SUBMITTED 7 MAY 24
REVISION REQ. 2 JUN 24; REVISION RECD. 10 JUN 24
ACCEPTED 25 JUN 24
ONLINE-FIRST: JULY 2024
DOI: https://doi.org/10.18295/squmj.7.2024.046

Clinical and Autoimmune Profiles of Omani Patients with True Versus False Positive Autoimmune Encephalitis Antibodies Panels

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Abstract:
The incidence of autoimmune encephalitis (AE) is rising due to increased awareness of the condition and detection of new autoantibodies. Coinciding with this rise are false positive autoantibodies without clinical correlates. ***Objective*:** To explore the clinical profiles of Omani patients who are truly positive for AE autoantibodies and compare them with those with false-positive autoantibodies. ***Methods*:** We reviewed the medical records of all patients who tested positive for AE antibody from May 2016 to December 2022. Cases were verified by three neurologists based on the existing criteria for AE. ***Results*:** The participants comprised N = 67 patients, 19 (28%) of whom fulfilled the criteria for AE. True-positive AE patients were younger with mean age of 35.3 ± 4.7 years (p = 0.010). They were also more likely to present with subacute memory disturbances (6/19; 32%; p = 0.030), seizures (12; 63%; p = 0.028), abnormal electroencephalogram (EEG) findings (10; 65%; p = 0.040), and

abnormal signals in limbic region on magnetic resonance imaging (MRI) (5; 26%; $p = 0.010$). Subacute memory disturbance was a significant predictor for true positivity (OR = 17.807, 95%CI = 1.608–197.202; $p = 0.019$). Anti-N-methyl-d-aspartate receptor (NMDAR) encephalitis was the most frequent type of AE (8; 42.1%), followed by anti-glutamic acid decarboxylase 65 (GAD65) (4; 21.1%). ***Conclusion*:** Of the 67 cases with positive AE autoantibody panel, 48 (72%) were false-positive. The presence of subacute memory impairment was a significant predictor of AE. Anti-NMDAR encephalitis was the most frequent AE encountered in our cohort.

Keywords: Autoimmune Encephalitis; Anti-N-Methyl-D-Aspartate Receptor Encephalitis; Limbic Encephalitis; Oman.

Advances in Knowledge:

- Explore the clinical and autoantibody profile of patient with positive AE antibody panels in a Middle East Arab ethnicity.
- Explore predictors of true positive AE in context of positive autoantibody panel.

Application to Patient Care:

- False positive autoantibodies fsuor AE is substantial and diagnosis of AE should be based on a sound clinical ground.
- Testing for autoimmune antibody should be guided by clinical history and physical signs in order to increase the meaningfulness of the antibody positivity.

Introduction

Autoimmune encephalitis (AE) is a group of diseases resulting from abnormal immune responses in the brain directed against neuronal cell surface proteins and intracellular antigens.[1] These responses could be triggered by malignancy (paraneoplastic encephalitis), infection (para-infectious encephalitis), or unknown trigger.[1,2] Various autoantibodies have been identified in AE patients, such as those directed against intracellular antigens (anti-Hu, Anti-Ma2 and anti-GAD) and those directed against synaptic receptor/cell surface proteins (Anti-NMDA, Anti-AMPA, Anti-Caspr2, Anti-LGi1) among others.[1]

The reported incidence rate of AE has tripled in the last decade due to the discovery of new autoantibodies, improved awareness of this condition, and readily available autoantibody

testing facilities.[3] However, the widespread availability of commercial AE autoantibody kits and indiscriminative testing could have raised the detection of false positive autoantibodies that lack appropriate clinical context. In addition, neuronal autoantibodies are detected in patients with other conditions like neurodegenerative disorders, primary psychiatric disorders, and cerebral neoplasms.[4,5] Thus mistaking false AE autoantibodies as true raises the risk of misdiagnosis and incorrect treatment.

