

PAPER • OPEN ACCESS

Effect Of Coal Dust Exposure To Serum Interleukin 6 (IL6) And Vascular Endothelial Growth Factor (VEGF) Level As Preeclampsia Induction In Pregnant Rattus Novergicus

To cite this article: S Wasilah *et al* 2019 *J. Phys.: Conf. Ser.* **1374** 012056

View the [article online](#) for updates and enhancements.



IOP | ebooks™

Bringing together innovative digital publishing with leading authors from the global scientific community.

Start exploring the collection—download the first chapter of every title for free.

Effect Of Coal Dust Exposure To Serum Interleukin 6 (IL6) And Vascular Endothelial Growth Factor (VEGF) Level As Preeclampsia Induction In Pregnant *Rattus Novergicus*

S Wasilah¹, F Rachman², D Rosadi³, A O Puteri⁴, N Laily², F Yulidasari⁵, L Anggraini⁵, B Setiawan⁶ and M S Noor^{4,7*}

¹Department of Biology, Faculty of Medicine, Lambung Mangkurat University, Banjarmasin, Indonesia; Email: wasilah77@gmail.com

²Department of Health Management, Public Health Study Program, Faculty of Medicine, Lambung Mangkurat University, Banjarbaru, Indonesia; Email: fauzie21@ulm.ac.id

³Department of Health Promotion, Public Health Study Program, Faculty of Medicine, Lambung Mangkurat University, Banjarbaru, Indonesia; Email: dian_rosadi@ymail.com

⁴Department of Reproductive Health, Public Health Study Program, Faculty of Medicine, Lambung Mangkurat University, Banjarbaru, Indonesia; Email: oputriandini@gmail.com

⁵Department of Nutrition, Public Health Study Program, Faculty of Medicine, Lambung Mangkurat University, Banjarbaru, Indonesia; Email: riniyulidasari@gmail.com

⁶Department of Biochemistry, Faculty of Medicine, Lambung Mangkurat University, Banjarmasin, Indonesia; Email: ganesh79setiawan@gmail.com

⁷Department of Public Health, Faculty of Medicine, Lambung Mangkurat University, Banjarmasin, Indonesia; Email: drmeitria@yahoo.com

*Corresponding author's email: drmeitria@yahoo.com

Abstract. South Kalimantan is one of provinces in Indonesia that has a lot of coal minings. south kalimantan living environment committee showed that there are 49 coal minings in 13 regions. the most coal minings are in Kotabaru, Tanah Laut and Balangan, each has 10 coal minings. Air pollution because of coal dust can effect endothelial function, such as hypertension in pregnant or preeclampsia. One of its mechanisms is coal dust can induce inflammation. One of inflammation's indicator is high level of IL6. Inflammation disturb angiogenesis which is showed by low level of VEGF. High inflammation and low angiogenesis can induce endothelial dysfunction which is found in preeclampsia. This research's goal was to analyze the effect of coal dust exposure to serum IL6 and VEGF level as preeclampsia induction in pregnant *rattus novergicus*. The design was experimental with *post test only with control group design*, consisted of 7 groups: control/K0 (group without coal dust exposure), group with coal dust exposure 6,25 mg/m³ for 1 hour/day (K1-1), group with coal dust exposure 12,5 mg/m³ for 1 hour/day (K1-2), group with coal dust exposure 25 mg/m³ for 1 hour/day (K1-3), group with coal dust exposure 6,25 mg/m³ for 2 hour/day (K2-1), group with coal dust exposure 12,5 mg/m³ for 2 hour/day (K2-2), and group with coal dust exposure 25 mg/m³ for 2 hour/day (K2-3).



