

OSA (Obstructive Sleep Apnea) Risk Factor-Based Predictive Model for New-onset Preeclampsia during Pregnancy in Indonesian Women

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ABSTRACT

Introduction: Preeclampsia is a potentially dangerous pregnancy complication characterized by high blood pressure and its prevalence is around 5-8% of all diseases that occur during pregnancy. However, obstructive sleep apnea causes inflammation and oxidative stress responses, endothelial damage, and metabolic disorders. **purpose:** the study to produce a risk factor model for OSA (Obstruction Sleep Apnea) predictors of preeclampsia in pregnancy. **Methodology:** This type of observational analytic study was retrospective Case Control design. carried out at Wahidin Sudirohusodo Mojokerto Hospital, Sakinah Mojokerto Hospital. Mojokerto in October 2020- February 2021., sampling with proportional random sampling of 272 people, inclusion criteria for preeclampsia pregnant 20-32 mg and normal pregnant > 32 mg. samples in the case group were 136 people and the control group was 136 people. Data analysis used is logistic regression analysis. **Results :** The result of data classification in the individual OSA risk factor model has a very good suitability value of 95.2%. The significant variables were: gestational age $p=0.000$, neck circumference $p=0.000$, history of hypertension $p=0.000$, ambient temperature $p=0.001$ and OSA $p=0.000$. **Conclusion:** OSA model is an appropriate, cheap and easy screening in predicting the incidence of preeclampsia. **Suggestion:** the OSA model can be applied to all pregnant women starting in the 2nd trimester.

Keywords: OSA model, predictor, preeclampsia

INTRODUCTION

Preeclampsia is the most serious complication in which the mother experiences high blood pressure during pregnancy, not due to hypertension but due to placental nidation. The impact of preeclampsia is the emergence of HELLP (*Hemolysis, Elevated Liver Enzymes and Low Platelet Count*) syndrome or hemolysis, (1–3).

The prevalence of preeclampsia is about 5-8% of all diseases that occurs during pregnancy (1). Syndrome of stopping breathing during sleep (Obstructive sleep apnea) emerged as a potential causative factor for several diseases cardiovascular (4,5). Epidemiological studies show a 2-13% prevalence of OSA (obstructive *sleep apnea*) in pregnancy . *Obstructive sleep apnea* causes inflammation and oxidative stress response, endothelial damage and metabolic disorders (6–8).

Obstructive sleep apnea (OSA) is a sleep disorder characterized by apnea causing intermittent airflow obstruction, hypoventilation, and nocturnal hypoxia (9). Anatomical narrowing and increased resistance in the respiratory system can occur due to Increased levels of estrogen and progesterone cause capillary swelling, hypersecretion and edema of the upper respiratory tract mucosa . Pregnancy cause changes in anatomy, physiology, and endocrine system, including upper airway narrowing | Objective: To produce a model of risk factors and OSA as predictors of preeclampsia in pregnancy .

MATERIALS AND METHODS

This type of research is an observational analytic study with a research design *Case Control* using a *retrospective approach*. The research location was carried out at Wahidin Sudiro Husoda Hospital, Mojokerto, Sakinah Mojokerto Hospital, Sooko Health Center and Gayaman Health Center, Kab. Mojokerto, research time in August 2019-April 2020. The technique or sampling used in this research is *proportional random sampling*. Population and sample: pregnant women with preeclampsia, totaling 272 people divided into 136 cases and 136 controls. Inclusion criteria: Pregnant women $\geq 20 - 38$ weeks who are preeclampsia, in control pregnant women ≥ 32 weeks. OSA instrument uses a Berlin questionnaire, Berlin questionnaire indicators: sleep quality, snoring, breathing stops, body fatigue. The Berlin questionnaire was assessed positive if there were ≥ 2 symptoms and negative if 1/ no symptoms. The results of the Berlin questionnaire test on 60 respondents: validity 0.254 and reliability 0.700 means the questionnaire is good and preeclampsia is measured blood pressure, edema and proteinuria. The stages in this study were to obtain a population and sample, data collection, data processing, statistical tests to determine the predictive model of OSA risk factors for PE, then in the Data Analysis Test. The inferential analysis used was Analyst a logistic regression, (7,10,11).

RESULTS

Table 1, it is known that significant variables are the influence of risk factors on OSA, namely: neck circumference, parity, R. Hypertension, R. DM, R. snoring, family income, and environmental temperature. of risk factors and OSA in logistic regression analysis using the Backward Stepwise (Wald) method of preeclampsia.