The diagnostic algorithm and criteria for AE were published in 2016. [1] To fulfil the criteria for possible AE, all three of the following must be met: subacute onset (rapid progression in less than three months) of working memory deficits (short-term memory loss), altered mental status (altered levels of consciousness, lethargy, or personality change), or psychiatric symptoms and at least one of the following: new focal central nervous system (CNS) findings, seizures not explained by a previously known seizure disorder, cerebrospinal fluid (CSF) pleocytosis or features suggestive of encephalitis in MRI. The last criterion is the reasonable exclusion of alternative causes. The same paper also established the criteria for subtypes of AE, such as definite limbic encephalitis and definite anti-NMDAR encephalitis. [1]

Our tertiary center in Oman introduced neuroimmunology testing facilities in 2016, and began to offer paraneoplastic and limbic encephalitis screens. Soon non-neurological subspecialties also began to order these tests. This may have also contributed to the rise in detection of false positive autoantibodies. However, the problem has not been investigated in depth.

To our knowledge, this is the first study to characterize the clinical and antibody profile of autoimmune encephalitis in the Arabian Peninsula. Studies from North America and Europe have showed a false positive rate of 70% approximately.[5,6] Though a few Middle Eastern studies have looked at AE clinical and antibody profiles, none has investigated the clinical impact of the rising rates of false positivity.[7–9]

Thus, the primary aim of this retrospective study was to characterize the clinical profiles of Omani patients with true-positive AE autoantibodies and compare them to those with false-positive autoantibodies. The secondary objective was to explore the clinical profiles and treatment outcomes of the most prevalent form of AE in our cohort.

Methods

Study design and data collection

This retrospective study was conducted at Sultan Qaboos University Hospital (SQUH), a tertiary teaching hospital in Muscat, Oman. From 2016 May, SQUH began to provide in-house immunology services. Therefore, we examined the electronic medical records of all patients who tested at least moderately positive for autoimmune limbic or paraneoplastic encephalitis panels from May 1, 2016 to December 31, 2022 (6 years, 7 months). The study was approved by the Medical & Research Ethics Committee of the College of Medicine and Health Sciences, Sultan Qaboos University, Muscat.

Demographic and clinical data of the participants were extracted from their medical records. Clinical data included past medical history, initial clinical presentation, duration of symptoms, serum neutrophils to lymphocytes ratio, CSF analysis, EEG results, and neuroimaging findings.

SQUH procedure to investigate for neuronal antibodies is as follows: antibodies against cell-surface or synaptic antigens (anti-NMDRA, anti-AMPA, anti-LG1, anti-CASPR2, anti-GABA) are detected using indirect immunofluorescence cell-based assay (Euroimmun, Lübek, Germany) and immunoblot for antibodies against intracellular antigens (anti-Hu, anti-Yo, anti-Ri, anti-Ma2, anti-CRMP5, anti-amphiphysin, anti-GAD65, anti-Zic4, anti-titin, anti-SOX1, anti-Rec, anti-Tr) (Euroimmun, Lübek Germany). Serum and CSF samples are tested and labeled positive or negative as per the manufacturer's instructions. As per hospital records, the above procedure was followed in respect of all cases selected for our study.

Case definition and outcome measures

The actual positive autoimmune limbic and paraneoplastic encephalitis were identified by two neurologists (AQ, HA) after independently reviewing each patient record. Any conflict was resolved by a third neurologist (AA) alone. To be labeled true positive, a case had to fulfil the Graus et al. criteria for definite autoimmune limbic encephalitis or definite anti-NMDAR encephalitis .[1] To label a case as false positive, it must not fulfil the three criteria for possible AE. In addition, these cases were reviewed independently by the same neurologist's panel, which includes checking the final alternative diagnoses and follow-up records of false positive cases. We compared the true positives and false positives with the respective clinical profiles. For each true positive case, we extracted the type of

immunotherapy used, follow-up duration, and outcome using the modified Rankin score (MRS) in the last follow-up visit. Finally, we characterized our study's most frequent true positive AE. Statistical analysis

