

Patogenesis prolaps uteri perempuan menopause: kajian variasi gen HOXA11, COL3A1, protein HOXA11, COL3A1, MMP2, MMP9, TIMP, P53, dan berbagai faktor klinis = Pathogenesis of uterine prolapse in menopausal woman research of gene variation hoxa11 col3a1 protein hoxa11 col3a1 colla1 mmp2 mmp9 timp p53 and clinical factors

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Abstrak

**ABSTRAK**

Prolaps uteri merupakan kondisi yang sering dialami oleh perempuan dan dapat menurunkan kualitas hidup. Penyebab prolaps uteri multifaktorial, pada umumnya berupa faktor klinis. Penelitian ini bertujuan untuk mengetahui adanya variasi gen berupa mutasi gen HOXA11 dan COL3A1 pada penderita prolaps uteri, mengetahui adanya perbedaan ekspresi protein HOXA11, COL3A1, COL1A1, MMP2, MMP9, TIMP, dan p53 pada penderita prolaps uteri dibandingkan pada perempuan tanpa prolaps uteri, serta mengetahui faktor risiko yang berhubungan dengan prolaps uteri. Studi potong lintang ini melibatkan 22 pasien prolaps uteri dan 22 tanpa prolaps uteri mulai Juni 2016 sampai Februari 2017 di RSUP dr. Kariadi Semarang. Dilakukan pencatatan data karakteristik berupa usia, paritas, IMT dan berat lahir bayi. Dilakukan pemeriksaan sekuens DNA gen HOXA11 dan Col3A1, pemeriksaan imunohistokimia pada ligamentum sakrouterina untuk menilai ekspresi protein HOXA11, COL1A1, Col3A1, MMP2, MMP9, TIMP, dan p53 pada perempuan menopause dengan prolaps uteri dan tanpa prolaps uteri. Tidak didapatkan variasi berupa mutasi gen HOXA11 pada perempuan dengan prolaps uteri sepanjang fragmen yang digunakan untuk sekuensing DNA. Didapatkan mutasi pada gen COL3A1 pada 10 pasien dengan prolaps uteri dan 6 pasien tanpa prolaps uteri  $p = 0,719$  sepanjang fragmen yang digunakan untuk sekuensing DNA. Ekspresi protein COL1A1, MMP-9 dan p53 lebih tinggi pada kelompok prolaps  $p < 0,05$ . Rerata usia, rerata paritas dan rerata berat lahir bayi, berbeda secara uji statistik pada kedua kelompok. Pada fragmen yang diperiksa tidak didapatkan mutasi gen HOXA11, namun didapatkan mutasi gen COL3A1 pada penderita prolaps maupun perempuan tanpa prolaps uteri. Tampak adanya faktor internal yang berperan untuk terjadinya prolaps uteri selain berbagai faktor risiko klinis. Faktor eksternal berupa usia, berat bayi lahir, dan paritas memiliki hubungan dengan prolaps uteri. Kata kunci: COL1A1, COL3A1, faktor klinis, HOXA11, menopause, MMP2, MMP9, mutasi gen, p53, prolaps uteri, TIMP.

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**ABSTRACT**

Uterine prolapse is a condition that decreases the quality of life of women. Multiple factors, mostly clinical, affect the course of uterine prolapse. The aims of the study were to investigate the genetic variation in the form of HOXA11 and Col3a2 gene mutations in women with uterine prolapse. This study also aimed to investigate different expression of HOXA11, COL3A1, COL1A1, MMP2, MMP9, TIMP, and p53 proteins in women with and without uterine prolapse, and to understand risk factors associated with uterine prolapse. A total of 44 women were enrolled in this cross sectional study, 22 of which with uterine prolapse and 22 others without uterine prolapse. This study was conducted between June 2016 and February 2017 in

RSUP dr Kariadi, Semarang. demographic data including age, parity, BMI, and birth weight were recorded. HOXA11 and COL3A1 gene sequencing, immunohistochemistry testing of uterosacral ligament were conducted to assess HOXA11, COL1A1, COL3A1, MMP2, MMP9, TIMP, and p53 protein expressions. A mutation in COL3A1 gene along the fragment used in DNA sequencing was found among 10 women with uterine prolapse and 6 women without uterine prolapse although this did not reach statistical significance  $p = .719$ . No genetic variation in the form of HOXA11 gene mutation was found in women with uterine prolapse. Higher expression of COL1A1, MMP 9 and p53 proteins were found in prolapse group  $p = .05$ . The average of age, parity, and birth weight in two groups were statistically different. Only the COL3A1 gene mutation was detected in women with and without uterine prolapse. Beside, various clinical factors, it was confirmed that some internal factors also play important role in the course of uterine prolapse. Examples of external factors are age, birth weight, and parity. Key word COL1A1, COL3A1, clinical factors, gen mutation, HOXA11, menopause, MMP2, MMP9, p53, TIMP, uterine prolapse.