



Original research article

# Obstructive sleep apnea syndrome and high-risk pregnancy

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## Abstract

**Introduction:** According to the available data, OSAS (Obstructive Sleep Apnea Syndrome) occurs in the fourth decade in 1 to 5% of women in the total population, and over 90% of women with OSAS do not know about their problems. Approximately 15% of obese pregnant females are thought to suffer from SAS. The aim of this work is to explore OSAS incidence in high-risk pregnant women and the association of OSAS with risk factors for pregnancy.

**Material:** 85 women of a group of 480 monitored high-risk pregnant females were examined, and 61 of these were involved in this study.

**Methods:** We statistically evaluated the relation between OSAS and hypertension, obesity, preeclamptic placental changes, low pH values of umbilical cord blood, and low PlGF levels in the group of high-risk pregnant women with AHI < 5 and in the group with AHI ≥ 5.

**Results:** In the monitored group there was a statistical significant coherence between OSAS and gestational diabetes and obesity in high-risk gravid women. Surprisingly, an association with hypertension was not found. From a statistical point of view, evaluations of histomorphological preeclamptic placental changes, low pH values of umbilical cord blood and low PlGF levels was not significant for a small number of respondents with these disorders.

**Keywords:** High-risk pregnancy; Hypertension; Obesity; OSAS; Preeclampsie

## Introduction

According to epidemiologic studies, sleep breathing disorders affect approximately 15% of the population (Slouka et al., 2015). About half of these disorders are caused by sleep apnea syndrome (SAS). This syndrome is divided into three forms: obstructive (OSAS), central and mixed. The seriousness of sleep apnea syndrome is definitely assessed in accordance with an average number of breathing events per hour of sleep (apnea-hypopnea index, AHI): mild SAS (AHI 5–14.9), moderate (AHI 15–29.9) and severe (AHI ≥ 30) (Sonka and Nevšimalová, 2011).

Sleep breathing disorders related to OSAS are associated with cardiovascular disorders (Monahan and Redline, 2011). OSAS may cause hypertension or complicate its treatment. Myocardial infarction, heart failure, cerebral vascular events, as well as a higher probability of recurrent atrial fibrillation after successful cardioversion essentially rank among other related cardiovascular disorders (Kasai, 2012). The risk of cardio-

vascular events in patients with non-treated SAS is three times higher than in the common population (Barbé et al., 2012).

Other common symptoms and complications of OSAS include memory and concentration disorders, daytime sleepiness, nocturnal polyuria and worsened response to treatment of diabetes (Slouka et al., 2015). Poor quality of life in patients with non-treated severe OSAS is connected with social aspects (Slouka et al., 2018).

Endocrine and metabolic disorders associated with OSAS are among the lesser-known disturbances. Changes in the endocrine system and metabolism (Slouka et al., 2015) influence the hypertrophy of tissues (as well as space in the upper airways) and breathing control. Fragmented sleep causes lower secretion of the growth hormone (Xu et al., 2018) and decreases testosterone levels (Cho and Duffy, 2017). Some epidemiologic studies show that a decrease in progesterone and estrogen levels after the menopause is directly connected with a higher risk of OSAS (Polo-Kantola et al., 2003). Coherence between hypothyreosis and OSAS has not been sufficiently proven up to now, even if clinical experience with OSAS im-

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provement after compensated hypothyreosis is mentioned (Slouka et al., 2015), thyreopathic myositis makes muscular functions (including airway dilators) worse and submucosal deposition of mucoproteins also causes narrowing of the upper airways. There are different opinions on the relationship between Cushing's syndrome (hypercortisolism) and apnea (Shipley et al., 1992). Nocturnal polyuria, mentioned above, is associated with higher secretion of atrial natriuretic peptide and decreased activity of the renin-angiotensin-aldosterone system (Tanaka et al., 2017). Subsequent higher sodium secretion may be one of the co-factors related to OSAS impact on hypertension (Tsuda, 2017). Sleep breathing disorders bring about increased catecholamine excretion and a higher activity of the sympatheticus, leading to hyperinsulinemia as well as potentiating hypertension (Slouka et al., 2014).