The data was analyzed using IBM SPSS Version 25 (IBM Corp., Armonk, NY). Descriptive statistics were used for demographic and clinical data. Continues variables were represented by mean and standard deviation ±) for normally distributed data, and median and interquartile range (IQR) for non-normally distributed data. Categorical data was represented by frequencies and percentages. Between-group comparison of categorical variables was performed using the Chi-Square test or Fisher exact test as appropriate. For measures with non-normal distribution, we applied the nonparametric Mann-Whitney test for between-group comparisons. Student-t test was used for normally distributed variables. $P < 0.050$ was considered statistically significant. We performed binary logistic regression with positivity status (true or false) as the outcome and demographic data and relevant clinical characteristics as predictors. Relevant clinical characteristics of $p < 0.250$ were included in the regression equation.

Results

The participants comprised N = 67 patients who had autoimmune and/or paraneoplastic limbic encephalitis panels with at least moderate positivity in serum or CSF during the study period [Table 1]. Of them, only 19 (28%) patients had true-positive AE as defined in the method section. The remaining 48 (72%) had false-positive AE. The true-positive group had 9/19 (47%) males against 17/48 males (35%) in false-positive group ($p = 0.370$). The true-positive group was significantly younger (mean age: 35.3 ± 4.7 years) than the false-positive group (53.0 ± 3.3 years); $p = 0.010$. The two groups were comparable in terms of comorbidities except for hypertension, which was significantly more prevalent in the false-positive group (17; 35%; $p = 0.010$).

Among patients with true-positive AE, the most prevalent first presenting symptom was subacute memory disturbance (6/19; 32%) compared to 4/48; 8% for the false-positive group ($p = 0.030$). When taken collectively, seizure presentation (breakthrough or first onset) was more prevalent in true-positive patients (12/19; 63%) than in false positive patients (15/48; 31%) ($p = 0.028$). Serum neutrophil-to-lymphocyte ratio was higher in true positives, but not

significantly. There was also a non-significant trend for higher CSF white blood cells and CSF protein among the true-positives.

EEG showing evidence of epileptogenicity through different forms of epileptiform discharges was more frequent in the true-positive group (10/19; 65%; $p = 0.040$). Neuroimaging modality includes CT-brain (true positive: 2/19; 10%; false positive: 13/48; 27%) and MRI-brain (true positive: 17/19; 90%; false positive: 26/48; 54%). Neuroimaging results were normal among comparable proportion of patients in the two groups (true positives: 8/19; 42%; false positives: 12/48; 32%). Abnormal signals in the limbic region were seen in 5/67 (26%) patients with true positive encephalitis; none was detected in false positives ($p = 0.010$).

Among true-positive AE patients, anti-NMDAR was the most frequently detected antibody in both serum and CSF (8/19; 42.1%), followed by anti-GAD65 (4; 21.1%) and anti-Caspr2 (3; 15.8%) [Table2]. On the contrary, the most frequent antibody in patients with false-positive results was anti-GAD65 (n = 8/48; 17%) followed by anti-Yo, anti-SOX1, and anti-Rec (each 6; 13%). None of the false-positive patients had antibodies detected in CSF. The most frequent diagnoses in false-positive group were epilepsy (14; 29%), primary psychiatric disorder (5; 10%), dementia (5; 10%), infection (systemic and CNS) (5; 10%), myasthenia gravis (4; 8%), peripheral neuropathy (4; 8%), spinocerebellar ataxia (2; 4%), myositis (2; 4%), stroke (2; 4%) and others (5; 10%) [Supplementary Table 1].

The mean treatment lag for true AE positive group was 45 ± 18.6 days, and the mean follow-up duration, 43 ± 4.3 months. Three different cancers were detected in three patients in the true-positive group: lung cancer with anti-CRMP5, Hodgkin lymphoma with anti-Tr, and testicular cancer with anti-Ma2. One patient with known cancer, leukemia, had anti-NMDAR encephalitis. The overall treatment outcome for true positive patients was excellent, with 12/19 (63%) achieving modified Rankin score of 0–1 [Figure 1].

