An Observational Study of, EEG Abnormalities and Clinical Outcome in Schizophrenia, Conducted in Government Hospital for Mental Care in Visakhapatnam

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ABSTRACT

BACKGROUND
Schizophrenia is a chronic mental illness with severe disruptions in thought, perception, language, and sense of self. Although there are a lot of recent advances in pharmacotherapy, a large percentage of persons with Schizophrenia remain treatment resistant or at least partially non-resistant to drugs. The recent increase of interest in the neurobiology of Schizophrenia and other psychiatric disorders, the emergence of neuropsychiatry, and the recent advances in computerized analyses of EEG have resulted in a revival of interest in electrophysiology among mental health professionals.

METHODS
This is a prospective observational study. A total of 84 subjects who were drug naïve and diagnosed with Schizophrenia were included in the study by convenience sampling. General information sheet to collect the socio-demographic and clinical details, Positive and Negative Syndrome Scale (PANSS), Clinical Global Impression scale, Electroencephalogram recordings were used. Data analysis was performed by using the SPSS Software version 23. Descriptive statistics and correlational statistics were used to analyse the collected data.

RESULTS
A total of 84 subjects who were diagnosed with Schizophrenia were included in the study. Out of 84 patients, 22 were lost to follow up bringing the valid sample of the study to 62. EEGs of the sample subjects were classified based on the modified sample, EEGs of 45 (72.58 %) subjects were normal, EEGs of 13 (20.97 %) subjects were essentially normal, and EEGs of 4 (6.45 %) subjects were classified as abnormal.

CONCLUSIONS
No statistically significant differences were found in Positive and negative syndrome scale scores at baseline when compared between normal, essentially normal and abnormal EEG groups of first episode schizophrenia subjects.

KEYWORDS
Electroencephalogram (EEG), Schizophrenia, PANSS, CGI Scale, SPSS Software Version 23.0

BACKGROUND

Schizophrenia is a chronic mental illness with severe disruptions in thought, perception, language, and sense of self. Schizophrenia with lifetime prevalence of 1 % and incidence of 1.5 in every 10000 population[1] is one of the most disabling psychiatric disorders in the world. Data from western countries shows moderate to sever degree of persisting disability in around 40 % of males and 25 % females with schizophrenia.[2] Death rates are almost double in people with schizophrenia compared to general population.[3] Although there are a lot of recent advances in pharmacotherapy, a large percentage of persons with Schizophrenia remain treatment resistant or at least partially non-resistant to drugs. An investigation which can predict poorer outcome in Schizophrenia will help in planning the management thereby decreasing health care expenditure, unnecessary side effects of drugs and improves the outcome. Identifying such early prognostic indicators will have significant clinical value helping in early identification of individuals who have an increased risk of poor prognosis.at present electroencephalogram is used in psychiatry only as an investigating tool for epilepsy or other central nervous system disorders. While abnormal EEGs are seen in around 20 % of people with schizophrenia[4] no significant correlation has been found between psychiatric disorders and results. It will give an opportunity to research into treatment resistance and methods to overcome it. The recent increase of interest in the neurobiology of Schizophrenia and other psychiatric disorders, the emergence of neuropsychiatry, and the recent advances in computerized analyses of EEG have resulted in a revival of interest in electrophysiology among mental health professionals. Few early studies of resting EEG and subsequent quantitative EEG supported the hypothesis that abnormal EEG is associated with poorer prognosis in Schizophrenia.[5]

Most of those studies used quantified EEGs in subjects with prolonged exposure to antipsychotic drugs. The recent increased interest in the study of the first episode of schizophrenia spectrum disorders provides an opportunity to assess individuals before prolonged exposure to antipsychotics and help in identifying characteristics at the beginning that predict the outcome.[6] In recent years few studies were done to assess the association between EEG abnormalities and prognosis in first episode psychosis. The current study attempts to assess the relation between EEG abnormalities at baseline and clinical outcome at six months follow up in first-episode schizophrenia patients.

Objectives
1. To study the association between Electroencephalogram abnormalities and clinical outcome in First-episode Schizophrenia
2. To examine whether an abnormal Electroencephalogram in First-episode Schizophrenia subjects is associated with poorer treatment response compared to subjects with normal E.E.G.