Continuous positive airway pressure (CPAP) is considered to be first-line therapy in patients with moderate and severe OSAS. It takes effect very quickly in the common population if treatment is performed successfully. Over the course of several weeks, we can see considerable subjective (feeling of rest after nocturnal sleep) and objective improvements of OSAS (reduction of breathing events and hyposaturation) (Slouka et al., 2018).

According to the available data, OSAS occurs in the fourth decade in 1 to 5% of women in the total population, and over 90% of women with OSAS do not know about their problems (Redline et al., 1994; Young, 1993).

OSAS affecting pregnant females has not been sufficiently explored until now. The presence of OSAS in women of reproductive age is often underdiagnosed (Bixler et al., 2001). The real and objectively documented prevalence of OSAS in gravid women is not known so far. However, approximately 15% of obese pregnant women are thought to suffer from SAS (Louis et al., 2012). Polysomnographically documented studies show that OSAS is associated with pathologies related to a higher incidence of preeclampsia (Champagne et al., 2009; Iczl et al., 2005; Ursavas et al., 2008).

The aim of this work is to detect OSAS incidence in high-risk pregnant females and the statistical relationship between OSAS incidence and risk factors, such as gestational hypertension, diabetes mellitus (GD, Gestational Diabetes), obesity, histomorphological preeclamptic placental changes, low pH values of umbilical cord blood, and low PlGF levels (Placental Growth Factor). If these findings are positive, it will be necessary to adjust the scheme of taking care of high-risk pregnant patients with respect to early diagnosis of OSAS as a factor increasing the occurrence of health complications in these patients. Our next aim will be to identify these patients early, set the way of care and to prove adequate decrease in their perinatal morbidity up to the level identical to that of mothers without OSAS, in a similar way to PAP administration in patients with SAS (Pien et al., 2005).

## Materials and methods

### Materials

A group of 480 high-risk pregnant patients monitored in the Department of Gynaecology and Obstetrics in Pilsen from 2014 to 2016 were used for the purpose of this study. 85 women from this group were involved in the research. 24 women did not meet the classification criteria and had to be excluded. The final studied group included 61 women (Group 1 and Group 2) (Table 1).

**Table 1. Characteristics of the studied group**

High-risk pregnant females	480	Age	
Involved patients	85		
Used group	61	100,0%	31.09 ± 5.83
AHI ≥ 5 (Group 1)	21	34,4%	33.0 ± 5.62
AHI < 5 (Group 2)	40	65,6%	30.1 ± 5.77

Classification criteria: high-risk pregnancy, screening records of nocturnal sleep, complete records of input data including BMI, changes in blood pressure (normotension, pregestational and gestational hypertension), gestational diabetes mellitus and perinatal and neonatal outcome.

Elimination criteria: multiple pregnancy, non-valid screening records of nocturnal sleep, poor cooperation and missing input data.

### Methods

This work is a monocentric prospective cohort study dealing with the group of high-risk pregnant women. Commonly measured data were compared between the sample of patients with and without OSAS. The aim of the work was to create a prospective study with subsequent statistical evaluation. This statistical assessment was calculated with respect to the total of 61 patients included in the study. The patients' personal data was only accessed by authorized medical staff and it was completely anonymized before the evaluation.

*The following variables were recorded and analysed:*

Hypertension was defined as blood pressure above 140/90 during two measurements over the course of 6 hours or if systolic pressure increased by 30 mmHg and diastolic pressure was rising by 15 mmHg (WHO, 1999).

BMI (Body Mass Index) was defined as body weight divided by the height squared; a measure of the degree of obesity.

AHI (apnea-hypopnea index) was defined as the average number of apnea and hypopnea during one hour of sleep.