The clinical profiles of the eight patients with anti-NMDAR encephalitis are shown in Figure 2. Their mean age was 20.4 ± 3.6 years and 6/8 (75%) were female. The most frequent presentation was seizures (first onset or breakthrough combined) (6; 75%), followed by psychiatric manifestation (4; 50%) and memory disturbance (2; 25%). Four (50%) had a prior history of epilepsy, while five (63%) had epileptiform activities on their EEGs

[Supplementary Figure 1]. Two (25%) patients were treated with a combination of steroid, intravenous immunoglobulin (IVIG), and rituximab. IVIG was part of immunotherapy in six (75%) patients. Five (62%) patients were asymptomatic at last follow up but two had severe deficits (MRS 3–4). One patient had slight deficit (MRS-2). There were no deaths.

As shown in Table 3, binary regression analysis identified memory disturbance and symptom duration as significant predictors of true AE positivity. Our patients with subacute memory disturbances and positive AE antibodies had 17-fold risk of having true positive AE (OR = 17.807, 95%CI = 1.608–197.202; $p = 0.019$). Longer symptom duration slightly reduced the odds of having true positive AE (OR = 0.995; 95%CI = 0.990–0.999; $p = 0.030$).

Discussion

In this retrospective review of hospital records spanning more than six years, we identified 67 patients with at least moderate positivity of AE antibody panels. Of them only 19 (28%) met the inclusion criteria for AE. They were significantly younger, which might explain the lower prevalence of hypertension in this group. Epilepsy was prominently prevalent in both true- and false-positive groups. Seizures in true-positive patients can be explained by the nature of AE presentation. In false-positive patients, there has been mounting evidence of co-occurrence of AE autoantibodies and epilepsy, especially temporal lobe epilepsy.[10,11]

Frequent requests from non-neurologists for panels for epilepsy and primary psychiatric conditions could have contributed to the proliferation of non-relevant positives. Neurologists and epileptologists, on the other hand, tend to limit autoantibody tests to essential cases, such as refractory epilepsy and normal or nonspecific white matter changes in neuroimaging. In the current study, in terms of clinical presentations, subacute memory disturbance and seizures (new onset and breakthrough combined) were significantly more frequent in the true-positive group. This was anticipated as presentations of AE frequently include both these symptoms.[12]

The prevalence of false-positive antibodies in our cohort was comparable with those in prior studies.[5,6] In one study that used Mayo paraneoplastic panel, 62 of 87 (71.3%) patients were false positive for paraneoplastic antibodies[5]. A study from Sweden included 94 patients with positive AE antibodies; only 31 (32.9%) met the criteria for definitive AE.[6]

There was a trend of higher neutrophil-to-lymphocyte ratio in our true AE positive group, albeit non-significantly, possibly due to absence of a healthy control group for comparison. In another study, this ratio was significantly higher in AE than in normal control.[13] In another study higher neutrophil to lymphocytes ratio was associated with severity in AE.[14] Perhaps for the same reason (no control group), we observed non-significant higher trends of CSF WBC count and CSF protein in true AE patients. Meanwhile, 42% of our true AE patients had normal neuroimaging results, similar to reports elsewhere.[15,16] Epileptiform discharges were common in our true AE patients, similar to prior findings.[7,17]

The most frequent AE type encountered in our study was anti-NMDAR encephalitis, prevalent in 42.1% of true AE patients, followed by anti-GAD65 4 (21.1%). Previous reports suggest that anti-NMDAR encephalitis may be the most frequent AE in the Middle Eastern region.[8,9] It accounted for 68% of the AE cases in an Iranian cohort of 39 patients.[9] A study from India included 31 patients with AE, of whom 13 patients had anti-NMDAR encephalitis.[8] Similar trend was also reported from more distant regions such as Latin America and China.[12,18]

