Red Cell Distribution Width to Platelet Ratio: in a Search of Non-Invasive Liver Fibrosis Biomarker

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Liver cirrhosis is the end stage of various chronic liver diseases which is known to have high prevalence and low survival rate. It's affected about 2.8 million people worldwide with mortality of 1.3 million death in 2015.[1] Multiple repeated injuries such as metabolic dysfunction, alcohol abuse, viral hepatitis, and autoimmune diseases progressively lead to liver fibrosis and eventually liver cirrhosis. The degree of liver fibrosis is not only important for patient's prognosis, but also a critical aspect for chronic liver disease treatment and management. Therefore, liver fibrosis diagnosis is mandatory for every chronic liver disease.

As the disease burden grows, the need for liver fibrosis diagnosis also increases. For chronic hepatitis B virus (HBV) infection alone, more than 5 million patients in Indonesia will require liver fibrosis assessment in 2020. As the gold standard, invasive procedure of liver biopsy alone is not practical since it is associated with various complications including hospitalization in 1-5% of cases and mortality in 0.01-0.1% of cases as well as poor patient adherence for repeated biopsies.[2] Therefore various non-invasive approaches such as scoring systems using several serum biomarkers and imaging technology have been investigated intensively.

Transient elastography (TE) is one of the non-invasive methods for diagnosing liver fibrosis. It uses a low frequency vibration transmitted through the right lobe of the liver.[3] Recent systematic review and meta-analysis by Geng et al, showed that TE has high sensitivity and specificity of 81% and 88% respectively for detecting liver fibrosis with area under the receiver operating characteristic (AUROC) curve of 0.931.[4] However, TE is only available in larger hospital and not evenly distributed across region in Indonesia. Therefore, several, more affordable and widely available, serum biomarkers have been studied for diagnosing liver fibrosis.

Red cell distribution width (RDW) to platelet ratio (RPR) is one of the non-invasive serum biomarkers that has been investigated recently for diagnosing liver fibrosis. It was known that RDW was positively correlated with liver fibrosis and cirrhosis whereas platelet and haemoglobin were negatively correlated with fibrosis and cirrhosis.[5] Chen et al in 2013 demonstrated RPR had high area under receiver operating characteristic/ROC curve (AUCs) for predicting liver fibrosis and cirrhosis in chronic hepatitis B (CHB) patients with 0.825 and 0.884 respectively.[5] More recent study in Indonesia by Tubung et al showed that RPR using cut off of 0.0666 also had high AUC of 0.816 with sensitivity and specificity of 76.9% and 78.6% respectively for predicting severe liver fibrosis in CHB patients. RPR was not inferior to aspartate aminotransferase to platelet ratio index (APRI) which is also a liver fibrosis serum biomarker for predicting sever liver fibrosis in CHB patients.[6]

Although RPR is not the only serum biomarker for liver fibrosis diagnostic, other biomarkers such as FibroTest, Fibroindex, aspartate aminotransferase (AST)/alanine aminotransferase (ALT) ratio, APRI and FIB-4 were mostly used in hepatitis C virus (HCV) infection patients that might produce conflicting result for predicting patients with HBV infection.[6] Therefore RPR is a promising, more affordable and widely available, non-invasive biomarker for diagnosing liver fibrosis particularly in Indonesia where HBV infection is dominant.

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