

## ABSTRAK

### Latar belakang:

Alkohol merupakan zat adiktif yang sering disalahgunakan di masyarakat. Data epidemiologi di negara berkembang khususnya di Indonesia belum diketahui secara pasti, namun alkohol banyak dikonsumsi secara ilegal. Penyalahgunaan alkohol menimbulkan kerusakan hati, namun tidak semua mengalami sirosis hepatis. Polimorfisme genetik pada enzim-enzim pemetabolisme alkohol memiliki peran pada penyakit hati yang disebabkan oleh alkohol.

**Tujuan penelitian:** tujuan penelitian ini mengetahui pengaruh polimorfisme gen *alkohol dehydrogenase3* dan *aldehid dehydrogenase2* terhadap kerusakan sel hati pada peminum alkohol suku Jawa di Yogyakarta.

**Metode penelitian:** penelitian ini merupakan penelitian *observasional* diskriptif. Rancang penelitian secara *case control*, dilakukan pada peminum alkohol dan bukan peminum alkohol suku Jawa di Yogyakarta. Sampel darah diambil melalui vena cubiti, setelah *informed consent* pemeriksaan polimorfisme gen *ADH3* dan gen *ALDH2* dengan PCR-RFLP, aktivitas ADH dan status fungsi hati (SGOT, SGPT, GGT) dengan spektrofotometri. Distribusi dan frekuensi polimorfisme gen *ADH3* dan gen *ALDH2*, dianalisa secara deskriptif, sedang perbedaan aktivitas ADH, pengaruh gen *ADH3* dan *ALDH2* terhadap kerusakan sel hati antara peminum alkohol dan bukan peminum alkohol dianalisa dengan  $X^2$ .

**Hasil penelitian:** Frekuensi distribusi polimorfisme gen *ADH3* dan gen *ALDH2*, pada peminum alkohol dan bukan peminum alkohol suku Jawa berturut-turut adalah tipe gen *ADH3\*1* (3,4%, 1,0%); *ADH3\*2* (76,4%, 88,2%); *ADH3\*1/3\*2* (20,2%, 10,8%), nilai  $P > 0,05$  dan tipe gen *ALDH2\*1* (17,7%, 35,9%); *ALDH2\*2* (82,3%, 63,1%); *ALDH2\*1/2\*2* (0,0%, 0,1%), nilai  $p < 0,05$ . Aktivitas enzim ADH berdasar konsentrasi etanol pada peminum alkohol (0,074891 mM) dan bukan peminum alkohol (0,052603 mM). Terdapat perbedaan pengaruh polimorfisme gen *ADH3\*2* dan *ADH3\*1/3\*2* serta gen *ALDH2\*2* terhadap kerusakan sel hati antara peminum alkohol dan bukan peminum alkohol suku Jawa, berdasarkan nilai kimia darah GGT, bermakna secara statistik dengan  $p < 0,05$

**Kesimpulan:** Tipe *ADH3* dan *ALDH2* baik pada peminum alkohol maupun bukan peminum alkohol sebagian besar adalah *ADH3\*2* (76,4%, 88,2%), dan *ALDH2\*2* (82,3%, 63,1%). Aktivitas enzim ADH kedua subyek lambat. Terdapat perbedaan pengaruh polimorfisme gen *ADH3\*2* dan *ADH3\*1/3\*2* serta gen *ALDH2\*2* terhadap kerusakan sel hati antara peminum alkohol dan bukan peminum alkohol suku Jawa, berdasarkan nilai kimia darah GGT

**Kata kunci:** polimorfisme gen *ADH3*, gen *ALDH2*, aktivitas enzim ADH, peminum alkohol, suku Jawa

## ABSTRACT

**Background:** Alcohol is an addictive substance which is frequently abused by people. Epidemiologic data from developing countries, particularly Indonesia, is not known for certain, but alcohol is frequently consumed illegally. Alcohol abuse can cause liver damage, although not all progress to liver cirrhosis. Genetic polymorphism in enzymes which metabolize alcohol play a role in the development of liver diseases caused by alcohol.

**Objectives:** The purpose of this study is to understand the effect of polymorphism in *alcohol dehydrogenase3* and *aldehyd dehydrogenase2* genes on liver cell's damage in Javanese alcoholics in Yogyakarta.

**Methods:** This was a descriptive observational study, with case-control design. The subject were Javanese alcoholics and non-alcoholics in Yogyakarta. Blood samples were collected from cubital vein after informed consents were acquired. Polymorphism of *ADH3* and *ALDH2* genes were tested using PCR-RFLP, while ADH activity and liver function status (SGOT, SGPT, GGT) were checked using spectrophotometry. Distribution and frequency of polymorphism in *ADH3* and *ALDH2* genes were analyzed descriptively, while differences in ADH activity, and effect of *ADH3* and *ALDH2* genes in liver cell's damage between alcoholics and non-alcoholics were analyzed using chi square test.

**Results:** Distribution frequency of *ADH3* and *ALDH2* genes polymorphism between Javanese alcoholics and non-alcoholics in each gene types respectively were: *ADH3\*1* (3,4%, 1,0%); *ADH3\*2* (76,4%, 88,2%); *ADH3\*1/3\*2* (20,2%, 10,8%), with  $p\text{-value} > 0,05$ ; and *ALDH2\*1* (17,7%, 35,9%); *ALDH2\*2* (82,3%, 63,1%); *ALDH2\*1/2\*2* (0,0%, 0,1%), with  $p\text{-value} < 0,05$ . ADH enzyme activity according to ethanol concentration in alcoholics was 0,074891 mM and in non-alcoholics was 0,052603 mM. There was a difference in effect of polymorphism in gene *ADH3\*2*, *ADH3\*1/3\*2*, and *ALDH2\*2* in liver cell's damage between Javanese alcoholics and non-alcoholics, according to blood GGT value, with statistically significant  $p\text{-value} < 0,05$

**Conclusions:** The most common *ADH3* and *ALDH2* gene polymorphism in both alcoholics and non-alcoholics were *ADH3\*2* (76,4%, 88,2%) and *ALDH2\*2* (82,3%, 63,%). ADH enzyme activity in both groups were low. There was a difference in effect of polymorphism in gene *ADH3\*2*, *ADH3\*1/3\*2*, and *ALDH2\*2* in liver cell's damage between Javanese alcoholics and non-alcoholics, according to blood GGT value.

**Keywords:** genetic polymorphism, *ADH3* gene, *ALDH2* gene, ADH enzyme activity, alcoholics, Javanese