Anti-LGi1 encephalitis was not detected in our cohort, unlike in Western countries, where it is more prevalent.[12] Perhaps genetic and environmental factors play a part in this pattern. Interestingly, 10% of our cohort has hypothyroidism (true positive: 2/19; 10%; false positive: 5/48; 10%), which brings in another potential cause of AE, such as Hashimoto encephalopathy. Furthermore, anti-thyroid peroxidase antibodies (TPO) were detected in most of these patients with low titer except for one patient with clear anti-GAD syndrome (ataxia and epilepsy) with anti-TPO titer of >500 IU/ml. None of these patients fulfilled the criteria for Hashimoto encephalopathy proposed by Graus et al.[1]

Our cohort's most frequent false positive antibodies were those directed against intracellular antigens. This perhaps relates to multiple factors including the pathogenicity of the autoantibody, the specificity of the assay used, and the frequency of these antibodies in the general Omani population. For example, anti-GAD65 antibody was frequent in both our true-positive AE and false-positive AE groups. A similar trend was demonstrated in a Mayo Clinic study, where 108 of 323 patients with high anti-GAD65 titer did not have anti-GAD65-related neurological autoimmunity.[19]

The most frequent clinical diagnoses in our false positive group were epilepsy, primary psychiatric disorders and dementia. These clinical presentations may explain why autoantibody testing was conducted, as they broadly share some of the features found in AE criteria. Over three and half years of follow-up, cancer was detected in three out of 19 true positive AE cases; each of the three AE types having known association with the cancer type detected.

Epilepsy, primary psychiatric conditions, and dementias were the most frequent conditions associated with false positive antibody profiles in our cohort. In addition, many ataxias, polyneuropathies, and myopathies might not need autoantibody profile studies. We strongly recommend physicians to refer such cases for expert evaluation prior to requesting autoantibody panels.

The demographic and clinical profiles of anti-NMDAR encephalitis patients in our cohort were similar to previously known epidemiology of the syndrome, with younger age onset and female predominance.[20] Seizure was the most frequent presentation followed by psychiatric and memory disturbance, respectively. These are similar to the reported initial presentations of anti-NMDAR encephalitis in the literature.[15,16,20] Of note, almost half of our cohort with anti-NMDAR encephalitis had a history of epilepsy. A retrospective study of 37 patients with anti-NMDAR encephalitis reported that 33% developed epilepsy.[21] Furthermore, a systematic review on the risk of AE with epilepsy (and vice versa) found that the incidence of epilepsy to be 73% after anti-NMDAR encephalitis. However, only 1% of patients with prior epilepsy later developed anti-NMDAR positivity; the overall rate of autoantibodies in epilepsy was 4%.[22] The outcome in our patients with anti-NMDAR encephalitis was excellent. This could be attributed to early initiation of therapy, absence of malignancy in all but one case, and use of combined immunotherapies.[15,20]

In our regression analysis exploring predictors of true positive autoantibodies versus false positive autoantibodies, presence of subacute memory disturbance increased the odds of having true AE by 17-fold. This is in keeping with the diagnostic criteria of AE, where subacute memory impairment is a core feature.[1] The importance of time factor is demonstrated by the presence of a negative relation between true AE positive and false-positive autoantibodies, thereby shorter duration of symptoms in appropriate context could

predict true AE. Again, symptoms duration of three months or less is part of the diagnostic criteria for AE.[1]

Our study has limitations. First, it has the typical limitations of a retrospective study. We had missing data like CSF analysis, EEGs and neuroimages in some cases, especially among the false-positive group. This could have led to misclassification bias or influenced statistical power. To minimize this, we used AE clinical criteria and charts reviewed by three senior neurologists independently for case ascertainment. Another limitation is that we included all positive autoantibodies related to different AE syndromes and compared them, in one group, with false positive antibodies in patients with various diagnoses, which could have affected the strength of association. We could not do separate analyses for each syndrome due to the small sample size. The fact that we did not include a healthy control group affected the significance of some of our findings, such as neutrophil-to-lymphocytes ratio. Furthermore, the autoantibody panels were not comprehensive and could have missed certain rare forms of AE, which could have affected the results. Finally, the single-centre nature of our study may affect the generalizability of its results.

