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Predictive Value of Hepatitis B Core-Related Antigen (HBcrAg) during Natural History of Hepatitis B Virus Infection

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Abstract : The natural history of HBV infection could experience immune tolerant (IT), immune clearance (IC), HBeAg-negative inactive/quienscent carrier (ENQ), and HBeAg-negative hepatitis (ENH). As current biomarkers for discriminating these four phases have some weaknesses, additional serological indicators are needed. Hepatits B core-related antigen (HBcrAg) encoded with precore/core gene contains denatured HBeAg, HBV core antigen (HBcAg) and a 22KDa precore protein (p22cr), which was demonstrated to have a close association with natural history of hepatitis B infection, but no specific cutoff values and diagnostic parameters to evaluate the diagnostic efficacy. This study aimed to clarify the distribution of HBcrAg levels and evaluate its diagnostic performance during the natural history of infection from a Western Chinese perspective. 294 samples collected from treatment-naïve chronic hepatitis B (CHB) patients in different phases (IT=64; IC=72; ENQ=100, and ENH=58). We detected the HBcrAg values and analyzed the relationship between HBcrAg and HBV DNA. HBsAg and other clinical parameters were quantitatively tested. HBcrAg levels of four phases were 9.30 log U/mL, 8.80 log U/mL, 3.00 log U/mL, and 5.10 logU/mL, respectively ($p < 0.0001$). Receiver operating characteristic curve analysis demonstrated that the area under curves (AUCs) of HBcrAg and quantitative HBsAg at cutoff values of 9.25 log U/mL and 4.355 log IU/mL for distinguishing IT from IC phases were 0.704 and 0.694, with sensitivity 76.39% and 59.72%, specificity 53.13% and 79.69%, respectively. AUCs of HBcrAg and quantitative HBsAg at cutoff values of 4.15 log U/mlmL and 2.395 log IU/mlmL for discriminating between ENQ and ENH phases were 0.931 and 0.653, with sensitivity 87.93% and 84%, specificity 91.38% and 39%, respectively. Therefore, HBcrAg levels varied significantly among four natural phases of HBV infection. It had higher predictive performance than quantitative HBsAg for distinguishing between ENQ-patients and ENH-patients and similar performance with HBsAg for the discrimination between IT and IC phases, which indicated that HBcrAg could be a potential serological marker for CHB.

Keywords : chronic hepatitis B, hepatitis B core-related antigen, hepatitis B surface antigens, hepatitis B virus
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