Table 2, it is known that OSA and preeclampsia were 51 people (18.75%). The number of OSA patients was 71 people and the total PE was 136 people (50%). OSA variable has an effect on the incidence of preeclampsia, because it has a significant value below 0.005. included in the OSA event model.

Table 3, it is known that OSA factors have a significant effect in the direction of preeclampsia. The higher the OSA level of pregnant women, the higher the tendency for preeclampsia. Significant variables include: gestational age, neck circumference, history of hypertension, ambient temperature and OSA. further strengthen the incidence of OSA has an influence relationship on preeclampsia in pregnant women (12–14). The logistic equation model for the incidence of preeclampsia is used to predict the incidence of preeclampsia. The

results of the probability equation predicting the regression model for the incidence of preeclampsia are as follows:

$$\begin{aligned} \text{Indeks Preeklamsia} = & -3.726 + 1.392 \text{ Umur Kehamilan (minggu)} + 1.321 \text{ Suhu} \\ & \text{Lingkungan (}^\circ\text{C)} + 1.467 \text{ lingkar Leher (cm)} + 1.866 \text{ OSA (ya)} + \\ & 2.173 \text{ R. Hipertensi (ya)}. \end{aligned}$$

DISCUSSION

Gestational age affects OSA, that gestational age, especially in the third trimester, increases body weight, obesity and fat accumulation. Pregnant women, especially in the third trimester, show an increase in the frequency of snoring, sleep disturbances, and poor sleep quality. The increasing gestational age in the supine position, so that *cardiac output* increases. The upper airway collapses more easily in the supine position due to compression of the diaphragm by a large intra-abdominal mass, especially in third trimester pregnant patients (12,15,16).

Neck circumference is a relatively new anthropometric method for preeclampsia. Neck fat is positively correlated with visceral fat, insulin resistance and metabolic syndrome. Fat deposits around the neck produce inflammatory substances that cause plaque buildup in the carotid arteries in the neck, causing heart health to be disturbed. In preeclampsia, it is caused by nocturnal fluid shifting from the legs to the neck or oedema, lipolytic activity of upper body fat indicates a risk of cardiovascular disease (16–18).

Obstructive Sleep Apnea (OSA) has a major effect on causing hypertension. OSA raises blood pressure through the effects of hypoxemia, namely increased sympathetic nerve stimulation and endothelial dysfunction, impaired endothelial function, increased blood cell activity, decreased cerebral blood flow/blood flow to the brain, causing thickening of the carotid blood vessel walls. History of hypertension before pregnancy or pregnancy <20 weeks increases the incidence of hypertension in pregnancy by about 5-10% and the incidence of OSA by 2-3 times, and doubles the risk of coronary disease or heart attack (18,19).

Environmental temperature is one of the risk factors for preeclampsia, global warming causes an increase in ambient temperature of 0.74°C during the 21st century or 3F, every 10F increase is 4.3% risk of OSA and PE. The study was conducted in the Mojokerto area which is an industrial area. The results of the study were temperature 32°C at risk of preeclampsia. High temperatures cause abnormal migration, trophoblast distribution is disrupted at the time of migration, resulting in impaired initiation of placental development which in turn causes

preeclampsia. This is relevant to global warming and affects the health of the mother and fetus (19–21). All factories emit waste either by air, land or noise. Pollution is also closely related to climate change. Temperature thresholds for warmth and cold were determined in the oropharyngeal mucosa of 15 patients with obstructive sleep apnea (OSA). Enlarged koncha, can cause blockage in the nose / nasal congestion (20–22).

OSA is collapse of the retrolingual airway and pharynx. The relaxation and loosening of the soft palate located at the base of the uvula and tongue causes blockage in the airways which makes breathing tiring and may even obstruct it so much that it eventually stops completely. In pregnant women with OSA, there is an increase in sympathetic activity in response to hypoxemia and hypercapnia increases peripheral vascular tone, causing an increase in systemic blood pressure. The study was conducted in 2019-2021, during the COVID-19 pandemic. Corona viruses cause upper respiratory tract infections, and contribute to the development of preeclampsia through suboptimal trophoblast invasion and induction of maternal systemic inflammation. There are great similarities between COVID-19 positive patients and preeclampsia (23–25).

The results of the calculation of the preeclampsia index value will then be known to describe the index ranking, based on the respondent's variables or characteristics, consisting of an index of gestational age, neck circumference, environmental temperature, history of hypertension and OSA. This tool can be easily and quickly used in clinical practice without relying on the awareness of the patient experiencing symptomatic apnea. It is used to assess the risk of OSA during pregnancy and has shown predictive value (26,27).