Conclusion

To our knowledge, this is the first study to examine patients with positive limbic and paraneoplastic antibody profiles in a Middle Eastern population of Arab ethnicity. We retrospectively explored the clinical profiles of 67 patients who tested positive for paraneoplastic and limbic encephalitis panel, of whom 19 had true positive AE. The most frequent AE was anti-NMDAR encephalitis. The presence of subacute memory impairment predicted true AE positivity. The overall outcome of the AE patients in this study was good. Epilepsy, psychiatric disorders, and dementias were more likely to be associated with false-positive antibody profiles; for patients with such conditions we recommend expert evaluation prior to testing. Larger prospective and retrospective studies on specific AE syndromes, with expanded autoantibody panels, are needed in the Middle Eastern region.

Conflict of Interest

The authors declare no conflicts of interest.

Funding

No funding was received for this study.

Authors' Contribution

AA-Q contributed to the conception, design, data gathering, intellectual content, writing of the first draft and revision of the manuscript. HA-A, MAK, AA-A, JA and ARG contributed to the intellectual content, design and revision of the manuscript. SAF, RAH and IAL contributed to data collection, intellectual content and revision of the manuscript. All authors approved the final version of the manuscript.

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Table 1: Demographic and baseline clinical characteristics of participating patients (N = 67)

Characteristic	**All cohort N=67 (100%)**	**True Positive Group (n=19; 28%)**	**False Positive Group (n=48; 72%)**	***p*-value[$]**
Age, years	43.5 ± 5.9	35.3 ± 4.7	53.0 ± 3.3	0.010
Sex, Male	26 (39%)	9 (47%)	17 (35%)	0.370
Medical history				
None	17 (25%)	7 (37%)	10 (21%)	0.180
Hypertension	18 (27%)	1 (5%)	17 (35%)	0.010
Diabetes	15 (22%)	3 (16%)	12 (25%)	0.530
Epilepsy	22 (33%)	9 (47%)	13 (27%)	0.110
Cerebrovascular event	3 (5%)	0	3 (6%)	0.270
Psychiatric history	4 (6%)	1 (5%)	3 (6%)	0.880
Cancer	7 (10%)	2 (10%)	5 (10%)	0.980
Hypothyroidism	7 (10%)	2 (10%)	5 (10%)	0.980
Other	27 (39%)	5 (26%)	21 (44%)	0.190
Presenting symptoms				
Altered sensorium	5 (8%)	1 (5%)	4 (8%)	0.670
New onset seizure*	11 (16%)	5 (26%)	6 (12%)	0.170
Breakthrough seizure*	16 (24%)	7 (37%)	9 (19%)	0.200
Subacute memory issues	10 (15%)	6 (32%)	4 (8%)	0.030
Psychiatric	11 (16%)	5 (25%)	6 (12%)	0.340

Characteristic	All cohort N=67 (100%)	True Positive Group (n=19; 28%)	False Positive Group (n=48; 72%)	*p*-value[$]
Movement disorder	1 (2%)	0	1 (2%)	0.710
Headache	3 (5%)	1 (5%)	2 (4%)	0.640
Focal neurological deficit	16 (24%)	2 (11%)	14 (29%)	0.390
Fever	3 (5%)	2 (10%)	1 (2%)	0.430
Others	9 (18%)	6 (32%)	6 (12%)	0.080
Duration of symptoms (days)	124.9 ± 37.6	120 ± 35	192 ± 25	0.210
Neutrophils-to-lymphocytes ratio	2.87 ± 0.85	3.39 ± 0.94	2.75 ± 0.70	0.610
CSF analysis	19 (28%)	12 (63%)	7(15%)	0.010
CSF WBC (count)	4.3 ± 2.8	6.2 ± 4.2	0.4 ± 0.3	0.310
CSF Protein (g/L)	0.53 ± 0.14	0.55 ± 0.21	0.42 ± 0.07	0.620
Electroencephalogram	37 (52%)	15 (79%)	22 (46%)	0.010
Normal	8 (22%)	2 (13%)	6 (27%)	0.430
Slowing	12 (32%)	3 (20%)	9 (41%)	0.280
Epileptiform	17 (46%)	10 (65%)	7 (30%)	0.040
Neuroimaging	56 (85%)	19 (100%)	38 (79%)	0.030
Normal	20 (35%)	8 (42%)	12 (32%)	0.43
Abnormal signals in limbic system	5 (9%)	5 (26%)	0	0.010
Other abnormalities	33 (59%)	6 (33%)	27 (71%)	0.010