Exposure started since first day of pregnant until 19th day of pregnant, and termination was in the 19th of pregnant after exposure. Serum IL6 level in all of groups was in normal distribution (p value $> 0,05$) but not homogen (p value $< 0,05$), So IL6 was analyzed by nonparametric Kruskal Wallis test with p value = 0,000. It meant that there was effect of coal dust exposure to serum IL6 level as preeclampsia induction in pregnant *Rattus novergicus*. Serum VEGF level was not in normal distribution (p value $< 0,05$), so it was analyzed by nonparametric Kruskal Wallis test with p value = 0,002. It meant that there was effect of coal dust exposure to serum VEGF level as preeclampsia induction in pregnant *rattus novergicus*. Coal dust exposure caused high inflammation and disturb angiogenesis. So it could induce endothelial dysfunction in preeclampsia process. The conclusion was there was effect of coal dust exposure to serum IL6 and VEGF level as preeclampsia induction in pregnant *Rattus novergicus*.

Keywords: Coal dust exposure, IL6, VEGF, preeclampsia.

1. Introduction

South Kalimantan is one of provinces in Indonesia that has a lot of coal minings. South Kalimantan Living Environment Committee showed that there are 49 coal minings in 13 regions. The most coal minings are in Kotabaru, Tanah Laut and Balangan, each has 10 coal minings. Pollutant evidence in those 3 regions in 2017 were Kotabaru Region with sulfur dioxide 403 ug/Nm³, Nitrogen Dioxide 78,5 ug/Nm³ and Carbon Monoxide 5.032 ug/Nm³; Tanah Laut Region with Sulfur Dioxide 132,34 ug/Nm³, Nitrogen Dioxide 95,35 ug/Nm³ and Carbon Monoxide 3.393 ug/Nm³; Balangan Region with Sulfur Dioxide 58,92 ug/Nm³, Nitrogen Dioxide 34,65 ug/Nm³ and Carbon Monoxide 1.199 ug/Nm³ [1].

Pollutant exposure to pregnant women can cause negative effects into mother and foetus. It also increases risk for preeclampsia and neonatal condition [2]. Air pollution also causes hypertension in pregnant such as preeclampsia that can induce high risk of premature delivery, low birthweight, small of gestation, stillbirth, and neonatal mortality [3].

Coal dust in epithel of alveolare will be fagocyted by macrofag to produce potential factors. Active macrofag will produce high level of inflammation [4]. One of inflammation cytocin that is involved in this process is interleukin 6 (IL6) [5]. Inflammation process can effect pregnant.

The result of normal process in early pregnant is placentation. It is signed by spiralis artery remodelling. This remodelling supplies oxygen and nutrition for foetus. Spiralis artery remodelling is a description of angiogenesis. Angiogenesis can be shown by vascular endothelial growth factor (VEGF) [6].

Some researches had shown that there was effect of oxidative stress and inflammation to pregnant women. One of the effect was preeclampsia. That effect's mechanism happened because of placental angiogenesis [7]. Until now, there were not a lot of researches that had evaluated effect of coal dust to serum IL6 and VEGF level as the induction of preeclampsia. The goal of this research was to analyse effect of coal dust to serum IL6 and VEGF level as the induction of preeclampsia.

2. Materials and Methods

2.1. Research Design

This research design was experimental with *post test only with control group design*. The subjects were *Rattus novergicus* in 12 weeks. Female *Rattus novergicus* will be mated by male *Rattus novergicus*. Sample size was calculated by Frederer formula, with minimal sample was 5/group. Total samples were 35 *Rattus novergicus*.

Samples were divided into 7 groups: *control/K0* (group without coal dust exosure), group with coal dust exposure 6,25 mg/m³ for 1 hour/day (K1-1), group with coal dust exposure 12,5 mg/m³ for 1 hour/day (K1-2), group with coal dust exposure 25 mg/m³ for 1 hour/day (K1-3), group with coal dust exposure 6,25 mg/m³ for 2 hour/day (K2-1), group with coal dust exposure 12,5 mg/m³ for 2 hour/day (K2-2), and group with coal dust exposure 25 mg/m³ for 2 hour/day (K2-3). Variables that were measured were serum IL6 and VEGF serum

2.2. Research Location

Research was done in Biochemistry Laboratory in Faculty of Medicine, Lambung Mangkurat University.

