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The Role of MMP-9 rs 3918242 genetic variant in association between MMP-9 serum level with risk factors of acute ischemic stroke

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ABSTRACT

Background: Increased serum MMP-9 level is known to be biomarker of atherosclerotic events and risk of cerebrovascular disease. Risk factors for acute ischemic stroke are known to be related to serum MMP-9 level. The genetic variant of MMP-9 rs3918242 is known to have a role in serum MMP-9 level. The aim of the study is to determine the role of MMP-9 rs 3918242 genetic variant in association between MMP-9 serum level with risk factors of acute ischemic stroke.
Methods: This was a cross-sectional study with an observational analytic design. 62 subjects of acute ischemic stroke treated at Dr. Kariadi Hospital Semarang from October 2018 to February 2019 were involved in this study. Statistical analysis was assessed by the bivariate test and followed by a logistic regression test.
Results: From 62 subjects in this study, 45 (72.6%) had high serum MMP-9 level. The association between serum MMP-9 level with risk factors of acute ischemic stroke was statistically significant in hypertension, diabetes mellitus, dyslipidemia, obesity, and hyperuricemia. There is a positive correlation of serum MMP-9 level with a number of acute ischemic stroke factors. In multivariate analysis, the most influential variables were obesity and hyperuricemia. CC Genetic Variant has a role in the association between serum MMP-9 level with risk factors of acute ischemic stroke, which are hypertension, diabetes mellitus, dyslipidemia, obesity, and hyperuricemia. Meanwhile, CT genetic variants only play a role in the association of serum MMP-9 levels with obesity and hyperuricemia as the risk factors for acute ischemic stroke.
Conclusion: CC genetic variants with high serum MMP-9 levels are associated with more acute ischemic stroke risk factors than CT genetic variants with high MMP-9 serum levels. Therefore, CC genetic variants have the potential to pose more risk of acute ischemic stroke.

Keywords: CIMT, Genetic variant, MMP-9, Acute ischemic stroke.
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INTRODUCTION

Ischemic stroke occurs due to obstruction of blood flow caused by endothelial interactions with blood constituents that can cause thrombosis and blockage of blood flow. The number of ischemic strokes is about 87% of all strokes.[1] The well-known risk factors contribute to ischemic stroke are hypertension, diabetes, dyslipidemia, and obesity, but there are still many other risks.[1,2] Evidence from twin and familial aggregation studies suggested that genetic risk factors predisposed to ischemic stroke.[3] The genes involved in the inflammatory response are under investigation to look for genetic variants that predispose to ischemic stroke. Buraczynska et al. stated that the risk factors for stroke that could not be modified were also closely related to the MMP-9 gene polymorphism.[3]

Stroke has been shown to be a cause of long-term disability and death. Ischemic stroke involves hypoperfusion around the infarct area where the cells are still viable, but the cascade leading to the apoptotic process has begun.[4] Acute cerebral blood flow obstruction results in many pathological conditions, including disturbances in homeostasis, neuronal excitotoxicity, intracellular calcium build-up, depolarization per infarction, free radical accumulation, lipid peroxidation, and protein synthesis disorders that lead to irreversible neuronal damage. The dead neurons will trigger the release of an immune response, which triggers the activation and infiltration of pro-inflammatory cells. Activation of these cells will produce cytotoxic agents, including Matrix Metalloproteinases (MMPs).[5-9]

The study which associates serum MMP-9 level with risk factors of ischemic stroke by looking at the genetic background of MMP-9 is promising.[8,10] Thus, this study aims to determine the role of MMP-9 rs 3918242 genetic variant in association between MMP-9 serum level with risk factors of acute ischemic stroke.

METHODS

This was an observational analytic study, involving 62 subjects determined by consecutive sampling. Subjects were