METHODS

Subjects for the study were recruited from the admitted patients of Government Hospital for Mental Care, Visakhapatnam. This is a Prospective observational study conducted over a period of 18 months (February 2017 to August 2018). A total of 84 subjects who were drug naïve and diagnosed with Schizophrenia were included in the study.

Inclusion Criteria
Subjects who were of age group 18 years to 55 years.
Subjects who fulfilled the ICD - 10 criteria for research of Schizophrenia.
Subjects who were drug-naive at the time of admission.
Subjects who gave consent to the study.

Exclusion Criteria
Subjects with comorbid psychiatric disorders.
Subjects with any known substance dependence pattern.
Subjects with organic psychotic disorders.
Subjects with epilepsy, head trauma, and stroke.
Subjects who were not willing to be part of the study.

Operational Procedure
Patients fulfilling the inclusion criteria were assessed with Positive and negative syndrome scale and Clinical Global Impression scale. Electroencephalograms of the sample were recorded. They were reported and classified by a neurologist based on the Modified version of Mayo clinic classification of EEG results. Subjects were followed up for six months. At six months subjects were reassessed using PANSS and CGI scale. In subjects, remission was assessed using PANSS total scores, Remission in Schizophrenia working group criteria and clinical global impression severity scale. Subjects were classified based on EEG reports, and relevant statistics were applied to assess the relation between EEG reports at baseline and remission statuses at six months follow up. Prior permission from Institutional Ethics Committee, Andhra Medical College, Visakhapatnam has been taken.

Instruments of the Study
- Informed consent form General Information sheet to collect the socio-demographic and clinical details.
- Positive and Negative Syndrome Scale (PANSS).
- Clinical Global Impression scale. Electroencephalogram recordings.

Statistical Analysis
Data analysis was performed by using the SPSS Software version 23. Descriptive statistics and correlational statistics were used to analyse the collected data.

RESULTS

A total of 84 subjects who were diagnosed with Schizophrenia were included in the study. Out of 84 patients, 22 were lost to follow up bringing the valid sample of the study to 62.

Age Wise Distribution of the Sample
In the valid sample (N = 62) the mean age was 30.2742 with a standard deviation of ± 7.284. In the sample 14 patients were from the age group of 18 to 24, 30 patients were from age group 25 to 34, 16 patients were from age group 35 to 44, and 2 patients were from age group 45 to 54. Minimum age in the sample is 18 years, and the maximum age is 45 years with a range of 27 years.

Gender-Wise Distribution of the Sample
In the sample 39 patients belong to male gender (62.90 %), and the other 23 to female gender (37.10 %).

Distribution of Domicile
In the sample majority of the subjects are from the rural area (74.2 %), followed by urban area (19.4 %) and very few are from the tribal area (6.4 %).

Literacy Distribution of the Sample
In the sample only 3.2 % of the patients were illiterate, 19.4 % of patients studied up to primary education, 38.7 % studied up to secondary education, 25.8% studied up to intermediate, and 12.9 % of the sample were graduates.

Religion-Wise Distribution of the Sample
Majority (N = 47, 75.8 %) of the sample were Hindu by religion, followed by Christians (N = 13, 21 %) and rest (N = 2, 3.2 %) were Muslims.

Marital Status
In the sample, 64.5 % were married, remaining 35.5 % were unmarried. Among the married, 2 were divorced.

Employment Status
In the sample, 29 of subjects were unemployed whereas the rest of 33 were employed which includes various types of professions. Of them unskilled workers were 8, semi-skilled were 7, farmers were 11, clerical were 5 and semi-professional were 2.

Socioeconomic Status
According to Modified Kuppuswamy scale, in the sample, 3 (4.8 %) subjects belonged to lower socioeconomic status, 21 (33.9 %) belonged to the upper lower group, 28 (45.2 %) belonged to the lower middle group, and 10 (16.1 %) subjects belonged to the upper middle group.

Type of Family
In the sample, 41 (66.12 %) subjects were from nuclear families whereas rest of the 21 (33.88 %) were from joint families.