[$] *Between Group A & B; * If seizure presentation is taken collectively, the difference between A and B is significant at p = 0.028; CSF: cerebrospinal fluid; WBC: White blood cells.*

Table 2: Frequency of autoantibodies in true positive and false positive groups.

Antibody Panel	True Positive Group, n=19 (28%)		False Positive Group, n=48 (72%)	
Paraneoplastic and limbic Autoantibodies	Serum	CSF	Serum	CSF
Anti-Ma2	1(5%)	0	2 (4%)	0
Anti-Yo	0	0	6 (13%)	0
Anti-GAD65*	4 (21%)	1 (5%)	8 (17%)	0
Anti-SOX1	0	0	6 (13%)	0
Anti-NMDAR**	7 (37%)	6 (32%)	2 (4%)	0
Anti-Caspr2	3 (16%)	0	3 (6%)	0
Anti-Zic4	1 (5%)	0	3 (6%)	0
Anti-Rec	0	0	6 (13%)	0
Anti-Amphiphysin	0	0	5 (10%)	0
Anti-Titin	0	0	4 (8%)	0
Anti-CRMP5***	0	1 (5%)	2 (4%)	0
Anti-Tr	1 (5%)	0	0	0
Anti LGi1	0	0	1 (2%)	0

*CSF: cerebrospinal fluid. *One patient had Anti-GAD65 in both CSF and serum; **5 patients had anti-NMDAR antibodies in both serum and CSF; *** This true AE positive patient was also positive for Anti-Hu in CSF.*

Table 3: Clinical predictors of autoimmune encephalitis in antibody positive patients.

Demographic and Clinical Characteristics	**B**	**S.E.**	***p*-value**	**Odds ratio (OR)**	**95% C.I. for OR**
Sex	-0.028	0.022	0.192	1.029	0.986–1.073
History of Hypertension	-1.423	1.460	0.330	0.241	0.014–4.220
History of Epilepsy	0.904	1.185	0.446	2.470	0.242–25.222
First Episode of seizure	1.047	0.928	0.259	2.849	0.462–17.566
Breakthrough seizure	0.037	1.298	0.977	1.038	0.081–13.219
Subacute Memory Disturbance	2.880	1.227	0.019*	17.807	1.608–197.202
Symptoms duration (days)	-0.005	0.002	0.030*	0.995	0.990–0.999
Constant	0.324	0.905	0.721	1.382	

