

## Detection of serum levels of human telomerase reverse transcriptase (*hTERT*) mRNA in non-alcoholic steatohepatitis (NASH) related hepatocellular carcinoma (HCC) in Sri Lanka

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NAFLD is a spectrum that can progress from simple liver steatosis to NASH-HCC, which is the most advanced and life-threatening stage, with increasing incidence and prevalence globally. This is attributed to its several predisposing risk factors, including genetic factors. Dysregulation of one of the critical key driver genes called human telomerase reverse transcriptase (*hTERT*) was reported to influence HCCs' pathogenesis. Traditionally, *hTERT* catalyses the insertion of the short DNA sequences (TTAGGG) to newly replicated telomere ends during normal cell division. However, its overexpression prevents the hepatocytes from undergoing traditional apoptosis, making them immortal. Currently, there is no study on the impact of *hTERT* expression levels specifically from NASH-HCC patients in Sri Lanka. Hence, this study aimed to be the first study to quantify the serum level of *hTERT* mRNA from NASH-HCC patients, hoping to contribute to identifying it as a potential non-invasive diagnostic biomarker for early diagnosis of NASH-HCC. Quantitative PCR (qPCR) was used to quantify the expression of *hTERT* mRNA levels from NASH-HCC and cirrhotic age, BMI and gender-matched controls. The analysis revealed an elevated expression of *hTERT* mRNA in the NASH-HCC cohort, with a mean level of  $9.11 \pm 8.44$ , representing a sevenfold increase compared to the cirrhotic age, BMI, and gender-matched controls, which exhibited a mean expression level of  $1.3 \pm 1.49$ . Furthermore, alanine aminotransferase (ALT) and tumor nodularity correlated with *hTERT* mRNA expression from NASH-HCC patients. We noted higher expression of *hTERT* in NASH-HCC patients than in the cirrhotic matched-control cohort. However, it is recommended to further evaluate the link between *hTERT* mRNA expression levels and some of its predisposing genetic driving risk factors, such as pathogenic *hTERT* promoter's SNPs and related key transcription factors, using a larger sample size of NASH-HCC patients; this may suggest *hTERT* level as a promising NASH-HCC diagnostic biomarker.

**Keywords:** HCC, NASH-HCC, *hTERT* mRNA, Diagnosis, Biomarker

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