Clinical Variables
Duration of Untreated Illness
The mean duration of untreated illness in the sample was 9.84 months with a standard deviation of ± 7.59. Out of total sample, 47 (75.81 %) subjects had a duration of untreated illness less than one year whereas 14 (22.58 %) subjects had a duration of untreated illness between 1 to 2 years and only 1 (1.61 %) subject had a duration of untreated illness between 2 to 3 years.

Duration of Illness
As the study subjects were first episode drug naive patients of Schizophrenia, duration of illness is as same as that of untreated illness with a mean duration of 9.84 months with a standard deviation of ± 7.59.

Electroencephalogram Classification
EEGs of the sample subjects were classified based on the modified version of the Mayo Clinic classification of EEG abnormalities. Out of the total sample, EEGs of 45 (72.58 %) subjects were normal, EEGs of 13 (20.97 %) subjects were essentially normal, and EEGs of 4 (6.45 %) subjects were classified as abnormal.

Psychopathological Variables
a) Positive and Negative Syndrome Scale Scores at the Time of Diagnosis
In the sample (N = 62), at the time of diagnosis, the mean Positive Scale score is 22.71 with a standard deviation of 3.58. Mean Negative Scale score is 15.55 with a standard deviation of 2.21. Mean General Psychopathology Scale score is 46.28 with a standard deviation of 6.51. Mean total PANSS score was 84.54 with a standard deviation of 7.09.

In the subjects with normal EEG (N = 45) at the time of diagnosis, the mean Positive Scale score is 22.58 with a standard deviation of 3.78. Mean Negative Scale score is 15.66 with a standard deviation of 2.28. Mean General Psychopathology Scale score is 47.96 with a standard deviation of 6.56. Mean total PANSS score was 86.18 with a standard deviation of 7.29.

In the subjects with essentially normal EEG (N = 13) at the time of diagnosis, the mean Positive Scale score is 23.22 with a standard deviation of 2.90. Mean Negative Scale score is 15.33 with a standard deviation of 2.17. Mean General Psychopathology Scale score is 46.22 with a standard deviation of 6.87. Mean total PANSS score was 84.78 with a standard deviation of 6.94.

In the subjects with abnormal EEG (N = 4) at the time of diagnosis, the mean Positive Scale score is 22.33 with a standard deviation of 2.08. Mean Negative Scale score is

15.67 with a standard deviation of 1.53. Mean General Psychopathology Scale score is 44.67 with a standard deviation of 4.93. Mean total PANSS score was 82.66 with a standard deviation of 3.22.

In the current study, no statistically significant differences were found between group means of total scores of PANSS among different EEG groups as determined by one way ANOVA (F = 0.013, p > 0.05).

EEG	Mean	N	Std. Deviation	F	Sig
Abnormal	85.75	4	6.70		
Essentially Normal	85.62	13	6.74	0.013	0.987
Normal	85.98	45	7.53		
Total	**85.87**	**62**	**7.21**		
Table 1. Total PANSS Scores Group Means Comparison at the Time of Diagnosis					

b) Positive and Negative Syndrome Scale Scores at 6 Months Follow Up

In the sample (N = 62), at 6 months follow up, the mean Positive Scale score is 11.45 with a standard deviation of 3.84. Mean Negative Scale score is 10.39 with a standard deviation of 2.69. Mean General Psychopathology Scale score is 24.18 with a standard deviation of 5.74. Mean total PANSS score was 45.92 with a standard deviation of 9.57.

In the subjects with normal EEG (N = 45) at 6 months follow up, the mean Positive Scale score is 12.22 with a standard deviation of 4.12. Mean Negative Scale score is 11.24 with a standard deviation of 2.85. Mean General Psychopathology Scale score is 25.36 with a standard deviation of 6.154. Mean total PANSS score was 48.42 with a standard deviation of 11.322. In the subjects with essentially normal EEG (N = 13) at 6 months follow up, the mean Positive Scale score is 11.89 with a standard deviation of 2.261. Mean Negative Scale score is 10.44 with a standard deviation of 1.67. Mean General Psychopathology Scale score is 23.44 with a standard deviation of 3.57. Mean total PANSS score was 45.78 with a standard deviation of 6.261.