Histomorphological (preeclamptic) placental changes were defined as placental spiral arteries vasculopathy with atherosclerosis causing limited vascular flow and partial placental infarction.

Low pH value (potential of hydrogen) of umbilical cord blood was defined as  $X \leq 7.25$ .

Low PlGF level (placental growth factor) was defined as  $X < 12$ .

The Ethics Committee of the University Hospital Pilsen granted the approval of the data analyses.

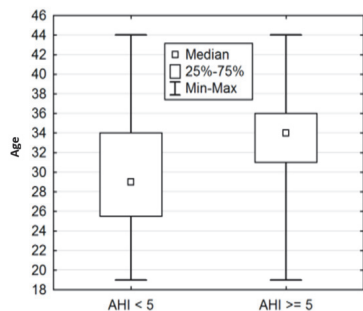
### Statistical methods

#### Basic statistics

The Shapiro-Wilk test shows significantly non-normal distributions of most quantitative variables. Non-parametric tests were used for the subsequent analysis. The tested relationship between AHI parameters and age, BMI, GDM, histomorphological placental changes, low PlGF levels and low pH values were compared between the women's groups with AHI ≥ 5 and AHI < 5 by carrying out the Mann-Whitney *U* test. Mutual correlations between the quantitative variables were analysed using the Spearman's correlation coefficient. All mentioned *p*-values were two-tailed and the level of statistical significance was set at  $\alpha = 0.05$ . The basic statistical analysis was performed in STATISTICA (StatSoft, Inc. 2013. Version 12. www.statsoft.com).

## Results

The Chart 1 shows that pregnant females with  $AHI \geq 5$  (Group 1) are statistically significantly older than pregnant women of the group with  $AHI < 5$  (Group 2).

