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Corresponding author:
Karolina Dżaman

kfrydel@poczta.onet.pl

Author Affiliation:
Centre of Postgraduate Medical Education.

A Relation Between Obstructive Sleep Apnea in Pregnancy and Delivering Small for Gestational Age Infant – A Systematic Review

Grajczyk, A[1]; Dżaman, K[2]; Czerwaty, K[3]; Kasperczak, M[4]; Zgliczyńska, M[5]; Stępień, A[6]; Kosińska-Kaczyńska K[7].

ADMINISTRATIVE INFORMATION

Support - Centre of Postgraduate Medical Education.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 11 August 2023 and was last updated on 11 August 2023.

INTRODUCTION

Review question / Objective To investigate and understand the association between obstructive sleep apnea (OSA) and small for gestational age (SGA) infants.

Rationale Limited and conflicting data exist on the possible relationship between maternal sleep disturbances and perinatal outcomes. In animal studies, intermittent maternal hypoxia, a model of OSA, led to low birth weight (LBW) of rat pups. Moreover, the fluctuations in oxygen partial pressure were translated from maternal to fetal blood, but transfer across the placenta reduced the magnitude of oxygenation fluctuations in a sheep model of gestational sleep apnea. OSA is related to repetitive nocturnal oxygen desaturation, and recurrent episodes of hypoxia and cortical arousal may lead to sympathetic activation and inflammation, subsequently leading to endothelial dysfunction. It results in placental dysfunction and preeclampsia development. An association between OSA and preeclampsia has been established. However, placental dysfunction may also impair fetal growth. Some authors report an increase in placental weight and obesity in newborns of mothers with OSA. Therefore, there is still a clear need for a profound study of available data on the relationship between OSA and SGA in pregnancy.

Condition being studied OSA is characterized by repetitive upper airway obstruction and significant reductions in airflow during sleep, which leads to repetitive hypoxia and fragmentation of rest. It is a common disorder in the general population, with a prevalence of 12% in US adults. During pregnancy, specific physiological changes in the women's body contribute to a higher prevalence of OSA. They include edema, increased body weight, reduced upper airway dimensions due to hyperemia of pregnancy, and increased upper airway collapsibility due to hormonal changes. Airway closure increases during tidal ventilation, especially in the supine position. On the other hand, the high level of progesterone has a

potentially protective effect because it significantly upregulates ventilatory drive by influencing the central chemoreceptors. Clinical factors associated with OSA in pregnancy include obesity, asthma, hypertension, and gestational diabetes mellitus, although the association between OSA and gestational diabetes mellitus is uncertain. In addition, a higher risk of OSA is associated with pre-pregnancy BMI and Perceived Stress Scale score.

Diagnosis and definition of OSA are usually based on the American Academy of Sleep Medicine (AASM) recommendations [20]. The gold standard for OSA diagnosis is overnight polysomnography (PSG). It is a susceptible and specific method, however, not widely available. Therefore, research including large study groups screened by PSG is lacking. For this reason, the prevalence of OSA has also been examined based on subjective questionnaires like the Epworth Sleepiness Scale (ESS), Berlin Questionnaire (BQ), and STOP-Bang. Unfortunately, the BQ has limited effectiveness in screening for OSA due to its predominant reliance on obesity identification. On the other hand, STOP-Bang had positive predictive values of over 70% in the pregnant population but had limited performance, and asking about snoring may be a more straightforward, effective predictor of OSA. Another tool that may be applied to predicting OSA in pregnancy is the Sleep Apnea Symptom Score, which, when combined with patient characteristics, i.e. age, BMI, and partner-reported snoring and breathing pauses, shows reasonable sensitivity and specificity. The pooled overall prevalence of OSA during pregnancy was 15% (95% CI 12-18%), but it can reach even more than 40% in a pregnant population with significant obesity (BMI >35kg/m2). It should also be noted that the prevalence and severity of OSA deteriorate throughout pregnancy.

METHODS

Search strategy The systematic literature search was completed using three databases: MEDLINE via PubMed, Scopus, and Cochrane Library.