In the subjects with abnormal EEG (N = 4) at 6 months follow up, the mean Positive Scale score is 10.25 with a standard deviation of 3.05. Mean Negative Scale score is 9.50 with a standard deviation of 2.08. Mean General Psychopathology Scale score is 23.75 with a standard deviation of 2.09. Mean total PANSS score was 43.5 with a standard deviation of 5.56.

In the current study, no statistically significant differences were found between group means of total scores of PANSS among different EEG groups as determined by one way ANOVA (F = 0.008, p > 0.05).

EEG	Mean	N	Std. Deviation	F	Sig
Abnormal	48.75	4	11.02		
Essentially Normal	48.08	13	6.99	0.008	0.992
Normal	48.40	45	11.09		
Total	**48.35**	**62**	**10.21**		
Table 2. Total PANSS Scores Group Means Comparison at Six Months Follow Up					

c) Clinical Global Impression Scale – Severity Score of Illness at Diagnosis

In the sample (N = 62), at the time of diagnosis severity of illness measured through clinical global impression scale. In total, 5 subjects (8.07 %) were moderately ill

group, 27 subjects (43.54 %) were markedly ill group, and 30 subjects (48.38 %) were severely ill group. When classified according to EEG type, in normal EEG group (N = 45), 5 subjects (11.12 %) were moderately ill group, 18 subjects (40.00 %) were markedly ill group, and 22 subjects (48.88 %) were severely ill group. In essentially normal EEG group (N = 13), 7 subjects (53.85 %) were markedly ill group, and 6 subjects (46.14 %) were severely ill group. In abnormal EEG group (N = 4), 2 subjects (50.00 %) were markedly ill group, and 2 subjects (50.00 %) were severely ill group.

	Moderately Ill	Markedly Ill	Severely Ill
Normal (N = 45)	11.2 %	40 %	48.88 %
Essentially Normal (N = 13)	0 %	53.85 %	46.15 %
Abnormal (N = 4)	0	50 %	50 %
Total (N = 62)	**8.07 %**	**48.38 %**	**43.55 %**
Table 3. CGI Severity Scale Comparison at the Time of Diagnosis			

d) Clinical Global Impression Scale – Severity of Illness at 6 Months Follow Up

In the sample (N = 62), at the time of 6 months follow up severity of illness measured through clinical global impression scale. In total, 20 subjects (32.27 %) were Borderline mentally ill group, 16 subjects (25.81 %) were mildly ill group, 23 subjects (37.09 %) were moderately ill group, and 3 subjects (4.83 %) were markedly ill group.

When classified according to EEG type, in normal EEG group (N = 45), 15 subjects (33.33 %) were Borderline mentally ill group, 11 subjects (24.44 %) were mildly ill group 17 subjects (37.78 %) were Moderately ill group, and 2 subjects (4.44 %) were Markedly ill group. In essentially normal EEG group (N = 13), 3 subjects (23.07 %) were Borderline mentally ill group, 4 subjects (30.76 %) were mildly ill group 5 subjects (38.46 %) were Moderately ill group, and 1 subject (7.69 %) was markedly ill group. In abnormal EEG group (N = 4), 2 subjects (50.00 %) were Borderline mentally ill group, 1 subject (25.00 %) was mildly ill group, and 1 subject (25.00 %) was moderately ill group.

	Borderline Mentally ill	Mildly ill	Moderately ill	Markedly ill
Normal (N = 45)	33.33 %	24.44 %	37.78 %	4.44 %
Essentially Normal (N = 13)	23.07 %	30.76 %	38.46 %	7.69 %
Abnormal (N = 4)	0	50 %	25 %	25 %
Total (N = 62)	**32.27 %**	**25.81 %**	**37.09 %**	**4.83 %**
Table 4. CGI Severity Scale Comparison at 6 Months Follow Up				

e) Remission Data of Sample
1) Positive Symptoms Criteria

In the sample (N = 62), at the time of 6 months follow up subjects who had reduction of positive symptoms by 50 % or greater are considered to be under remission. In total sample, 50 subjects (80.64 %) were in remission and remaining 12 subjects (19.36 %) were not in remission.