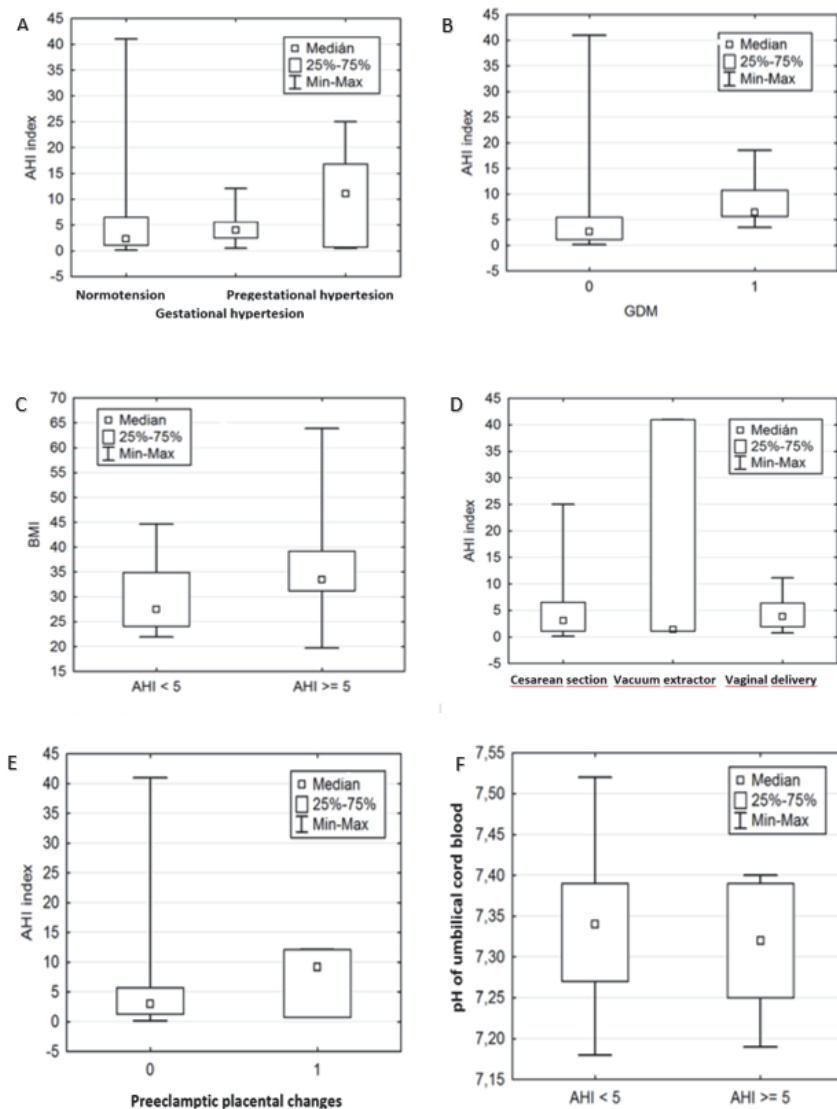


**Chart 1.** Coherence between the age of pregnant females and groups with  $AHI \geq 5$  and with  $AHI < 5$

Regarding blood pressure examination in the first group ( $AHI \geq 5$ ) of pregnant females with detected OSAS, we diagnosed normotension in ten gravid women, gestational hypertension in eight patients, and pregestational hypertension in three of them. In the other group ( $AHI < 5$ ) of pregnant females without detected OSAS, there were twenty-five women with normotension, thirteen women with gestational hypertension and two women with pregestational hypertension. From a statistical point of view, there was no difference in both defined groups (Chart 2a).

GD (gestational diabetes mellitus requiring a diet or insulin therapy) was diagnosed in four women of the first group ( $AHI \geq 5$ ). GD was detected in one patient of the other group ( $AHI < 5$ ). From a statistical point of view, this is a significant dependence of any GDM on AHI (Chart 2b). With regards to potential confounding related to obesity, the result is almost beyond the statistical significance due to a small number of pregnant females with detected GD; that is why it is not mentioned.

In the case of the first group ( $AHI \geq 5$ ), sixteen patients had  $BMI \geq 30$ , and five patients had  $BMI < 30$ . Regarding the



**Chart 2.** Coherence between (A) AHI and blood pressure; (B) AHI and any GD; (C) BMI and groups with  $AHI \geq 5$  and with  $AHI < 5$ ; (D) AHI and the way to end pregnancy; (E) AHI and histological preeclamptic changes; (F) low values of umbilical cord blood, and groups with  $AHI \geq 5$  and with  $AHI < 5$ .

other group ( $AHI < 5$ ), nineteen women had  $BMI \geq 30$  and twenty-one had  $BMI < 30$ . A statistically significant positive correlation was proved in relation to BMI and AHI (Chart 2c).

In terms of the method used to end the pregnancy, cesarean section was performed twelve times, the vacuum extractor was used once, and seven women delivered vaginally in the first group ( $AHI \geq 5$ ). In the other group ( $AHI < 5$ ), pregnancy was ended by performing cesarean section in twenty-two patients, twice by using the vacuum extractor, and eleven women delivered vaginally. From a statistical point of view, there was no substantial difference in both groups (Chart 2d).

Histomorphological preeclamptic changes were detected in two patients of the first group with OSAS. In the case of the other group (without diagnosed OSAS), placental changes were only found in one patient. According to the statistical evaluation, there was no significant difference in both groups for a very small number of affected placentas (Chart 2e).

The pH values of umbilical cord blood were only monitored in thirty-six of sixty-one pregnant women involved in the study. For technical reasons, related results were not available in the other ones. In the first group ( $AHI \geq 5$ ), low pH was detected in four pregnant women out of the fifteen observed. In the other group ( $AHI < 5$ ), low pH was only found in two of twenty-one women. According to the statistical evaluation, this equates to no significant dependence (Chart 2f).