2.3. Research Procedure

2.3.1. Mating of *Rattus novergicus*. Female *Rattus novergicus* were injected by pregnant mare serum gonadotropine (PMSG) 10 IU 10 IU intraperitoneal. 48 hours after that, they were injected by human chorionic gonadotropin (HCG) 10 IU intraperitoneal. After HCG injection, they were mated by male *Rattus novergicus* with 1:1. 17 hours after mating, vaginal plug was observed in female. If it was positive, it was called as pregnant day 0.

2.3.2. Coal dust exposure. Coal dust exposure was done since in the first day of pregnant. Exposure used specific tools with dose of coal dust in each groups. Exposure finished in the day of 19.

2.3.3. Termination and sample taking. In the day of 19 of exposure, all of *Rattus novergicus* were terminated and heart blood was taken. Blood sample was made into serum and then checked for IL6 and VEGF.

2.4. Data analyzes

All of data was tabulated and analysed by homogeneity and normality test. If distribution data was normal and homogen, the test would use Anova test with 95% significant level. If data was not in normal distribution and not homogen, the test would be Kruskal Wallis test with 95% significant level.

3. Results and Discussion

This research was done in 7 groups: *control/K0* (group without coal dust exposure), group with coal dust exposure 6,25 mg/m³ for 1 hour/day (K1-1), group with coal dust exposure 12,5 mg/m³ for 1 hour/day (K1-2), group with coal dust exposure 25 mg/m³ for 1 hour/day (K1-3), group with coal dust exposure 6,25 mg/m³ for 2 hour/day (K2-1), group with coal dust exposure 12,5 mg/m³ for 2 hour/day (K2-2), and group with coal dust exposure 25 mg/m³ for 2 hour/day (K2-3). Variables that were observed were serum IL6 dan VEGF level.

Mean of serum IL6 level was in normal distribution (p value > 0.05) but not homogen (p value < 0.05). Statistic analyzes used Kruskal Wallis in Table 1.

Table 1. Analyzes of serum IL6 level.

GROUP	MEAN (pg/ml)	DEVIATION STANDARD	KRUSKAL WALLIS TEST
K0	5.26700	.994593	p = 0.000
K1-1	6.44983	.169871	
K1-2	7.15233	.514288	
K1-3	7.25033	.948923	
K2-1	6.17200	.105119	
K2-2	11.87650	4.123804	
K2-3	13.11650	6.010984	

IL6 is one of inflammation cytocin. It is included in preeclampsia process. Table 1 showed that mean of serum IL6 level in control group (without coal dust exposure) was lower than in coal dust exposure groups. Longer exposure and higher dose tend to cause higher serum IL6 level. Kruskal Wallis test showed that there was significant different between research's groups. So, inflammation happened in coal dust exposure with longer and higher doses.

The other variables was serum VEGF level. Mean of serum VEGF level was not in normal distribution (p value < 0.05), so the analyses test used Kruskal Wallis test in Table 2.

Table 2. Analyzes of serum VEGF level.

GROUP	MEAN (pg/ml)	DEVIATION STANDARD	KRUSKAL WALLIS TEST
K0	714.550	52.2709	p = 0.002
K1-1	717.133	.169871	
K1-2	937.133	148.5728	
K1-3	816.133	144.5831	
K2-1	700.133	224.0310	
K2-2	665.133	180.8963	
K2-3	571.633	48.2718	

VEGF is one of factors that is involved in angiogenesis to make spiralis artery remodeling. Spiralis artery remodeling in preeclampsia decreases. Table 2 showed the mean of serum VEGF level in control group (without coal dust exposure) was higher than in coal dust exposure groups. Longer and higher dose of exposure tend to make serum VEGF level became lower. Kruskal Wallis test showed that there was significant different between research groups. That data showed there was disturbances of angiogenesis and spiralis artery remodeling process because of coal dust exposure. This process started early clinical manifestation of preeclampsia.

