Journal of Clinical and Nursing Research, 2025, Volume 9, Issue 5
http://ojs.bbwpublisher.com/index.php/JCNR
Online ISSN: 2208-3693
Print ISSN: 2208-3685

Research Status and Progress of Related Indicators for Early Diagnosis and Prognosis Evaluation of Autoimmune Encephalitis

Dandan Shi*

School of Clinical Medicine, Affiliated Hospital of Hebei University, Baoding 071000, Hebei, China

**Author to whom correspondence should be addressed.*

Abstract: Addressing the challenges of difficult early diagnosis and the incomplete prognosis evaluation system for Autoimmune Encephalitis (AE), this study comprehensively reviews the relevant indicators for early diagnosis and prognosis evaluation of AE. The analysis reveals that multiple indicators currently exhibit unique value in the diagnosis and treatment of AE, but each has its limitations. This article aims to systematically review these indicators and clarify their current application in clinical practice, to help improve the accuracy of early diagnosis and prognosis evaluation of AE, and provide a theoretical basis for clinicians to develop more effective treatment strategies.

Keywords: Autoimmune Encephalitis; Early diagnosis; Prognosis evaluation; Biomarker

Online publication: May 30, 2025

1. Introduction

Within the scope of neurological diseases, Autoimmune Encephalitis (AE) is experiencing a significant increase in incidence and has become a focus of clinical and scientific research. The clinical manifestations of AE are extremely complex, including severe abnormalities in mental behavior. Patients may experience unexplained mania, depression, or hallucinations. Cognitive function can also be severely impaired, with significant decreases in memory and attention. Frequent epileptic seizures are also one of the common symptoms. These manifestations are highly similar to a variety of neurological diseases, posing significant challenges for early and accurate diagnosis. Relevant clinical data shows that more than half of AE patients are misdiagnosed during their first visit, resulting in the loss of valuable treatment opportunities. If AE is not intervened in a timely and effective manner early on, patients may face severe neurological sequelae, such as permanent cognitive dysfunction and limb movement disorders, which seriously affect daily life and social integration, and increase the burden of family care and economic pressure. Some critically ill patients may even lose their lives due to rapid deterioration

of the disease. Currently, there is a lack of specific and sensitive indicators for the early diagnosis of AE, and the prognosis evaluation system also needs to be improved. Therefore, in-depth research on relevant indicators for early diagnosis and prognosis evaluation of AE, and the construction of a more precise and efficient diagnosis and treatment system are crucial to improving patients' clinical outcomes and reducing the disease burden. This is an important topic that urgently needs to be broken through in the current field of neuromedicine.

2. Pathogenesis of AE

2.1. Abnormal immune system

The core function of the human immune system is to recognize and eliminate foreign pathogens while maintaining immune tolerance to its own tissues [1]. In patients with AE, this balance is disrupted, leading to abnormal activation of the immune system [2]. Generally speaking, T and B lymphocytes work together to fight foreign antigens. However, in AE, the antigen-presenting cells mistakenly present their own neuronal antigens to T lymphocytes, leading to the activation of T lymphocytes and triggering an immune response. Activated T lymphocytes further stimulate B lymphocytes, promoting their differentiation into plasma cells and secreting a large number of antibodies targeting their own neurons. Additionally, regulatory T cell dysfunction fails to effectively inhibit overactive immune responses, leading to continuous immune attacks and ultimately causing brain tissue damage. For example, in anti-N-methyl-D-aspartate receptor (NMDAR) encephalitis, the immune system produces specific antibodies against the NMDAR on the surface of neurons, triggering a series of immune responses and disrupting normal neuronal function.