PlGF levels were tested in forty-nine of the sixty-one pregnant women involved in the study. These values were not examined in twelve patients for technical reasons. Very low PlGF levels were only measured in four patients of both groups. No significant difference was proved in a statistical way.

## Discussion

The incidence of high-risk pregnancies is increasing, resulting in more demanding care for these patients. This is followed by indirectly increasing costs of this care (Liu et al., 2009). At the same time, OSAS occurrence increases in pregnant females (Bourjeily et al., 2010). Some authors mention that OSAS affects more than one third of women during the third trimester of pregnancy (Duley, 2009), which corresponds to the findings related to our group where OSAS occurred in 34.4%. In the course of the last few years, we can also see a rising frequency of risk factors in pregnant females leading to preeclampsia. Early detection of risk factors, detection of preeclampsia and subsequent treatment are not only prevention against serious complications, such as organ affection (e.g. liver or kidneys), but also against mothers' death or fetal damage (Högborg, 2005). Another crucial fact is the high risk of cardiovascular diseases in mothers with preeclampsia (O'Brien et al., 2014). That is why subsequent education on appropriate changes in lifestyle related to eating, gradual loss of weight, motion activities and stress prevention is important. Education should be focused on the women who are put at high risk of cardiovascular diseases as well as on those ones who already suffer from one of these diseases (Olišarová et al., 2016).

In our compared groups (Group 1  $AHI \geq 5$  versus Group 2  $AHI < 5$ ), there is a statistically significant age difference. After clinical correlation, this difference becomes less high and less important ( $33.0 \pm 5.62$  versus  $30.1 \pm 5.77$ ) and does not influence the validity of results.

Blood pressure disorders affect approximately 10% of pregnant females and are factors that increase the risk of undesirable events during pregnancy (Duley, 2009). Surprisingly, we proved no difference of the statistical occurrence of hyperten-

sion in high-risk pregnant women (with and without OSAS) in our group. Our conclusions differ from those of O'Brien et al. (2012), where the dependence of OSAS on gestational hypertension was proved in a large group of pregnant females. Reid et al. (2011) also came to similar conclusions to O'Brien. The results of O'Brien et al. (2012) and Reid et al. (2011) correspond, even with the clearly proven connection of OSAS to hypertension in the common population (Townsend et al., 2016). The difference between the statistical results is thought to have been caused by a larger number of respondents' in the compared group.

The result concerning the statistical independence of the occurrence of GD and OSAS was a surprising conclusion of the O'Brien study mentioned above (O'Brien et al., 2012). Their results do not correlate with diabetes mellitus (DM) and OSAS in the common population. The statistical relation between GD and OSAS was proved by a strong association between GD and OSAS in our work, and so it conforms with the study work of Reutrakul et al. (2013).

In the monitored group, we also explored the connection between obesity ( $BMI$  over 30) and OSAS within the completeness of results. A statistical significant dependence was proved in compliance with the study work of Olivarez et al. (2011). Considering overweight and obesity, hidden patterns of behaviour and motives (e.g. cultural conditionality of eating habits in pregnant women) may also be found in gravid women. Their identification can help them to lose weight (Olišarová et al., 2016).

The dependence of the way to end the pregnancy on OSAS was not proved in our group. Our results differ from the conclusion of Spence et al. (2017) who detected a higher probability of cesarean section to end the pregnancy in a group of 350 pregnant women. Nevertheless, the difference in results may arise from the fact that two groups of high-risk pregnant females with OSAS and without OSAS were compared in our group of patients, unlike the work of Spence et al. (2017) in which a common sample of the pregnant population with OSAS was statistically compared to a sample of risk-free pregnant patients.

Unfortunately, no available study has explored the occurrence of histomorphological changes, low pH values of umbilical cord blood (potential of hydrogen) and low PlGF levels in connection with OSAS. The detection of these disorders was so low in our group that statistical results could not be considered valid.