When assessed as per EEG type, in normal EEG group (N = 45) 37 subjects (82.22 %) were in remission and remaining 8 subjects (17.78 %) were not in remission. In essentially normal EEG group (N = 13) 10 subjects (76.92 %) were in remission and remaining 3 subjects

(23.08 %) were not in remission. In abnormal EEG group (N = 4) 3 subjects (75.00 %) were in remission and remaining 1 subject (25.00 %) was not in remission. In current study, no statistically significant differences were found between number of subjects in remission in different EEG groups as determined by chi-square analysis.

	Normal	Essentially Normal	Abnormal	Total	Test & P Values
Remission	37 (59.68 %)	10 (16.13 %)	03 (4.53 %)	51 (82.26 %)	X² value = 1.1139; d.f. = 2; P = 0.5730; P > 0.05
No Remission	08 (12.90 %)	03 (4.84 %)	01 (1.92 %)	11 (17.74 %)	
Total	45 (72.58 %)	13 (20.97 %)	04 (6.45 %)	62 (100.0 %)	
Table 5. PANSS Positive Symptoms Remission Criteria Statistics					
(χ² value = 1.1139; p = 0.5730; p > 0.05)					

2) Remission in Schizophrenia Working Group criteria for remission

In the sample (N = 62), at the time of 6 months follow up subjects who scored mild or less in severity level in eight items P1, P2, P3, G5, G9, N1, N4, and N6 were considered to be under remission according to Remission in Schizophrenia Working Group criteria. In total sample, 39 subjects (62.90 %) were in remission and remaining 23 subjects (37.10 %) were not in remission. When assessed as per EEG type, in normal EEG group (N = 45) 28 subjects (62.22 %) were in remission and remaining 17 subjects (37.78 %) were not in remission. In essentially normal EEG group (N = 13) 8 subjects (61.54 %) were in remission and remaining 5 subjects (38.46 %) were not in remission.

In abnormal EEG group (N = 4) 3 subjects (75.00 %) were in remission and remaining 1 subject (25.00 %) was not in remission.

In this study, no statistically significant differences were found between number of subjects in remission in different EEG groups as determined by chi-square analysis.

	Normal	Essentially Normal	Abnormal	Total	Test & P Values
Remission	28 (45.16 %)	08 (12.90 %)	03 (4.84 %)	39 (62.90 %)	X² value= 0.2702; D.f = 2; P = 0.8729; P > 0.05
No Remission	17 (27.42 %)	05 (8.06 %)	01 (1.61 %)	23 (37.10 %)	
Total	45 (72.58 %)	13 (20.97 %)	04 (6.45 %)	62 (100.0 %)	
Table 6. R.S.W.G. Criteria Remission Statistics					
(X² value = 0.2702; p = 0.8729; p > 0.05)					

3) Clinical Global Impression-Severity Criteria for Remission

In the sample (N = 62), at the time of 6 months follow up subjects who scored Clinical Global Impression-Severity scale score less than or equal to 3 is considered as remission. In total sample, 36 subjects (58.06 %) were in remission and remaining 26 subjects (41.94 %) were not in remission. When assessed as per EEG type, in normal EEG group (N = 45) 26 subjects (57.77 %) were in remission and remaining 19 subjects (42.23 %) were not in remission. In essentially normal EEG group (N = 13) 7 subjects (53.84 %) were in remission and remaining 6 subjects (46.16 %) were not in remission. In abnormal

EEG group (N = 4) 3 subjects (75.00 %) were in remission and remaining 1 subject (25.00 %) was not in remission.

In this study, no statistically significant differences were found between number of subjects in remission in different EEG groups as determined by chi-square analysis.

