ABSTRACT

Colorectal cancer (CRC) is one of the most prevalent types of cancer in both genders worldwide. In Indonesia alone, CRC ranks second in men and third in women for its prevalence. Microsatellite instability (MSI) occurs in 15% of all CRC cases from hereditary and sporadic origins. In sporadic cases, more than 90% of MSI cases results from mismatch repair (MMR) *MLH1* gene promoter hypermethylation. The analysis of *MLH1* methylation plays a crucial role in the decision-making algorithm towards having genetic testing for CRC with MSI phenotype. Methylation-sensitive high-resolution melting (MS-HRM) analysis has shown a future potential as a tool for detecting DNA methylation and determining methylation status. This study aims to optimize the detection of methylation of *MLH1* promoter in CRC samples using MS-HRM analysis. There were 14 CRC patient samples used (8 MSS samples and 6 MSI samples). The methods included bisulfite conversion of isolated DNA samples of CRC, quality control using *MYOD1* PCR, MS-HRM analysis for *MLH1*, and data analysis to determine the *MLH1* methylation status of each sample. This study showed that 50% of the samples with loss of *MLH1* expression and MSI scoring was able to be detected for partial methylation of *MLH1*. Meanwhile, the other 50% of the MSI samples were determined as *MLH1*-unmethylated. The results of this study suggested the importance of *MLH1* methylation analysis in the genetic testing algorithm of CRC, as well as the potential of MS-HRM as the analysis method.

Keywords: colorectal cancer, microsatellite instability, *MLH1*, promoter hypermethylation, MS-HRM