The expressions of cd44, cd90 and alpha fetoprotein biomarkers in Indonesian patients with advanced liver disease: An observational study

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Abstrak

Background: increased serum alpha fetoprotein (AFP) levels are often found in patients with advanced hepatocellular carcinoma (HCC). Cluster Differentiation 44 (CD44) and CD90 are stem cell biomarkers that have been assumed as the early HCC markers and associated with onset and progressivity of HCC. The study related to HCC stem cell has not been available in Indonesia. The present study aimed to evaluate the expression of cancer stem cell markers (CD44, CD90) and AFP levels in patients with advanced liver disease.

Methods: an observational study was conducted in 41 patients with chronic hepatitis B and/or C infection, liver cirrhosis, and HCC at dr. Saiful Anwar General Hospital. CD44 and CD90 expressions were measured with flow cytometry, and AFP serum levels with ELISA. Data on patient characteristics were evaluated using bivariate and multivariate statistical analysis (One-way ANOVA, Mann-Whitney, Chi-Square, Kruskal-Wallis). Data of CD44, CD90 and AFP were analyzed using Kruskal Wallis test with a significance value of $p < 0.05$, and diagnostic power was analyzed using receiver operating characteristic (ROC).

Results: the subjects of our study were 16 patients with chronic hepatitis, 15 patients with liver cirrhosis, and 10 patients with HCC. There was a significant difference regarding CD44+CD90+ and AFP among those three groups ($p=0.001$; $p=0.000$) specifically in chronic hepatitis compared to liver cirrhosis ($p=0.002$; $p=0.000$) and HCC ($p=0.002$; $p=0.000$) respectively. ROC analysis showed the best diagnostic power for the combination of CD44+CD90+ and AFP (AUC=0.981; $p=0.000$).

Conclusion: there are higher expressions of CD44+CD90+ and serum AFP levels in patients with HCC compared to the other two groups (those with chronic hepatitis and liver cirrhosis). The combination of both parameters has the best diagnostic power of HCC.

......Latar belakang: meningkatnya kadar alfa fetoprotein (AFP) serum seringkali ditemui pada pasien karsinoma sel hati (KSH) tahap lanjut. Cluster Differentiation 44 (CD44) dan CD90 adalah biomarker sel punca yang diduga merupakan penanda awal KSH dan berhubungan dengan onset dan progresivitas KSH. Hingga kini masih belum ada studi terkait sel punca KSH di Indonesia. Studi ini bertujuan untuk mengevaluasi ekspresi penanda sel punca kanker CD44, CD90 dan kadar AFP pada pasien dengan penyakit hati lanjut.

Metode: studi observasional dilakukan pada 41 pasien dengan hepatitis B dan/ atau C kronis, sirosis hati, dan KSH di RSUD dr. Saiful Anwar Malang. Ekspresi CD44 dan CD90 dalam darah diukur menggunakan flow cytometri dan kadar AFP serum menggunakan ELISA. Data karakteristik pasien dilakukan analisa statistik bivariat dan multivariat (One way ANOVA, Mann-Whitney, Chi-Square, Kruskal-Wallis). Data CD44, CD90 dan AFP dianalisis menggunakan uji Kruskal Wallis dengan signifikansi $p < 0,05$, serta uji kekuatan diagnostik dengan analisis receiver operating characteistic (ROC).

Hasil: subjek penelitian ini adalah 16 pasien hepatitis kronis, 15 pasien sirosis hepatis, dan 10 pasien KSH. CD44+CD90+ dan AFP pada ketiga kelompok mempunyai perbedaan signifikan ($p=0.001$; $p=0.000$),

khususnya pada hepatitis kronis yang dibandingkan dengan sirosis hepatis (p=0.002; p=0.000) dan KSH (p=0.002; p=0.000). Analisa ROC menunjukkan kekuatan diagnostik paling baik pada kombinasi CD44+CD90+ dengan AFP (AUC=0.981; p=0.000;).

Kesimpulan: ekspresi CD44+CD90+ dan kadar AFP serum pada pasien dengan KSH lebih tinggi dibandingkan hepatitis kronis dan sirosis hepatis. Kombinasi kedua parameter ini memiliki kekuatan diagnostik KSH yang paling baik