## Conclusions

High-risk pregnancies increase the costs of medical care of these patients and make the occurrence of life-threatening health complications in mothers as well as children higher, too.

Our study detected a coherence between OSAS in high-risk gravid women and obesity and GD. Owing to the low occurrence, the association with OSAS related to histomorphological placental changes, low pH values of umbilical cord blood (potential of hydrogen) and low PlGF levels was not clarified in our patients. The conclusion will be completed and added after the number of new respondents involved in the study increases. Our results show the significance of education for common people in the prevention of obesity as a clear co-factor of OSAS and an increase in the probability of complications in high-risk pregnant women. This education should be aimed at patients at risk, as well as at people who have already been treated for some disease.

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## Conflict of interests

The authors have no conflict of interests to declare in this article.

## Syndrom obstrukční spánkové apnoe a vysoce rizikové těhotenství

### Souhrn

**Úvod:** Podle dostupných pramenů trpí syndromem obstrukční spánkové apnoe (OSAS) ve čtvrté dekádě života 1–5 % ženské populace a více než 90 % žen s OSAS o svém problému neví. Přibližně 15 % obézních těhotných žen má pravděpodobně SAS (Sleep Apnoe Syndrome). Cílem práce je průzkum výskytu OSAS v populaci rizikové těhotných a průzkum souvislosti OSAS s rizikovými faktory pro těhotenství.

**Charakteristika souboru:** Ze 480 sledovaných těhotných bylo zkoumáno 85 a do studie zařazeno 61 rizikové těhotných respondentek.

**Metody:** Statisticky jsme zhodnotili vztah OSAS k hypertenzi, obezitě, preeklamptickým změnám placenty, nízkému pH pupečníkové krve, nízké hladině PlGF ve skupině rizikové těhotných s AHI < 5 a ve skupině s AHI ≥ 5.

**Výsledky:** Ve studovaném souboru byla prokázána významná statistická souvislost výskytu OSAS s gestačním diabetem a obezitou u rizikové těhotných. Nebyla prokázána souvislost s výskytem hypertenze. Pro nízký záchyt respondentek s těmito potížemi nebyla statisticky přínosná hodnocení výskytu histomorfologických preeklamptických změn placenty, nízkého pH pupečníkové krve a nízké hladiny PlGF.