*: *Significant predictor; B: regression coefficient; S.E.: standard error*

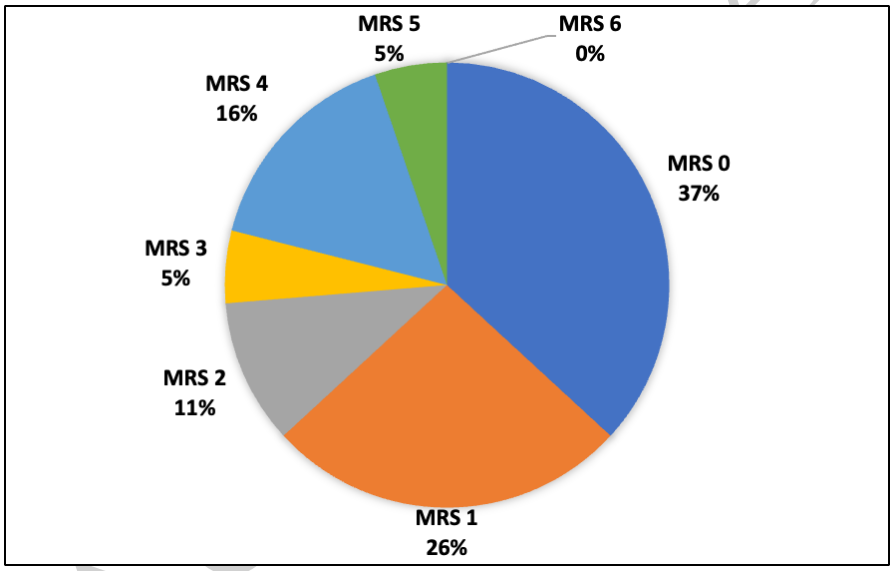

Figure 1: Outcome in patients with autoimmune encephalitis.
MRS: Modified Rankin Scale.

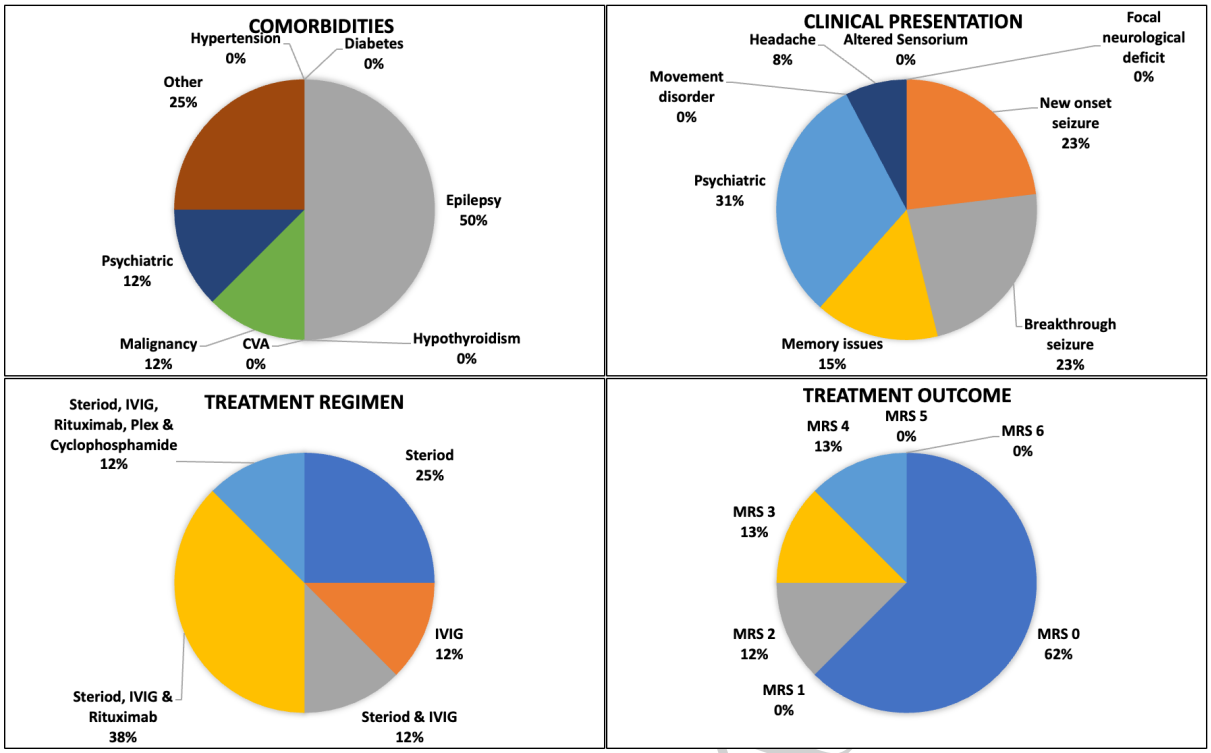

Figure 2: Clinical Profile and outcome of patients with Anti-NMDAR encephalitis (n=8). *NMDAR: N-methyl-D-aspartate receptor EEG: Electroencephalogram; MRS: Modified Rankin Scale; IVIG: Intravenous Immunoglobulin*.