Placentation in human was signed by wide utery spiralis artery remodelling. It also need the role of natural killer cell (NK cell) and invasive trophoblast. Normal pregnant has extravillous cytotrophoblast in foetus that invate spiralis artery in decidua and myometrium. Invasion of cytotrophoblast will replace mother's spiralis artery in endothelial layer and makes it becomes wider. In preeclampsia, the change is not complete. Invation of cytotrophoblast in spiralis artery is only in the surface of decidua and myometrium [8]. Abnormality of this spiralis artery remodelling can caused by inflammation.

Small coal dust can reach alveolar and make inflammation and fibrogenesis. Components of coal dust that can cause inflammation are Fe dan Si [9]. IL6 will cause inflammation in the body. Inflammation inhibits trophoblast invation and disturbs utery spiralis artery remodeling. Inhibition of placentation will cause hypoxia and induce preeclampsia [10].

Serum IL6 level in coal dust exposure groups was tend to increase, so high level of IL6 could cause wide inflammation in longer and higher dose of exposure. Inflammation was followed by decreasing of serum VEGF level. Serum VEGF level tend to decreased in longer and higer dose of exposure. It showed spiralis artery remodelling also decreased, and it could induce preeclampsia.

4. Conclusion

The conclusion was there was effect of coal dust exposure to serum il6 and vegf level as preeclampsia induction in pregnant *Rattus novergicus*.

5. Acknowledgement

We would like to thanks to Laboratory of Biochemistry Lambung Mangkurat University as the location of research. We also would like to show our thank for Faculty of Medicine, Lambung Mangkurat University for giving funding to this research.

References

- [1] Balai Lingkungan Hidup Daerah Provinsi Kalimantan Selatan 2017 *Laporan Data Pencemaran* (Banjarmasin: BLHD Prov. Kalsel)
- [2] Lu X, Lin C, Li Y, Yao T, Fung J C and Lau A K 2017 Assesment of Health Burden Caused by Particulate Matter in Southern China Using High-Resolution Satellite Observation *Environ. Int.* **98** 160-170

- [3] Lee H, Hyo J K, Yoo J L, Min Y L, Hyeonjin C, Hyemin L *et al* 2011 Kruppel-like factor KLF8 plays a critical role in adipocyte differentiation *PLoS ONE* **7** (12)
- [4] Armutcu F, Gun B D, Altin R, Gurel A 2007 Examination of lung toxicity, oxidant/antioxidant status and effect of erdosteine in rats kept in coal mine ambience *Environmental Toxicology and Pharmacology* **24** (2) 106-113
- [5] Perrone S, Maria L T, Simona N, Mariangela L, Maria S, Maria G A *et al* 2016 Placental histological examination and the relationship with oxidative stress in preterm infants *Placenta* **72-78**
- [6] Burton G J J A 2009 Oxygen, the Janus gas; its effects on human placental development and function *Epub* **215** (1) 27-35
- [7] Pereira R D, De Long N E, Wang R C, Fereshteh T, Yazdi, Alison C *et al* 2015 *Angiogenesis in the Placenta: The Role of Reactive Oxygen Species Signaling*. Biomed Research Internasional Hindawi Publishing Corporation
- [8] Kim Y J 2013 Pathogenesis dan promises non invasive markers for preeklmasia *Obstet. Gynecol. Sci.* **56** (1) 2-7
- [9] Errickson A and Arbour L 2014 The Shared Pathoetiological Effects of Particulate Air Pollution and the Social Environment on Fetal-Placental Development *Journal of Environmental and Public Health*
- [10] Laresgoiti-servitje E, Lopez N G and Olson D M 2010 An immunological insight into the origins of preeclampsia *Human Reproduction Update* **16** (5) 510-524