**Klíčová slova:** hypertenze; obezita; OSAS; preeklampsie; rizikové těhotenství

## References

- Barbé F, Durán-Cantolla J, Sánchez-de-la-Torre M, Martínez-Alonso M, Carmona C, Barceló A, et al. (2012). Effect of continuous positive airway pressure on the incidence of hypertension and cardiovascular events in nonsleepy patients with obstructive sleep apnea: a randomized controlled trial. *JAMA* 307(20): 2161–2168. DOI: 10.1001/jama.2012.4366.
- Bixler EO, Vgontzas AN, Lin HM, Ten Have T, Rein J, Vela-Bueno A, et al. (2001). Prevalence of sleep-disordered breathing in women: effects of gender. *Am J Respir Crit Care Med* 163(3): 608–613. DOI: 10.1164/ajrcm.163.3.9911064.
- Bourjeily G, Raker CA, Chalhoub M, Miller MA (2010). Pregnancy and fetal outcomes of symptoms of sleep-disordered breathing. *Eur Respir J* 36(4): 849–855. DOI: 10.1183/09031936.00021810.
- Champagne K, Schwartzman K, Opatrny L, Barriga P, Morin L, Mallozzi A, et al. (2009). Obstructive sleep apnoea and its association with gestational hypertension. *Eur Respir J* 33(3): 559–65. DOI: 10.1183/09031936.00122607.
- Cho JW, Duffy JF (2017). Sleep, sleep disorders, and sexual dysfunction. *World J Mens Health* 45(7): 503–508. DOI: 10.5534/wjmh.180045.
- Duley L (2009). The global impact of pre-eclampsia and eclampsia. *Semin Perinatol* 33(3): 130–137. DOI: 10.1053/j.semper.2009.02.010.
- Högberg U (2005). The world health report 2005: “Make every mother and child count” – including Africans. *Scand J Public Health* 33(6): 409–411. DOI: 10.1080/14034940500217037.
- Izci B, Martin SE, Dundas KC, Liston WA, Calder AA, Douglas NJ (2005). Sleep complaints: snoring and daytime sleepiness in pregnant and pre-eclamptic women. *Sleep Med* 6(2): 163–169. DOI: 10.1016/j.sleep.2004.12.007.
- Kasai T (2012). Sleep apnea and heart failure. *J Cardiol* 60(2): 78–85. DOI: 10.1016/j.jcc.2012.05.013.
- Liu A, Wen SW, Bottomley J, Walker MC, Smith G (2009). Utilization of health care services of pregnant women complicated by preeclampsia in Ontario. *Hypertens Pregnancy* 28(1): 76–84. DOI: 10.1080/10641950802366252.
- Louis J, Auckley D, Miladinovic B, Shepherd A, Mencin P, Kumar D, et al. (2012). Perinatal outcomes associated with obstructive sleep apnea in obese pregnant women. *Obstet Gynecol* 120(5): 1085–1092. DOI: 10.1097/AOG.0b013e31826eb9d8.
- Monahan K, Redline S (2011). Role of obstructive sleep apnea in cardiovascular disease. *Curr Opin Cardiol* 26(6): 541–547. DOI: 10.1097/HCO.0b013e32834b806a.
- O'Brien LM, Bullough AS, Chames MC, Shelgikar AV, Armitage R, Guilleminault C, et al. (2014). Hypertension, snoring, and obstructive sleep apnea during pregnancy: a cohort study. *BJOG* 121(13): 1685–1693. DOI: 10.1111/1471-0528.12885.
- O'Brien LM, Bullough AS, Owusu JT, Tremblay KA, Brincat CA, Chames MC et al. (2012). Pregnancy-onset habitual snoring, gestational hypertension, and pre-eclampsia: prospective cohort study. *Am J Obstet Gynecol* 207(6): 487–489. DOI: 10.1016/j.ajog.2012.08.034.
- Olišarová V, Šedová L, Tóthová V, Bártlová S, Chloubková I, Michálková H, et al. (2016). Areas of health-education of physicians and nurses in care for cardiac patients from the perspective of citizens of the Czech Republic. *Neuroendocrinology Letters* 37 (Suppl. 2): 5–10.
- Olivarez SA, Ferres M, Antony K, Mattewal A, Maheshwari B, Sangi-Haghpeykar H, et al. (2011). Obstructive sleep apnea screening in pregnancy, perinatal outcomes, and impact of maternal obesity. *Am J Perinatol* 28(8): 651–658. DOI: 10.1055/s-0031-1276740.
- Pien GW, Fife D, Pack AI, Nkwuo JE, Schwab RJ (2005). Changes in symptoms of sleep-disordered breathing during pregnancy. *Sleep* 28(10): 1299–305. DOI: 10.1093/sleep/28.10.1299.
- Polo-Kantola P, Rauhala E, Helenius H, Erkkola R, Irjala K, Polo O (2003). Breathing during sleep in menopause: a randomized, controlled, crossover trial with estrogen therapy. *Obstet Gynecol* 102(1): 68–75. DOI: 10.1016/S0029-7844(03)00374-0.
- Redline S, Kump K, Tishler PV, Browner I, Ferrette V (1994). Gender differences in sleep disordered breathing in a community-based sample. *Am J Respir Crit Care Med* 149 (3 Pt 1): 722–726. DOI: 10.1164/ajrcm.149.3.8118642.