The value of the influence of OSA as a mediator of the relationship between environmental risk and preeclampsia is known to be positive at 0.029. This influence value means that if OSA is caused by the environment, it will have an impact on increasing the incidence of preeclampsia by 0.029 times. Based on the results of the relationship significance test, the value was concluded to have no significant effect (t-statistics 1,318). The family risk actor has a role in the individual's risk of OSA. So the alternative model by adding a moderating variable of family risk on the relationship between individual risk factors for OSA. this index can be used easily in clinical practice without relying on patient awareness to predict PE in pregnancy (12,28–30).

CONCLUSION

1. OSA gestational age, history of hypertension, neck circumference, ambient temperature

Has a significant effect on the incidence of preeclampsia.

2. The preeclampsia index equation is a fix predictor model of preeclampsia.

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Table 1. Distribution of the influence of risk factors on OSA in hospitals and health centers in the Mojokerto region in 2020-2021.

No	Indicator	B	SE	P	OR	95%CI	
						lower	high
1	Mother's age	0.031	0.028	0.269	1.031	0.977	1.089
2	Gestational age	0.009	0.024	0.696	1.050	0.963	1.058
3	BMI	-0.017	0.032	0.594	0.983	0.922	1.047
4	neck circumference	0.070	0.041	0.089	1.072	0.990	1,162
5	parity	0.546	0.134	0.000	0.726	1.327	2,245
6	upper respiratory problems						
	yes	-0.949	1.132	0.402	0.387	0.042	3,557
	no						
7	Wife's Job						
	yes	-0.619	0.639	0.332	0.538	0.154	1,883
	no						
8	History of Hypertension						
	Yes	2,583	0.422	0.000	13,233	5,791	30,237
	Not						
9	DM history						
	Yes	-1,853	1.068	0.085	0.159	0.019	1,290
	Not						
10	History of snoring						
	Yes	2,300	1.173	0.050	9,969	1,001	99,260
	Not						
10	Family income	0.000	0.000	0.203	1,000	1,000	1,000
11	Smoke						
	Yes	-0.005	0.367	0.988	0.995	0.484	2.042
	Not						
12	Ambient temperature	0.128	0.102	0.210	1.031	0.977	1.089

Table 2. Frequency distribution of the effect of OSA on preeclampsia in the Mojokerto region in 2020-2021 :

Variable	PE		No PE		Total	
	F	%	F	%	F	%
OSA	51	18.75	20	7.3	71	26.1
No OSA	85	31.25	116	42.6	201	73.8
Total	136	50	136	50	272	100

Indicator	B	SE	P	OR	95%CI	
					lower	Hight
OSA incident	1,247	0.300	.000	3,480	1,933	6,265

Table 3. Distribution of the influence of risk factors and OSA on PE in hospitals and health centers in the Mojokerto region in 2020-2021

Indicator	B	SE	P	OR	95% CI	
					lower	high
Mother's age risky no	0.290	0.346	0.386	1,286	0.728	2,271
Gestational age at risk no	1,570	0.283	0.000	4,806	2,761	8,367
BMI at risk no	0.028	0.025	0.261	1.028	0.980	1.079
Neck Circumference at risk no	1,785	0.270	0.000	5,958	3,508	10,121
parity at risk no	0.016	0.104	0.876	1,016	0.829	1,245
R. Hypertension yes no	2,225	0.284	0.000	9,257	5,310	16,137
R. DM yes no	1.535	0.954	0.108	4,640	0.715	30,118
R. Snoring yes no	-1.114	1,161	0.338	0.328	0.034	3,197
Temperature	1.434	0.294	0.001	4,196	2,360	7,461
OSA incident	1,247	0.300	0.000	3,480	1,933	6,265

Table 4. OSA-based Pre - eclampsia risk screening card (Respondent sample1)

OSA-based Preeclampsia risk screening						
	OSA and Risk Factors	category	Weight	px value	Respondent risk	Risk Weight (weight x risk)
1	R. hypertension	yes	5	1	1	5
2	OSA	yes	4	1	1	4
3	neck circumference	> 33 cm	1	39 cm	1	1
4	Gestational age	< 34 weeks	1	35	1	1
5	Ambient temperature	>32C	1	37	1	1
Total Score			12			12
Pre-eclampsia risk probability (respondent 1) = total risk score						

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