	Normal	Essentially Normal	Abnormal	Total	Test & P Values
Remission	26 (41.94 %)	7 (11.29 %)	03 (4.84 %)	36 (58.06 %)	X² value = 0.5677; d.f = 6; P = 0.7529; P > 0.05
No Remission	19 (30.65 %)	06 (9.68 %)	01 (1.61 %)	26 (41.94 %)	
Total	45 (72.58 %)	13 (20.97 %)	04 (6.45 %)	62 (100.0 %)	
Table 6. C.G.I. Severity Remission Criteria Statistics					
(X² value = 0.5677; p = 0.7529; p > 0.05)					

DISCUSSION

The current study was aimed to study the relation between EEG abnormalities at baseline and clinical outcome in the form of remission at six months follow up in individuals with first-episode schizophrenia who were admitted in Government hospital for mental care as inpatients on voluntary basis. In the sample around 63 % of the subjects are males, most of the subjects are literates with primary level and secondary level education, two-thirds of the sample are from the rural area. Majority of the subjects are Hindus, and almost half of the subjects are of 25 to 34 years age group.

Two-thirds of the total subjects are married as the majority of the women subjects are married in line with marriages around the age of 18 in rural females. Subjects were categorized into three groups. In this study among the valid sample of 62, 45 subjects had normal E.E.G.s with 72.58 %, 13 subjects had essentially normal E.E.G.s with 20.97 %, and four subjects had abnormal E.E.G.s with 6.45 %. In this study, there is no significant difference in psychopathology as assessed by PANSS scores at baseline when compared between subjects of different EEG groups. This finding of the study is similar to the baseline findings of Rahul Manchanda et al,[7] and R Norman et al.[8] even though SANS and SAPS were applied in those studies.

In the current study, the clinical outcomes at six months follow up were assessed to compare with EEG abnormalities. PANSS and C.G.I. Scales were applied. As a measure of clinical outcome, remission data of the sample were measured.

In this study as per PANSS positive symptom scores, 82.22 % of normal EEG subjects, 76.92 % of essentially normal EEG subjects and 75 % of abnormal EEG subjects were in remission at six months follow up. This finding is similar to the study of R Manchanda et al.[7] where 90.5 %, 64.3 % and 58.3 % respectively of normal, essentially normal and abnormal EEG groups were in remission.

Though percentages are in similar trend, this study did not have statistically significant differences between remission percent of different groups, X² value = 0.3525; P = 0.8375; P > 0.05 contrary to the study mentioned above which has significant relation (p = 0.045). The change in findings is probably due to the change in the selection of

sample and methodology where PANSS was used in this study and SAPS in that study.

In this study as per RSWG remission criteria 62.22 % of normal EEG subjects, 61.53 % of essentially normal EEG subjects and 50 % of abnormal EEG subjects were in remission at six months follow up. No statistically significant differences were found between the number of subjects in remission in different groups as determined by chi-square analysis. (P = 0.5728) however, a similar study done by R Norman et al.[8] has a contrary finding where borderline significant differences were present in remission of different EEG groups.(P < 0.09).

The difference in finding is probably due to different remission criteria. They used the score for all the items in SAPS and SANS as the definition of remission whereas this study used RSWG criteria for remission.

When Clinical global impression scale severity only is taken as criteria for remission 57.77 % of normal EEG subjects, 53.84 % of essentially normal EEG subjects and 50% of abnormal EEG subjects were in remission with no statistically significant differences. This finding is contrary to the finding of statistically significant differences in remissions among different EEG groups in a similar study done by R Manchanda et al.[9]

The probable reason for the differences are changes in the definition of remission and time frames of follow up which are six months and two years respectively in current and similar studies.

Strengths

1. This study is a prospective cohort study with six months follow up.
2. One of the very few studies where routine EEG recordings relation with remission in schizophrenia is assessed.
3. Valid scales and remission criteria were used.

Limitations

- This study is an uncontrolled study with a small sample.
- Electroencephalogram recording was done only once at the beginning of the study.
- Follow up at six months is done to assess remission due to study period limitations but follow up at two years and more extended periods to assess remission in schizophrenia would have been more accurate in par with similar studies.
- Only non-quantified E.E.G.s were recorded in this study.

CONCLUSIONS

In this study, no statistically significant differences were found in positive and negative syndrome scale scores at

baseline when compared between normal, essentially normal and abnormal EEG groups of first episode schizophrenia subjects.

No statistically significant differences were found in remission at six months follow up when compared with EEG abnormalities.

Future Recommendations

- A study with a larger sample of Schizophrenia may help to understand EEG pattern better.
- A study with follow up for longer periods may give a clear idea about remissions in schizophrenia.

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