20. Reid J, Skomro R, Cotton D, Ward H, Olatunbosun F, Gjevre J, et al. (2011). Pregnant women with gestational hypertension may have a high frequency of sleep disordered breathing. *Sleep* 34(8): 1033–1038. DOI: 10.5665/SLEEP.1156.
21. Reutrakul J, Zaidi N, Wroblewski K, Kay HH, Ismail M, Ehrmann DA, et al. (2013). Interactions between pregnancy, obstructive sleep apnea, and gestational diabetes mellitus. *J Clin Endocrinol Metab* 98(10): 4195–4202. DOI: 10.1210/jc.2013-2348.
22. Shipley JE, Scheingart DE, Tandom R, Starkman MN (1992). Sleep architecture and sleep apnea in patients with Cushing's disease. *Sleep* 15(6): 514–518. DOI: 10.1093/sleep/15.6.514.
23. Slouka D, Holoubková J, Frei J (2015). Obstrukční syndrom spánkové apnoe. In: Slouka D (Ed.). *Syndrom spánkové apnoe*. Plzeň: Euroverlag, pp. 55–71.
24. Slouka D, Honnerova M, Hosek P, Matas A, Slama K, Landsmanova, J, et al. (2018). Risk factors for failure of continuous positive airway pressure treatment in patients with obstructive sleep apnoea. *Biomed Pap Med* 162(2): 134–138. DOI: 10.5507/bp.2017.056.
25. Slouka D, Honnerova M, Hrabe V, Matas A (2014). The prediction of treatment failure of the continuous positive airways pressure. *Bratisl Lek Listy* 115(11): 704–707.
26. Sonka K, Nevšímalová S (2011). 60 years of sleep medicine at the Department of Neurology, First Faculty of Medicine, Charles University in Prague and General University Hospital in Prague. *Prague Med Rep* 112(3): 236–243.
27. Spence R, Allen RC, Lutgendorf MA, Gary VR, Richard JD, Gonzalez SC (2017). Association of obstructive sleep apnea with adverse pregnancy-related outcomes in military hospitals. *Eur J Obstet Gynecol Reprod Biol* 210: 166–172. DOI: 10.1016/j.ejogrb.2016.12.013.
28. Tanaka A, Inaguma D, Ito E, Kamegai N, Kato A, Mizutani M, et al. (2017). Factors associated with severity of sleep apnoea syndrome in patients with chronic kidney disease. *Acta Cardiol* 72(4): 440–445. DOI: 10.1080/00015385.2017.1335048.
29. Townsend R, Khalil A, Premakumar Y, Allotey J, Snell KIE, Chan C, et al. (2016). Prediction of pre-eclampsia: review of reviews. *Ultrasound Obstet Gynecol* 29(8): 542–546. DOI: 10.1002/uog.20117.
30. Tsuda K (2017). Associations among sodium intake, endothelial dysfunction and endothelial damage biomarkers in hypertension. *Am J Hypertens* 85(3): e8. DOI: 10.1093/ajh/hpy141
31. Ursavas A, Karadag M, Nalci N, Ercan I, Gozu RO (2008). Self-reported snoring, maternal obesity and neck circumference as risk factors for pregnancy-induced hypertension and preeclampsia. *Respiration* 76(1): 33–39. DOI: 10.1159/000107735.
32. WHO (1999). International society of hypertension guidelines for the management of hypertension. *J Hypertens* 17(2): 151–183.
33. Xu JH, Li WY, Jin HY, Ye Y, Wang W (2018). Effect of serum growth hormone releasing hormone levels on cognitive function in patients with moderate-severe obstructive sleep apnea-hypopnea syndrome. *Zhonghua Jie He He Hu Xi Za Zhi* 41(8): 606–609. DOI: 10.3760/cma.j.issn.1001-0939.2018.08.007.
34. Young T (1993). Analytic epidemiology studies of sleep disordered breathing – what explains the gender difference in sleep disordered breathing? *Sleep* 16 (Suppl. 8): S1–S2. DOI: 10.1093/sleep/16.suppl\_8.S1.