Potential plasma biomarkers: miRNA-29c, miRNA-21, and miRNA-155 in clinical progression of Hepatocellular Carcinoma patients

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Abstract	This study evaluated differences in the clinical appearance of patients with hepatocellular carcinoma (HCC) based on plasma level and regulation of microRNAs (miRNA-29c, miRNA-21, and miRNA-155). The observational-analytical study with a cross-sectional design was conducted on 36 HCC patients and 36 healthy controls. The blood samples were collected from 2 Province Hospitals (Dr. Sardjito Hospital and Prof. Dr. Margono Soekarjo Hospital) for HCC and the Blood Bank Donor of the Indonesian Red Cross for 36 healthy controls. These blood samples were treated as follows: plasma isolation, RNA isolation, cDNA synthesis, quantification by qRT-PCR using a sequence-specific forward primer, and normalization of miRNA using housekeeping-stably miRNA-16. There were only 27 HCC patients with complete clinical variables (neutrophil to lymphocyte ratio (NLR), platelet to lymphocyte ratio (PLR), platelet count, albumin, C-reactive protein (CRP), and cholinesterase (ChE)) that were able to analyses for regulation miRNAs based on its fold change expression miRNA target. All 27 HCC subjects were follow-up until 3-years of monitoring for their overall survival. The miRNA plasma expression was analyzed by Bio-Rad CFX 96 Manager software to determine the cycle of quantification, followed by the calculation of expression levels using Livak's methods. Data were analyzed using STATA 11.0, with a significant value of $p<0.05$. The miRNAs expression of HCC subjects were lower than that healthy control subjects in miRNA-29c (down-regulation 1.83-fold), higher than that healthy control subjects in miRNA 21 and miRNA-155 (up-regulation, 1.74-fold; 1.55-fold) respectively. NLR, CRP, ChE, and platelet count showed a significant difference in miRNA-29c regulation, though neutrophil count showed a significant difference in miRNA-21 and miRNA-155 regulation ($p<0.05$). Conclusion: Plasma biomarkers: miRNA-21 and miRNA155 might be potential biomarkers as onco-miR in HCC subjects, while miRNA-29c might act as a tumor suppressor. Significant evidence was identified with clinical progression based on the regulation of miRNAs, which was consistent with miRNA -29c.
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