

# Hubungan Biomarker Fibrosis Hati Transforming Growth Factor-B, Matrix Metalloproteinase-7, dan Ultrasonografi Acoustic Radiation Force Impulse Dengan Derajat Fibrosis Hati Pada Pasien Atresia Bilier = Correlation Between Liver Fibrosis Biomarkers Transforming Growth Factor-B, Matrix Metalloproteinase-7, and Acoustic Radiation Force Impulse Ultrasound with Degree of Liver Fibrosis in Biliary Atresia Patients

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## Abstrak

Latar belakang: Atresia bilier merupakan penyebab paling umum fibrosis hati pada anak, dan menjadi indikasi terbanyak transplantasi hati. Fibrosis hati dapat dinilai dengan pemeriksaan histopatologis dan kuantifikasi skor Laennec. Pemeriksaan biomarker dari darah dan metode pencitraan radiologis merupakan upaya lain untuk menilai derajat fibrosis hati. Penelitian ini dimaksudkan untuk meneliti perbandingan biomarker penanda fibrosis transforming growth factor (TGF-), matrix metalloproteinase (MMP)-7, dan ultrasonografi (USG) Acoustic Radiation Force Impulse (ARFI) dengan derajat fibrosis berdasarkan pemeriksaan histopatologi. Metode penelitian: Penelitian ini merupakan penelitian desain cross sectional pada pasien anak dengan kolestasis yang dicurigai akibat atresia bilier di ruang rawat anak RSUPN Cipto Mangunkusumo. Data penelitian ini adalah data primer dari anamnesis, pemeriksaan fisik, serta data sekunder dari rekam medis untuk melihat riwayat penyakit pasien. Dilakukan pemeriksaan serum biomarker TGF- dan MMP-7, dan USG ARFI oleh operator yang telah ditentukan. Dibandingkan hasil pemeriksaan TGF-, MMP-7, USG ARFI dengan hasil skoring fibrosis biopsi hati.

Hasil penelitian: Dari total 15 pasien dengan AB, terdapat 6 pasien F2-F3, dan 9 pasien F4 berdasarkan derajat fibrosis biopsi hati. Terdapat peningkatan kadar TGF- dengan adanya peningkatan derajat fibrosis biopsi hati, namun tidak terdapat hubungan bermakna antara derajat fibrosis hati dengan kadar TGF- (uji Mann-Whitney,  $p=0.768$ ). Pada penelitian ini, rerata kadar MMP-7 pada kelompok F2-3 dan F4 menunjukkan peningkatan, namun tidak terdapat hubungan yang bermakna (Uji Mann-Whitney,  $p=0.409$ ). Terdapat hubungan bermakna antara derajat fibrosis hati F2-F3 dengan derajat F4 yang diperoleh berdasarkan hasil USG ARFI dan hasil biopsi hati ( $p<0,01$ ). Kesimpulan: TGF- dan MMP-7 merupakan biomarker yang cukup efektif namun memiliki keterbatasan tidak spesifik untuk AB. USG ARFI merupakan pemeriksaan minimal invasive yang efektif untuk menentukan derajat fibrosis.

.....Background: Biliary atresia is the most common cause of liver fibrosis and the highest indication for liver transplantation in pediatrics. Liver fibrosis is quantified through Laennec score based on histopathology of liver biopsy. Blood serum biomarkers and radiological examinations are alternative methods that could determine liver fibrosis. This study aimed to compare the significance of serum biomarkers transforming growth factor (TGF-), matrix metalloproteinase (MMP)-7, and Acoustic Radiation Force Impulse (ARFI) ultrasonography (USG) in determining the degree of liver fibrosis compared to histopathology score from liver biopsy. Method: This was a cross-sectional study, on patients in the pediatric ward at dr. Cipto Mangunkusumo National Hospital, that were admitted with cholestasis with biliary atresia as the suspected etiology. Primary data was obtained through anamnesis, and physical

examination, and secondary data was obtained through patients' medical records. Serum biomarkers TGF- and MMP-7, and USG ARFI were examined by related experts and results were obtained through medical records. Results of TGF-, MMP-7, and USG ARFI were compared with fibrosis scores based on liver biopsy.

Result: From a total of 15 patients with AB, there were 6 F2-F3 patients, and 9 F4 patients according to the biopsy results. TGF- levels showed an increasing trend alongside increase in liver biopsy fibrosis score, however it was not statistically significant (Mann-Whitney test,  $p=0.768$ ). In this study, there was an increase in MMP-7 levels in F2-3 group compared to F4 group, however there was no statistically significant difference (Mann-Whitney test,  $p=0.409$ ). The ARFI USG results showed significant difference between F2-F3 group and F4 group based on ARFI USG compared to liver biopsy ( $p<0.01$ ). Conclusion: TGF- and MMP-7 are effective serum biomarkers, however, lacked specificity to determine fibrosis levels in biliary atresia. A minimally invasive test that is effective in determining the degree of fibrosis can be done through ARFI USG.