2.2. Role of the blood-brain barrier

The blood-brain barrier, formed by brain capillary endothelial cells, basement membrane, pericytes, and astrocytes, plays a crucial role in maintaining the stability of the central nervous system. Generally, the blood-brain barrier can effectively prevent the invasion of pathogens, toxins, and macromolecules. However, in the pathogenesis of AE, various factors can increase the permeability of the blood-brain barrier. Studies have found that under viral infection or inflammatory stimulation, the expression of adhesion molecules on cerebrovascular endothelial cells can absorb and cross the blood-brain barrier. Additionally, inflammatory mediators (such as TNF-α and IL-6) can damage the blood-brain barrier, leading to barrier impairment and increased permeability. When the permeability of the blood-brain barrier increases, autoantibodies and immune cells in the circulatory system can invade brain tissue, bind to surface antigen molecules on neurons, launch an "immune attack," trigger an inflammatory response, and ultimately induce AE.

2.3. Pathogenic mechanism of autoantibodies

The autoantibodies produced in AE patients can damage neurons through various mechanisms. Taking anti-NMDAR antibodies as an example, after binding to the GluN1 subunit of NMDAR, these antibodies reduce the receptors on the neuronal surface through endocytosis, leading to decreased neuronal reactivity to glutamate and affecting neurotransmitter transmission and neuronal excitability. Furthermore, antibody binding can also activate the complement system, forming membrane attack complexes that directly disrupt the integrity of neuronal cell membranes and trigger apoptosis. Anti-leucine-rich glioma-inactivated protein 1 (LGI1) antibodies, on the other hand, bind to LGI1 protein, interfering with its interaction with ADAM22 and ADAM23, and affecting potassium

channel function. This leads to abnormal neuronal excitability, which in turn causes typical symptoms such as faciobrachial dystonic seizures. Different types of autoantibodies damage neuronal function through their unique targets and mechanisms, ultimately resulting in the diverse clinical manifestations of AE.

3. AE early diagnosis indicators

3.1. Cerebrospinal fluid immunoglobulins

The detection of cerebrospinal fluid (CSF) immunoglobulin levels is significant in the early diagnosis of AE. Under normal circumstances, the immunoglobulin content in CSF is relatively low and mainly consists of IgG. In AE patients, due to the activation of the immune response within the central nervous system, the immunoglobulin level in CSF often rises significantly. This has been confirmed by studies such as that conducted by Hu *et al.* [3]. In particular, the appearance of oligoclonal bands (OCBs) has high suggestive value for the diagnosis of AE. OCBs are immunoglobulin bands that appear in the CSF but are not detected in the serum, indicating localized immunoglobulin synthesis within the central nervous system. Additionally, an elevated IgG index in the CSF (reflecting the proportion of IgG synthesis in the CSF relative to the serum) is also commonly seen in AE patients [4].

3.2. Features of head MRI - FLAIR

Fluid-attenuated inversion recovery (FLAIR) sequences in head magnetic resonance imaging (MRI) play a crucial role in the early diagnosis of AE. AE patients often show characteristic changes on FLAIR sequences, with the most common being high signals in the limbic system areas such as the medial temporal lobe (especially the hippocampus), insula, and cingulate gyrus [5]. For example, in anti-LGI1 encephalitis, approximately 80% of patients may exhibit bilateral medial temporal lobe high signals on FLAIR, and some patients may be accompanied by hippocampal atrophy. Although the overall MRI positivity rate in anti-NMDAR encephalitis is relatively low (approximately 20%–40%), some patients may still show nonspecific high signals in the cortex or subcortex on FLAIR sequences. Additionally, some AE patients may exhibit abnormal signals in other brain regions, such as the frontal and parietal lobes. It should be noted that MRI-FLAIR findings are not specific to AE, as similar imaging manifestations may also occur in certain viral encephalitis, cerebral infarction, and other diseases. Therefore, MRI-FLAIR results need to be comprehensively analyzed in combination with the patient's clinical symptoms, cerebrospinal fluid examination, and antibody detection to improve the accuracy of early AE diagnosis.

3.3. The weight of video electroencephalogram

Video electroencephalogram (VEEG) can continuously record patients' brain electrical activity and synchronously monitor their clinical manifestations, providing unique advantages in the early diagnosis of AE. VEEG in AE patients often shows an increase in focal or diffuse slow waves, and some patients may exhibit epileptiform discharges, including spike waves, sharp waves, and spike-and-wave complexes. Additionally, VEEG can be used to monitor changes in AE patients' condition and evaluate treatment effectiveness. For example, as treatment progresses, the patient's brain electrical activity gradually returns to normal, and epileptiform discharges decrease or disappear, indicating improvement in the condition [6]. However, the interpretation of VEEG results has a certain degree of subjectivity, and some AE patients may not show significant abnormalities in brain electrical activity

early in the disease. Therefore, analysis by experienced electroencephalogram physicians and comprehensive judgment based on other examination results are necessary.

