

**HUBUNGAN STATUS ASETILATOR
GEN N-ACETYLTRANSFERASE 2 (NAT2)
DENGAN KONSENTRASI PLASMA ISONIAZID
(INH) PADA PASIEN TB MDR YANG MENDAPAT
PADUAN TERAPI JANGKA PENDEK
DI SUMATERA BARAT**

TESIS



**Oleh:
MEGA SENJA
1550306202**

**PEMBIMBING:
DR. Dr. MASRUL BASYAR, Sp.P(K) FISR
Dr. Yessy Susanty Sabri, Sp.P(K) FISR
Dr.Afriani, Sp.P(K)**

**BAGIAN PULMONOLOGI DAN KEDOKTERAN RESPIRASI
FAKULTAS KEDOKTERAN UNAND/ RSUP. Dr. M. DJAMIL**

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Abstrak

Latar belakang: Isoniazid (INH) salah satu obat yang penting untuk pengobatan TB. INH dosis tinggi digunakan pada paduan terapi TB MDR jangka pendek. Status asetilator gen NAT2 berpengaruh terhadap konsentrasi obat. Pengetahuan status asetilator penting untuk mengetahui risiko hepatotoksisitas, kegagalan pengobatan dan resistensi obat. Penelitian ini bertujuan mengetahui hubungan status asetilator gen NAT2 dengan konsentrasi plasma INH 2 jam setelah pemberian oral.

Metode: Penelitian cross sectional pada pasien TB MDR yang mendapat paduan terapi jangka pendek di RSUP Dr M Djamil Padang, RSUD Dr Achmad Mochtar Bukittinggi dan RS Paru Sumatera Barat dari Oktober 2019 hingga Mei 2020. Pasien diperiksa status asetilator gen NAT2 dan konsentrasi INH plasma. Hasil konsentrasi INH plasma yang didapatkan dievaluasi berdasarkan kelompok status asetilator gen NAT2.

Hasil: Penelitian ini mendapatkan sebagian besar laki-laki (62,5%) dengan usia terbanyak 40-64 tahun (50%), komorbid terbanyak ditemukan diabetes mellitus (31,25%), dan 75% pasien normoweight. Sebanyak 7 alel ditemukan pada pasien TB MDR yang mendapat terapi jangka pendek diantaranya terdapat 1 alel yang belum bisa ditentukan karena terdapat mutasi di 776 C>A (rs1304162037) yang belum dipublikasikan di NAT2 *Gene Nomenclature Committee*. Alel terbanyak ditemukan adalah NAT2*12A (56,25%) dan status asetilator gen NAT2 terbanyak pada penelitian ini adalah asetilator cepat (NAT2*12A/*12A). Berdasarkan distribusi bimodal nilai median konsentrasi INH pada asetilator cepat 1,25µg/ml dan asetilator lambat 5,24µg/m. Tidak ada hubungan jenis status asetilator gen NAT2 dengan konsentrasi INH plasma.

Kesimpulan: Tidak ada hubungan konsentrasi INH plasma dengan jenis status asetilator gen NAT2

Kata kunci: NAT2, INH, Status asetilator, TB MDR

ABSTRACT

Background: Isoniazid (INH) is an important drug for TB treatment. High doses of INH are used in short-term MDR-TB therapy. The NAT2 gene acetylator status affects drug concentration. Knowledge of a patient's acetylator status is essential to determine the risk of hepatotoxicity, treatment failure, and drug resistance. This study aims to determine relationship between NAT2 gene acetylator status and plasma concentration of INH 2 hours after oral administration.

Method: Cross-sectional study on MDR-TB patients with short-term therapy at Dr. M. Djamil Hospital, Dr Achmad Mochtar Hospital, and West Sumatra Lung Hospital from September 2019 to February 2020. Patients were examined for the NAT2 Acetylator and plasma concentrations of INH. Plasma concentration of INH results were evaluated based on NAT2 gene acetylator status group.

Results: Results found that most of male (62.5%) with the age ranged 40-64 years (50%), the highest comorbid was diabetes mellitus (31.25%), and 75% of patients were normoweight. Seven alleles were found in MDR TB patients receiving short-term therapy, 1 allele could not be determined as there was mutation in 776 C>A (rs1304162037) unpublished in NAT2 Gene Nomenclature Committee. Alleles found were NAT2*12A (56.25%) and the most acetylator status of NAT2 genes was fast acetylators (NAT2*12A/*12A). Based on the bimodal distribution, median of INH concentration on fast acetylators was 1.25 µg/ml and slow acetylators was 5.24 µg/m. No relationship between NAT2 gene acetylator status and plasma INH concentration.

Conclusion: No relationship between plasma concentration of INH and NAT2 gen acetylator status group.

Keywords: NAT2, INH, acetylator status, MDR-TB