PubMed:

(("Sleep Apnea, Obstructive"[Mesh]) OR (sleep AND apnea*) OR (sleep AND hypopnea*) OR (Upper AND Airway AND Resistance) OR (OSAHS) OR (OSA)) AND (("Fetal Growth Retardation"[Mesh]) OR (IUGR) OR (SGA) OR (FGR) OR (intrauterine AND growth AND (restrict* OR retard*)) OR (fetal AND growth AND (restrict* OR retard*)) OR ("Infant, Small for Gestational Age"[Mesh]) OR (small AND for AND gestational AND age) OR ("Birth Weight"[Mesh]) OR (birthweight*) OR (birth* AND weight*))

Scopus:

TITLE-ABS-KEY (((sleep AND apnea*) OR (sleep AND hypopnea*) OR (Upper AND Airway AND Resistance) OR (OSAHS) OR (OSA)) AND ((IUGR) OR (SGA) OR (FGR) OR (intrauterine AND growth AND (restrict* OR retard*)) OR (fetal AND growth AND (restrict* OR retard*)) OR (small AND for AND gestational AND age) OR (birthweight*) OR (birth* AND weight*))) AND (LIMIT-TO (LANGUAGE,"English"))

Cochrane:

#1 "Sleep Apnea, Obstructive"[Mesh]

#2 (sleep AND apnea*) OR (sleep AND hypopnea*) OR (Upper AND Airway AND Resistance) OR (OSAHS) OR (OSA)

#3 "Fetal Growth Retardation"[Mesh]

#4 (IUGR) OR (SGA) OR (FGR) OR (intrauterine AND growth AND (restrict* OR retard*)) OR (fetal AND growth AND (restrict* OR retard*))

#5 "Infant, Small for Gestational Age"[Mesh]

#6 (small AND for AND gestational AND age)

#7 "Birth Weight"[Mesh]

#8 (birthweight*) OR (birth* AND weight*)

TRIALS.

Participant or population Studies on the impact of OSA on the prevalence of SGA/IUGR/FGR/LBW in human pregnancies.

Intervention Studies on the impact of OSA on the prevalence of SGA/IUGR/FGR/LBW in human pregnancies.

Comparator No comparator.

Study designs to be included Original studies (prospective and retrospective).

Eligibility criteria Inclusion Criteria: Studies on the impact of OSA on the prevalence of SGA/IUGR/FGR/LBW in human pregnancies; OSAwas diagnosed based on the examination of sleep of any kind (for example, PSG, watch pat home sleep test); Original studies; Finished study.

Information sources Electronic databases, contact with authors, trial registers.

Main outcome(s) Association between OSA and SGA.

Quality assessment / Risk of bias analysis Two independent reviewers assessed the risk of bias using the Newcastle-Ottawa quality assessment scale for cohort and case-control studies. Any inconsistencies in the ratings concerning the potential for bias or rationales behind such assessments were resolved through discussion to

establish a mutual agreement between the two review authors. A total score of 0-3 was considered unsatisfactory, 4-5 points satisfactory, 6-7 points good, and 8-9 points very good. Furthermore, the Discussion section outlines additional potential sources of bias that were not encompassed within the scale.

Strategy of data synthesis All results from included studies will be analyzed by two reviewers.

Subgroup analysis Degrees of OSA.

Sensitivity analysis Conducted by two investigators.

Language restriction English.

Country(ies) involved Poland.

Keywords small for gestational age; obstructive sleep apnea; pregnancy; upper airway resistance; sleep hypopnea; birth weight.

Dissemination plans Publication in a journal with impact factor.

Contributions of each author

Author 1 - Alicja Grajczyk.
Email: alicja.grajczyk@gmail.com
Author 2 - Karolina Dżaman.
Email: kfrydel@poczta.onet.pl
Author 3 - Katarzyna Czerwaty.
Email: katarzynaczerwaty@gmail.com
Author 4 - Monika Kasperczak.
Author 5 - Magdalena Zgliczyńska.
Author 6 - Anna Stępień.
Author 7 - Katarzyna Kosińska-Kaczyńska.