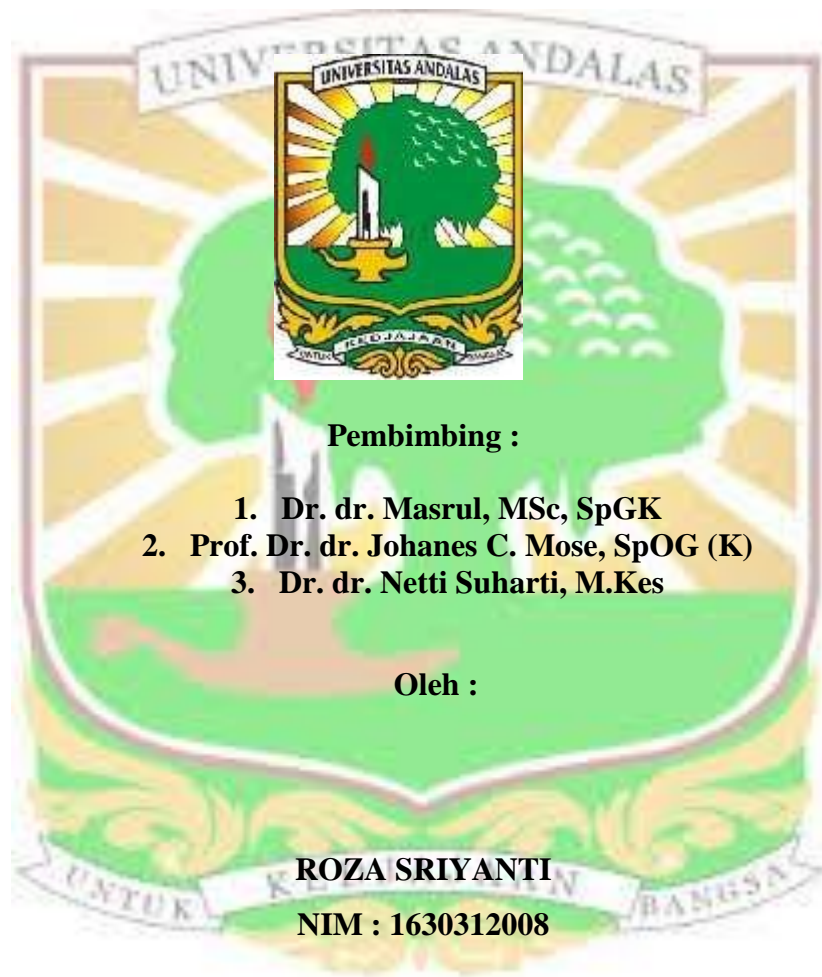


DISERTASI

**HUBUNGAN ANTARA POLIMORFISME PROMOTOR GEN LEPTIN
G-2548A, KADAR *HYPOXIA INDUCIBLE FACTORS- 1 α* DAN
KADAR LEPTIN DENGAN ONSET PREEKLAMPSIA**



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Abstrak

HUBUNGAN ANTARA POLIMORFISME PROMOTOR GEN LEPTIN G-2548A, KADAR *HYPOXIA INDUCIBLE FACTORS-1 α* DAN KADAR LEPTIN DENGAN ONSET PREEKLAMPSIA

Roza Sriyanti

Preeklamsia merupakan salah satu komplikasi kehamilan yang sering meningkatkan morbiditas dan mortalitas ibu. Patofisiologi preeklamsia sampai saat ini masih belum jelas. Adanya pengaruh faktor HIF-1 α dan leptin ikut berperanan terhadap perkembangan preeklamsia. Tujuan penelitian ini untuk mengetahui hubungan polimorfisme promotor gen leptin G-2548A, kadar hypoxia inducible factors - 1 α dan kadar leptin dengan onset preeklamsia

Penelitian dilakukan dengan menggunakan desain *cross sectional comparative study*. Penelitian ini dilakukan dari bulan Mei 2018 - April 2019 yang dilaksanakan dibagian/ SMF Obstetri dan Ginekologi RSUD dr. M. Djamil Padang, RSUD Achmad Mochtar, RSUD Solok, RST Reksodiwiryo. Sampel terdiri dari 69 orang ibu hamil yang memenuhi kriteria inklusi dan eksklusi dan dikelompokkan berdasarkan onset preeklamsia yaitu 23 orang PEAD, 23 orang PEAL dan 23 orang kehamilan normal. Pengambilan sampel dengan *consecutive sampling*. Pemeriksaan kadar HIF-1 α dan kadar leptin dengan metode ELISA yang dilakukan di Laboratorium Biomedik Fakultas Kedokteran Universitas Andalas dan pemeriksaan polimorfisme promotor gen leptin G-2548A dengan metode sekuensing yang dilakukan di *First Base laboratories, Singapore* dan di Biotek Universitas Andalas. Analisis statistik menggunakan uji chi-square dan anova dengan signifikansi ($p < 0,05$).