4. AE prognostic indicators

4.1. Antibody titer

The antibody titer in serum has a certain reference value for the prognosis evaluation of AE. Generally speaking, the higher the antibody titer in serum, the more severe the patient's disease and the worse the prognosis [7, 8]. Taking anti-NMDA encephalitis as an example, before receiving treatment, patients with higher antibody titers in their serum have a higher frequency of acute seizures, longer durations of coma, and a higher risk of developing neurological sequelae. Therefore, monitoring changes in antibody titers in serum during treatment can evaluate the efficacy of the treatment. If the antibody titer in the serum gradually decreases after immunotherapy, it indicates that the treatment is effective and the patient has a better prognosis. Conversely, it suggests that the patient's condition is not well-controlled and prone to recurrence.

4.2. Neutrophil-to-lymphocyte ratio in peripheral blood

The neutrophil-to-lymphocyte ratio (NLR) in peripheral blood is an important parameter that can reflect inflammation and immune homeostasis in the body. AE patients often have significantly elevated NLR levels. This was confirmed by the research of Miao *et al.*, who compared the peripheral blood cell counts of AE patients and healthy patients and found that the NLR has certain significance for the prognosis of AE [9].

Studies have shown that an increase in NLR is associated with disease severity and poor prognosis. An elevated NLR indicates the presence of excessive inflammatory responses and immune dysfunction in the body, which may exacerbate damage to brain tissue and have a negative impact on the patient's prognosis. For example, a study on AE patients showed that the NLR of patients with poor prognosis was significantly higher than that of patients with better prognosis. Additionally, NLR can be used to monitor patients' inflammatory responses during treatment. If the NLR gradually decreases to normal levels during treatment, it indicates that inflammation has been effectively controlled, and the patient's prognosis will be better. However, NLR is affected by many factors such as infection and stress, so other interfering factors need to be considered when using NLR to evaluate patients' prognosis [10].

4.3. High-density lipoprotein cholesterol

High-density lipoprotein cholesterol (HDL-C) has a potential protective role in the prognosis of AE. HDL-C not only participates in reverse cholesterol transport but also has various functions such as anti-oxidation, anti-inflammation, and anti-thrombosis. Studies have found that decreased serum HDL-C levels in AE patients are associated with disease severity and poor prognosis. Lower HDL-C levels may weaken its neuroprotective effects, making neurons more susceptible to immune attacks and inflammatory damage [11]. Clinical studies have also shown that AE patients whose HDL-C levels rebound after treatment have better neurological recovery and prognosis. Therefore, HDL-C is expected to become an important indicator for evaluating the prognosis of AE and guiding treatment.

4.4. B Lymphocyte-related cytokines

B lymphocytes play a critical role in the pathogenesis of AE, and various cytokines secreted by them have an

impact on disease prognosis. Interleukin-6 (IL-6) is an important proinflammatory cytokine, and its levels are often significantly elevated in the serum and cerebrospinal fluid of AE patients. High levels of IL-6 can promote the activation and proliferation of B lymphocytes, enhance immune responses, lead to increased inflammatory damage to brain tissue, and affect prognosis. Conversely, interleukin-10 (IL-10) is a cytokine with anti-inflammatory effects that can inhibit the activation of B lymphocytes and the secretion of proinflammatory cytokines. Studies have shown that AE patients have relatively low levels of IL-10, and the lower the IL-10 level, the more severe the patient's condition and the worse the prognosis. By regulating the levels of B lymphocyte-related cytokines, it is possible to improve the immune status of AE patients, thereby affecting disease prognosis.

