

DISERTASI

HUBUNGAN ANTARA POLIMORFISME GEN *PROLINE DEHYDROGENASE* rs372055 dan rs2870984, KADAR PROLIN, KADAR KYNURENIC ACID DAN KADAR GLUTAMAT DENGAN FUNGSI KOGNITIF ORANG DENGAN SKIZOFRENIA DI SUMATERA BARAT



Oleh:

MUTIARA ANISSA

NIM. 1830312014

1. Prof. Dr. dr. Afriwardi, SH, SpKO, MA, Subsp. APK (K)
2. Dr. dr. Yaslinda Yaunin, Sp.KJ
3. dr. Rauza Sukma Rita, PhD

PROGRAM STUDI ILMU BIOMEDIS PROGRAM DOKTOR

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ABSTRAK

HUBUNGAN ANTARA POLIMORFISME GEN *PROLINE DEHYDROGENASE* rs372055 dan rs2870984, KADAR PROLIN, KADAR KYNURENIC ACID DAN KADAR GLUTAMAT DENGAN FUNGSI KOGNITIF ORANG DENGAN SKIZOFRENIA DI SUMATERA BARAT

Mutiara Anissa

Skizofrenia merupakan gangguan jiwa kronik yang ditandai oleh defisit kognitif yang signifikan dan berdampak pada kualitas hidup penderita. Beberapa studi menyebutkan adanya keterlibatan interaksi antara jalur metabolisme prolin, sistem glutamatergik, dan *kynurenine pathway* dalam patofisiologi skizofrenia, namun hasil tersebut belum konsisten. Penelitian ini bertujuan untuk mengetahui hubungan antara polimorfisme gen *Proline Dehydrogenase* (PRODH) rs372055 dan rs2870984, kadar prolin, kadar *kynurenic acid* (KYNA), kadar glutamat dengan fungsi kognitif pada Orang Dengan Skizofrenia (ODS).

Penelitian ini menggunakan desain *cross sectional* dengan responden ODS sebanyak 99 orang yang dipilih secara *consecutive sampling* di RSJ Prof. Dr. HB Saanin Padang. Diagnosis skizofrenia ditegakkan menggunakan *Structured Clinical Interview* DSM yang dilakukan oleh psikiater. Fungsi kognitif dievaluasi dengan serangkaian uji neuropsikologi yang meliputi *Rey Auditory Verbal Learning Test* (RAVLT), *Digit Span Test*, dan *Trail Making Test* (TMT). Pemeriksaan polimorfisme gen PRODH dilakukan dengan PCR, kadar prolin, KYNA, dan glutamat diukur menggunakan metode ELISA.

Hasil penelitian menunjukkan tidak terdapat ada perbedaan bermakna antara polimorfisme gen PRODH rs372055 dan rs2870984 dengan fungsi kognitif. Kadar prolin yang lebih tinggi berhubungan signifikan negatif dengan memori verbal dan memori kerja. Tidak ditemukan hubungan signifikan antara kadar KYNA dan glutamat serum dengan performa kognitif. Selain itu, ditemukan korelasi positif yang kuat antara kadar KYNA dengan glutamat, namun tidak ditemukan hubungan antara kadar prolin dengan KYNA maupun glutamat.

Penelitian ini membuktikan adanya peranan kadar prolin plasma yang lebih relevan sebagai biomarker fungsi kognitif pada skizofrenia dibandingkan KYNA dan glutamat serum. Hasil ini memperkuat hipotesis keterlibatan disregulasi metabolisme prolin terhadap gangguan kognitif pada skizofrenia. Studi lanjutan pemeriksaan pada gen PRODH komponen regulator, seperti promotor, *enhancer* dan faktor transkripsi.

Kata kunci: Skizofrenia, fungsi kognitif, PRODH, prolin, glutamat, KYNA, polimorfisme

ABSTRACT

THE RELATIONSHIP BETWEEN PROLINE DEHYDROGENASE GENE POLYMORPHISM rs372055 dan rs2870984, PROLINE LEVEL, KYNURENIC ACID LEVEL, AND GLUTAMATE LEVEL WITH COGNITIVE FUNCTION IN PEOPLE WITH SCHIZOPHRENIA IN WEST SUMATRA

Mutiara Anissa

Schizophrenia is a chronic psychiatric disorder characterized by significant cognitive deficits and has an impact on the quality of life of sufferers. Several studies have suggested an involvement of interactions between the proline metabolic pathway, the glutamatergic system, and the kynurenin pathway in the pathophysiology of schizophrenia, but they are still inconsistent. This study aimed to determine the relationship between the polymorphisms of the proline Dehydrogenase (PRODH) gene, rs372055 and rs2870984, and proline, kynurenic acid (KYNA), glutamate levels, as well as cognitive function in People With Schizophrenia (PWS).

This study employed a cross-sectional design with ODS subjects, comprising 99 people selected by purposive sampling at RSJ Prof. Dr. HB Saanin, Padang. Schizophrenic diagnosis is established using a DSM-5 Structured Clinical Interview conducted by a psychiatrist. Cognitive function was evaluated using a series of neuropsychological tests, including the Rey Auditory Verbal Learning Test (RAVLT), Digit Span Test, and Trail Making Test (TMT). PCR, examined the PRODH polymorphism, and proline, KYNA, and glutamate levels were measured using the ELISA method.

The results showed that there was no significant difference between the polymorphism of the prodh genes rs372055 and rs2870984 and cognitive function. Higher proline levels were significantly negatively associated with verbal memory and working memory. No significant association was found between serum KYNA and glutamate levels and mental performance. In addition, a strong positive correlation was found between KYNA and glutamate levels; however, no relationship was observed between proline levels and either KYNA or glutamate.

This study demonstrates the role of plasma proline levels as more relevant biomarkers of cognitive function in schizophrenia, compared to KYNA and serum glutamate. The results reinforce the hypothesis of the involvement of proline metabolic dysregulation in cognitive impairment in schizophrenia. Further studies on the examination of the PRODH gene regulatory components, such as promoters, enhancers, and transcription factor.

Keywords: Schizophrenia, cognitive function, PRODH, proline, glutamate, KYNA, polymorphism