HUBUNGAN POLIMORFISME GEN *TOLL LIKE RECEPTOR* 2 RS3804099, VITAMIN D RESEPTOR FOK1 RS2228570, KADAR *TUMOR NECROSIS FACTOR*-α DAN KADAR VITAMIN D DENGAN DERAJAT KEPARAHAN DAN LUARAN MENINGITIS TUBERKULOSIS

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ABSTRAK

HUBUNGAN POLIMORFISME GEN *TOLL LIKE RECEPTOR* 2 RS3804099, VITAMIN D RESEPTOR FOK1 RS2228570, KADAR *TUMOR NECROSIS FACTOR*-α DAN KADAR VITAMIN D DENGAN DERAJAT KEPARAHAN DAN LUARAN MENINGITIS TUBERKULOSIS

Fanny Adhy Putri

Latar Belakang:
Meningitis tuberkulosis (TBM) merupakan salah satu bentuk tuberkulosis paling berat dengan angka morbiditas dan mortalitas yang tinggi. Faktor genetik dan imunologis berperan penting dalam menentukan derajat keparahan serta luaran TBM. Polimorfisme pada gen *Toll-Like Receptor* 2 (TLR2) rs3804099 dan gen *Vitamin D Receptor* (VDR) Fok1 rs2228570 diduga dapat memodulasi respons imun terhadap infeksi tuberkulosis melalui jalur metabolisme vitamin D dan regulasi sitokin proinflamasi, seperti *Tumor Necrosis Factor*-α (TNF-α). Namun, hubungan antara variasi genetik tersebut, kadar vitamin D, TNF-α, tingkat keparahan, dan luaran TBM belum sepenuhnya dipahami.
Tujuan:
Penelitian ini bertujuan untuk menganalisis hubungan antara polimorfisme TLR2 rs3804099 dan VDR Fok1 rs2228570, kadar TNF-α dan kadar vitamin D, serta kaitannya dengan derajat keparahan dan luaran TBM.
Metode:
Dari total 50 pasien TBM yang direkrut, 35 pasien memenuhi kriteria inklusi penelitian. Analisis polimorfisme gen TLR2 rs3804099 dan VDR Fok1 rs2228570 dilakukan menggunakan metode PCR-RFLP, sedangkan kadar TNF-α dan vitamin D diukur dengan metode ELISA. Derajat keparahan TBM ditentukan berdasarkan kriteria *British Medical Research Council* (BMRC), dan luaran klinis dinilai menggunakan *Glasgow Outcome Scale* (GOS). Analisis statistik digunakan untuk mengevaluasi hubungan antara polimorfisme genetik dan biomarker biokimia dengan derajat keparahan serta luaran TBM.
Hasil:
Polimorfisme TLR2 rs3804099, VDR Fok1 rs2228570, serta kadar TNF-α tidak menunjukkan hubungan yang signifikan dengan derajat keparahan maupun luaran klinis TBM. Sebaliknya, kadar vitamin D dalam cairan serebrospinal (CSS) berhubungan dengan derajat keparahan dan luaran meningitis TBM ($p<0,05$).
Kesimpulan:
Kadar vitamin D dalam CSS menjadi biomarker penting dalam pengelolaan dan prediksi prognosis TBM. Polimorfisme gen TLR2, VDR Fok1, serta kadar TNF-α, tidak mempengaruhi keparahan TBM maupun luaran klinis.

Kata Kunci: TBM, Polimorfisme TLR2 rs3804099, Polimorfisme VDR Fok1 rs2228570, Vitamin D, TNF-α, Cairan Serebrospinal, Keparahan, Luaran Klinis.

ABSTRACT

THE RELATIONSHIP BETWEEN POLYMORPHISMS OF THE TOLL LIKE RECEPTOR2 RS3804099, VITAMIN D RECEPTOR FOK1 RS2228570, TUMOR NECROSIS FACTOR-α AND VITAMIN D LEVELS WITH THE SEVERITY AND OUTCOME OF TUBERCULOUS MENINGITIS

Fanny Adhy Putri

Background:
Tuberculous meningitis (TBM) is one of the most severe forms of tuberculosis, characterized by high morbidity and mortality rates. Genetic and immunological factors play a crucial role in determining the severity and outcomes of TBM. Polymorphisms in the Toll-Like Receptor 2 (TLR2) gene rs3804099 and the Vitamin D Receptor (VDR) gene Fok1 rs2228570 are believed to modulate the immune response against *Mycobacterium tuberculosis* infection through the vitamin D metabolic pathway and regulation of proinflammatory cytokines, such as Tumor Necrosis Factor-α (TNF-α). However, the relationship between these genetic variations, vitamin D levels, TNF-α, disease severity, and TBM outcomes remains incompletely understood.

Objective:
This study aims to analyze the relationship between TLR2 rs3804099 and VDR Fok1 rs2228570 polymorphisms, TNF-α and vitamin D levels, with the severity and clinical outcomes of TBM.

Methods:
A total of 50 TBM patients were recruited, of whom 35 met the study inclusion criteria. Polymorphisms of the TLR2 rs3804099 and VDR Fok1 rs2228570 genes were analyzed using the PCR-RFLP method, while TNF-α and vitamin D levels were measured by ELISA. TBM severity was assessed based on the British Medical Research Council (BMRC) criteria, and clinical outcomes were evaluated using the Glasgow Outcome Scale (GOS). Statistical analyses were performed to evaluate the associations between genetic polymorphisms and biochemical biomarkers with TBM severity and outcomes.

Results:
Polymorphisms in TLR2 rs3804099, VDR Fok1 rs2228570, and TNF-α levels did not show a significant association with TBM severity or clinical outcomes. Conversely, vitamin D levels in cerebrospinal fluid (CSF) were significantly associated with clinical outcomes ($p < 0.05$).

Conclusion:
Vitamin D levels in CSF serve as an important biomarker in the management and prognosis prediction of TBM. Polymorphisms in the TLR2 and VDR Fok1 genes, as well as TNF-α levels, do not influence TBM severity or clinical outcomes.

Keywords: TBM, TLR2 rs3804099 Gene Polymorphism, VDR Fok1 rs2228570 Gene Polymorphism, Vitamin D, TNF-α, CSF, Severity, Clinical Outcome.