

# Karakteristik Klinis, Penunjang, Dan Luaran Ensefalitis Autoimun Di RSUPN Dr. Cipto Mangunkusumo, Indonesia = Clinical, Ancillary Characteristics, And Prognosis Of Autoimmune Encephalitis In Dr. Cipto Mangunkusumo National Center General Hospital, Indonesia

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## Abstrak

Latar Belakang. Sejak laporan pertama ensefalitis antireseptor N-methyl-D-aspartate (NMDA) pada 2007, prevalensi ensefalitis autoimun (EA) serupa dengan ensefalitis infeksi (EI). Sayangnya, heterogenitas klinis EA, serupanya klinis dengan EI, penyakit autoimun seperti neuropsikiatrik lupus eritematosus sistemik, atau penyakit psikiatrik menjadi tantangan deteksi awal dan tatalaksana EA. Keterlambatan berhubungan dengan perburukan luaran, sedangkan kurang-tepatan menerapi EI sebagai EA dapat mengeksaserbasi infeksi. Studi ini bertujuan mengenali karakteristik EA, khususnya ensefalitis antireseptor NMDA definitif sebagai EA tersering, di era keterbatasan ketersediaan penunjang definitif di Indonesia.

Metode. Studi kohort retrospektif dengan rekam medis di RSUPN dr. Cipto Mangunkusumo dilakukan pada curiga EA yang menjalani pemeriksaan antireseptor NMDA cairan otak sejak Januari 2015-November 2022. Karakteristik klinis dan penunjang EA, EA seropositif NMDA, dan luarannya dinilai. Analisis univariat dan bivariat dilakukan sesuai kebutuhan.

Hasil. Dari 102 subjek yang melalui kriteria inklusi dan eksklusi, terdapat 14 EA seropositif dan 32 seronegatif NMDA. Temuan klinis EA terbanyak adalah gangguan psikiatri dan tidur (85,7%), gangguan kesadaran (78,3%), prodromal (76,1%), dan bangkitan (70,6%). Karakteristik penunjang EA adalah inflamasi sistemik (75,0%), inflamasi cairan otak (69,2%), abnormalitas MRI (57,9%) dominan inflamasi (42,2%), dan abnormalitas EEG (89,5%). Karakteristik klinis EA seropositif NMDA adalah psikosis (76,9% vs 24,1%,  $p=0,002$ ), delirium (71,4% vs 40,6%,  $p=0,06$ ), bangkitan (71,4% vs 46,7%,  $p=0,12$ ), takikardia (55,6% vs 17,6%,  $p=0,08$ ), dan gangguan otonom lainnya (55,6% vs 23,5%,  $p=0,19$ ), sedangkan klinis EA seronegatif NMDA adalah somnolen (34,4% vs 7,1%,  $p=0,07$ ) dan defisit neurologis fokal (31,3% vs 7,1%,  $p=0,13$ ). Leukositosis dan pleositosis cairan otak dengan dominasi mononuklear secara signifikan lebih ditemukan pada EA seropositif NMDA. Sebanyak 10,9% subjek meninggal.

Kesimpulan. Karakteristik klinis EA adalah gangguan psikiatri dan tidur, gangguan kesadaran, prodromal, dan bangkitan. Psikosis, delirium, bangkitan, dan disfungsi otonom cenderung lebih ditemukan pada EA seropositif NMDA. Inflamasi sistemik, cairan otak, MRI, dan abnormalitas EEG sering ditemukan pada EA, terutama seropositif NMDA.

.....Background. Since the first report of N-methyl-D-aspartate receptor (NMDAR) encephalitis in 2007, the prevalence of autoimmune encephalitis (AE) was similar to infectious encephalitis (IE). Unfortunately, heterogeneities of EA as well as similarities in the manifestation to IE, other autoimmune diseases including neuropsychiatric systemic lupus erythematosus, or psychiatric diseases compromised the early detection and management of EA. This delay correlated with worse outcome whereas the inaccuracy in treating IE as AE may exacerbate infection. This study aimed to describe the characteristics of EA, particularly definitive NMDAR encephalitis as the most common, in the era of limited availability of definitive ancillary test in Indonesia.

**Methods.** Retrospective study using medical records at Dr. Cipto Mangunkusumo National Center General Hospital was conducted for suspected EA cases tested for cerebrospinal fluid NMDAR autoantibody test from January 2015 to November 2022. Clinical, ancillary characteristics, and concordance between clinical diagnosis and diagnostic criteria were assessed. Univariate, bivariate, and multivariate analysis were performed as needed.

**Result.** Of 102 subjects following inclusion and exclusion criteria, there were 14 seropositive and 32 seronegative NMDA subject. Clinical characteristics of AE were psychiatric and sleep disorder (85,7%), altered consciousness (78.3%), prodromal (76.1%), and seizure (70.6%). Ancillary characteristics of AE were systemic inflammation (75.0%), cerebrospinal fluid inflammation (69.2%), MRI abnormalities (57.9%) with inflammatory predominance (42.2%), and EEG abnormalities (89.5%). Seropositive NMDA characteristics were psychosis (76.9% vs 24.1%,  $p=0.002$ ), delirium (71.4% vs 40.6%,  $p=0.06$ ), seizure (71.4% vs 46.7%,  $p=0.12$ ), tachycardia 95.6% vs 17.6%,  $p=0.08$ ), and other autonomic disorder (55.6% vs 23.5%  $p=0.19$ ) whereas seronegative NMDA characteristics were somnolence (34.4% vs 7.1%,  $p=0.07$ ) and focal neurologic deficit (31.3% vs 7.1%,  $p=0.13$ ). Leukocytosis and cerebrospinal fluid pleocytosis with mononuclear predominance were significantly found in seropositive NMDA AE. The mortality rate was 10.9%.

**Conclusion.** Clinical characteristics of AE were psychiatric and sleep disorder, altered consciousness, prodromal, and seizure. Psychosis, delirium, seizure, and autonomic dysfunction tended to be found in seropositive NMDA AE. Inflammation in systemic, cerebrospinal fluid, and MRI findings as well as EEG abnormalities commonly occurred in AE, especially seropositive NMDA.