Rerata kadar HIF-1 α pada PEAD paling tinggi dibandingkan PEAL dan kehamilan normal ($1366,96 \pm 733,40$ pg/ml vs $916,87 \pm 466,06$ pg/ml vs $716,77 \pm 541,08$ pg/ml), dan terdapat hubungan yang bermakna ($p = 0,001$). Rerata kadar leptin pada PEAD paling tinggi dibandingkan PEAL dan kehamilan normal ($64,07 \pm 78,27$ ng/ml vs $30,46 \pm 31,99$ ng/ml vs $16,61 \pm 24,49$ ng/ml) dan terdapat hubungan yang bermakna ($p = 0,007$). Pada polimorfisme promotor gen leptin G-2548A didapatkan genotipe AA (homozigot) pada PEAD lebih tinggi dibandingkan PEAL dan kehamilan normal ($60,86\%$ vs $52,18\%$ vs $43,47\%$) dan tidak terdapat hubungan yang bermakna ($p = 0,897$). Hubungan kadar leptin dengan polimorfisme promotor gen leptin G-2548A tidak didapatkan hubungan yang bermakna dari ketiga kelompok. Selain polimorfisme G-2548A, pada penelitian ini juga menemukan dua variasi basa baru yaitu pada lokasi 128.238.686 (A-2504G) dan 128.238.741 (C-2559T) pada data genom, dan belum terdaftar di NCBI. Berdasarkan uji statistik tidak didapatkan hubungan yang bermakna antara polimorfisme promotor gen leptin C-2559T dengan onset preeklamsia.

Kesimpulan penelitian ini terdapat hubungan kadar HIF-1 α , kadar leptin dengan onset preeklamsia dan tidak terdapat hubungan polimorfisme promotor gen leptin G-2548A dengan onset preeklamsia dan kadar leptin. Dari penelitian ini didapatkan dua varian baru (A-2504G dan C-2559T) yang kemungkinan berhubungan dengan onset preeklamsia.

Kata Kunci : PEAD, PEAL, HIF-1 α , Leptin, Polimorfisme promotor gen leptin G-2548A



ABSTRACT

RELATIONSHIP OF POLYMORPHISMS OF G-2548A LEPTIN GENE PROMOTER, HYPOXIA INDUCIBLE FACTORS-1A LEVEL AND LEPTIN LEVEL WITH THE ONSET OF PREECLAMPSIA

Roza Sriyanti

Preeclampsia is a complication that increases maternal morbidity and mortality in pregnancy. The pathophysiology of preeclampsia is still unclear. Some studies described that HIF-1 α and leptin play role in the development of preeclampsia. This study aims to determine the relationship of polymorphism of G-2548A leptin gene promoter, hypoxia inducible factors-1 α level and leptin level with the onset of preeclampsia.

The study was conducted using a cross sectional comparative study design. This research was conducted from May 2018 to April 2019 in Obstetrics and Gynecology Department of General Hospital Dr. M. Djamil Padang, Achmad Mochtar General Hospital Bukittinggi, Solok General Hospital, Reksodiwiryo General Hospital Padang. Subjects were 69 pregnant women who met the inclusion and exclusion criteria and divided based on the onset of preeclampsia, including 23 subjects of EOPE group, 23 subjects of LOPE group and 23 subjects of normal pregnancies group. Samples were selected using consecutive sampling. HIF-1 α levels and leptin levels were examined using ELISA method that was performed in the Biomedical Laboratory of the Faculty of Medicine of Andalas University and polymorphism of the G-2548A leptin gene promoter were examined using sequencing methods conducted at First Base Laboratories, Singapore and Andalas University Biotech. Statistical analysis was performed using Chi-square and Anova tests with significance of $p < 0.05$.

Mean HIF-1 α level in EOPE was the highest compared to LOPE and normal pregnancy group (1366.96 ± 733.40 pg/ml vs 916.87 ± 466.06 pg/ml vs 716.77 ± 541.08 pg/ml) and there was relationship between HIF-1 α levels with onset of preeclampsia (p value=0.004). Mean leptin level was the highest in EOPE group compared to LOPE and normal pregnancy group (64.07 ± 78.27 ng/ml vs 30.46 ± 31.99 ng/ml vs 16.61 ± 24.49 ng/ml) and there was relationship between leptin levels with onset of preeclampsia (p value=0.008). In the polymorphism of the G-2548A leptin gene promoter, genotype of AA (homozygous) in EOPE was higher than that in LOPE and normal pregnancy group (60.86% vs 52.18% vs 43.47%) and there was no relationship between polymorphism of the G-2548A leptin gene promoter with onset of preeclampsia. In addition to the G-2548A polymorphism, this study also found two new base variations, at 128,238,686 (A-2504G) and 128,238,741 (C-2559T) location in genome data, and have not yet been registered in NCBI and there was no relationship between polymorphism of

the C-2559T leptin gene promoter with onset of preeclampsia.

It was concluded that there is a relationship between HIF-1 α level and leptin level with the onset of preeclampsia but there is no relationship between the polymorphism of G-2548A leptin gene promoter with the onset of preeclampsia and leptin levels. In this study, two new variants (A-2504G and C-2559T) were obtained which might be related to the onset of preeclampsia.

Keywords: EOPE, LOPE, HIF-1 α , Leptin, Polymorphism of the G-2548A Leptin Gene Promoter