5. Conclusion

In summary, the early diagnosis and prognosis evaluation of autoimmune encephalitis involve multiple indicators. In terms of pathogenesis, immune system abnormalities, blood-brain barrier disruption, and autoantibody pathogenesis are key links. Early diagnostic indicators such as cerebrospinal fluid immunoglobulin, head MRI-FLAIR features, and video electroencephalogram have their respective advantages but also have certain limitations, requiring comprehensive application to improve diagnostic accuracy. Prognostic indicators include antibody titer, neutrophil-to-lymphocyte ratio in peripheral blood, high-density lipoprotein cholesterol, B lymphocyte-related cytokines, and neurobiological factors of nerve injury. These indicators reflect the severity of the patient's condition, immune status, and nerve damage from different perspectives and are important for evaluating prognosis. However, the early diagnosis and prognosis evaluation of AE still face many challenges, such as insufficient specificity of some indicators and differences in research results. In the future, further research is needed on the pathogenesis of AE, exploring more sensitive and specific biomarkers, optimizing existing detection methods, and establishing a comprehensive multi-indicator diagnosis and prognosis evaluation system to improve the diagnosis and treatment level of AE and improve patients' clinical outcomes.

Disclosure statement

The author declares no conflict of interest.

References

[1] Li W, Wen S, Chen J, et al., 2025, Relationship Between Serum Immunoglobulin Levels and Disease Prognosis in Children With Autoimmune Encephalitis. Journal of Clinical and Experimental Medicine, 24(01): 54–58.

[2] Ma H, Xu J, Hao F, et al., 2023, Clinical Characteristics and Treatment Analysis of Autoimmune Encephalitis. Chinese Journal of Practical Nervous Diseases, 26(05): 566–571.

[3] Hu X, Li J, Xu W, et al., 2024, Clinical Diagnostic Value of Cerebrospinal Fluid Immunoglobulins, Peripheral Blood Inflammatory Cell Indicators, and Cellular Immune Indicators in Children With Autoimmune Encephalitis. China Modern Medicine, 31(23): 105–108.

[4] Wang D, Zheng G, Shao C, et al., 2023, The Value of Cerebrospinal Fluid Indicators in the Differential Diagnosis of Autoimmune Encephalitis and Viral Encephalitis. Labeled Immunoassays and Clinical Medicine, 30(02): 186–190, 222.

[5] Cao D, Zhang L, Guo X, et al., 2017, Analysis of Clinical Manifestations and MRI Features of Autoimmune Encephalitis. Chinese Journal of Neurology and Psychiatry, 43(06): 341–345.

[6] Wu G, Wang C, Huang N, et al., 2024, Discussion on the Correlation and Weight of Diagnostic Elements of Autoimmune Encephalitis. Journal of Stroke and Nervous Diseases, 41(03): 264–269.

[7] Kuang Z, Liu B, Yang H, et al., 2020, Clinical Analysis and Dynamic Observation of Serum Antibodies in Anti-N-Methyl-D-Aspartate Receptor Encephalitis. Chinese Journal of Neuroimmunology and Neurology, 27(04): 270–275.

[8] Gresa-Arribas N, Titulaer M, Torrents A, et al., 2014, Antibody Titres at Diagnosis and During Follow-Up of Anti-NMDA Receptor Encephalitis: A Retrospective Study. Lancet Neurol, 13(2): 167–177.

[9] Miao C, Zhu Y, Liu P, 2023, Clinical Significance of the Neutrophil-to-Lymphocyte Ratio in Peripheral Blood of Patients With Autoimmune Encephalitis. Modern Medicine and Health, 39(12): 2049–2053.

[10] Zhang Q, Shi Y, Yuan Y, 2024, Current Status of Cognitive Impairment in Patients With Autoimmune Encephalitis and Its Relationship With Poor Prognosis. Chinese Journal of Practical Nervous Diseases, 27(10): 1189–1194.

[11] Liu Y, Ma L, Ma X, et al., 2022, Simple and Effective Serum Biomarkers With Potential for Predicting Status Epilepticus in Anti-N-Methyl-D-Aspartate Receptor Encephalitis. BMC Neurol, 22(1): 27.