± 4.4, *P < 0.001*
Facco et al. [19]	Cohort study: high-risk for OSA = Prepregnancy BMI ≥30 kg/m2, GHTN, pre-gestational DM, prior history of preeclampsia, and/or a twin gestation; N = 56 OSA, N = 132 no OSA PSG done between 6 and 20 weeks	Moderate-to-Severe OSA/Mild OSA/no OSA Preeclampsia: 20%/12.5%/18.9%, *P = 0.7* GDM: 62.5%/42.9%/26.5%, *P = 0.03* Preterm birth <34 weeks: 13.3%/7.5%/9.4%, *P = 0.8* SGA: 0/2.5%/0.8%, *P = 0.8* GDM in Mild OSA: AOR, 1.5; 95% CI, 0.4–6.0 GDM in Moderate-to-Severe OSA: AOR, 3.6; 95% CI, 0.6–21.8
Sahin et al. [20]	Prospective observational study: a non-high risk obstetric population at Afyonkarahisar Kocatepe University Hospital, Turkey was screened for OSA with Berlin Questionnaire. Women with self-reported snoring or any degree of apnea offered PSG after 34 weeks gestation. OSA N = 4, no OSA N = 31	OSA rate = 11.4% (N = 4; 2 mild and 2 moderate OSA) Preeclampsia: 0 vs. 6.4% GDM: 50% vs. 6.4% CHTN: 0% vs. 9.6% Cardiovascular disease: 25% vs. 6.4% Apgar 1 min: 7.5 ± 1.9 vs. 8.9 ± 0.2, *P = 0.006* Apgar 1 min: 9 ± 1.4 vs. 10 ± 0, *P = 0.000*

Note: Only included studies or results from studies, which reported polysomnography (PSG) or a diagnosis of OSA for inclusion of patients. RR = relative risk; OR = odds ratio; AOR = adjusted odds ratio; OSA = obstructive sleep apnea; GHTN = gestational hypertension; NICU = neonatal intensive care unit; GDM = gestational diabetes; SGA: small for gestational age; APO = adverse pregnancy outcome; CS = cesarean delivery; P-CS = primary cesarean delivery; LBW = low birth weight (<2500 g); Preterm Birth (<37 weeks gestation).