Original Article

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# Correlational Analysis of Socio-demographic and Clinical Profile in Determining the Treatment Response in Patients with Catatonia in the Psychiatric Inpatient Department of a Rural Tertiary Care Centre in Eastern India

Psychiatry/Mental Health Section

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## ABSTRACT

**Introduction:** Catatonia, a poorly understood syndrome challenging the clinician's diagnostic and management skills, has scarce literatures regarding the clinical correlates and determining factors towards treatment response.

**Aim:** To find the correlates of socio-demographic, clinical profile, catatonic features and identifying determining factors of treatment response to lorazepam and Modified Electroconvulsive Therapy (MECT) in catatonia.

**Materials and Methods:** This cross-sectional study was conducted at the Department of Psychiatry, North Bengal Medical College, Siliguri, West Bengal, India from January 2020 to February 2021. The catatonia cases satisfying the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) criteria were studied. A total of 66 patients were evaluated using the 23-item Bush Francis Catatonia Rating Scale (BFCRS) for severity and later grouped into lorazepam responder (Group I) and non responders (Group II) who received MECT. Background diagnoses using DSM-5 was made after symptom resolution. Statistical analyses like Chi-square and student's t-test to compare frequencies and means respectively, Pearson's and Spearman's correlation test for bivariate correlation and linear and logistic regression to predict factors for treatment outcome were employed using Statistical Package for the Social Sciences (SPSS) 16.0 with a p-value <0.05 considered significant.

**Results:** Among 66 patients, group I had total 54 patients (mean age=25.25±7.03 years) and group II had 12 patients (mean age=23.25±4.30 years). Schizophrenia spectrum disorders were the major underlying psychiatric diagnosis. The MECT was needed in 58.33% of patients with positive family history of psychiatric disorders as compared to 14.81% who responded to lorazepam (p-value=0.001). Severity of catatonia measured by the total BFCRS Scores was higher in the Group II (p-value <0.001). Positive family history (Spearman's rho=-0.512, p-value <0.001) and longer hospital stay (Spearman's correlation coefficient=0.344; p-value=0.005) had significant correlation to catatonic severity. The BFCRS subscale bivariate correlational analysis showed high scores on immobility, mutism, staring, grimacing, rigidity, negativism, withdrawal and autonomic abnormality correlated significantly with MECT response. High scores on stereotypy, waxy flexibility and excitement correlated significantly with lorazepam response.

**Conclusion:** Lorazepam was effective in most cases. Higher scores on BFCRS, positive family history of psychiatric illness, presence of mutism, rigidity, immobility, withdrawal and negativism correlated with lorazepam resistance and MECT response. Waxy flexibility, stereotypy and excitement correlated to lorazepam response. Severity of catatonic symptoms and positive family history were the determining factor for non response to Lorazepam. This could provide insight into the management strategies and treatment protocol in catatonia.

**Keywords:** Electroconvulsive therapy, Immobility, Lorazepam, Mutism, Waxy flexibility

## INTRODUCTION

Catatonia is a neuropsychiatric syndrome that can occur due to a spectrum of medical and psychiatric disorders chiefly mood, psychotic and neuro-developmental disorders. The term 'Catatonia' was primarily introduced by Kahlbaum KL and comprised of several clinical features of motor abnormalities occurring along with psychiatric disorders, epilepsy and tuberculosis [1]. Catatonia has been broadly classified into excited delirious type or retarded stuporous type where more than 40 catatonic signs can manifest [2]. Mutism, stupor, staring, negativism, rigidity, posturing, catalepsy and withdrawal were few signs commonly reported in Indian studies [3-5]. The Diagnostic and Statistical Manual of Mental Disorders (DSM-5) has enlisted 12 prominent signs of which three or more must dominate the clinical picture for a minimum 24 hours to meet the diagnostic criteria of catatonia [6,7]. The International Classification of Disorders (ICD-11) has also proposed separate diagnosis of catatonia [7,8].

Incidence of catatonia has been studied primarily in acutely ill-psychiatric inpatients [6]. The incidence has been reported to be approximately 10%, but estimates ranged from 5-20%, depending upon the study designs and operational definition of catatonia [9-12]. In a meta-analysis and meta-regression analysis of 74 studies, it was found that the mean prevalence rates ranged from 7.8 to 9% [13]. The four year period prevalence rate of catatonia in admitted patients in a psychiatric ward from Indian studies as per ICD-10 criteria and DSM-5 criteria were found to be 4.8% and 5.3% respectively [3,14].

Remission of catatonic features is often achieved by benzodiazepines initially and ECT, if needed [15]. Though it is fairly common, catatonia tests the clinician's skill owing to its difficulties in studying, understanding and recognition of the disorder [16]. In a review it was seen that in about 70% of cases benzodiazepines were effective [17]. Another study showed 87% response rate to lorazepam and diazepam in patients with catatonic schizophrenia [18]. A large prospective Indian study showed that there was significant early

response to lorazepam in 93% catatonic cases with 75% attaining remission and the rest 18% having partial response [9]. A cross-sectional study from India with 32 catatonic patients found a 50% response rate with lorazepam while the non responders responded to ECT [5]. Occasionally diazepam has also shown efficacy in similar situations [19,20]. Overall the complete remission ranged from 17.6% [3] to 32.3% [21,22] and partial remission upto 68.7% [22] in Indian retrospective studies. Role of benzodiazepines has been emphasised in recently updated management algorithm in early and chronic catatonia [23]. In cases resistant to pharmacological treatment, MECT has been shown to be a promising option in systematic reviews, double-blind randomised control trials and retrospective studies [24-26].

Although there are few Indian studies [3-5,21,22] regarding the socio-demographic and clinical features of catatonia, there is uncertainty about the factors that can determine the response to lorazepam in catatonia. Whatever studies are available, were mainly retrospective chart reviews which have their own limitations [3,4,21,22], The retrospective nature of these studies provide inferior levels of evidence, have recruitment by convenience sampling, have selection bias and as such have been recognised as inaccurate, incomplete or illegible documentation as well as variance in quality and location of informations recorded by medical professionals. [24] There is often no data on co-medications [3] which hamper interpretation of results. Moreover, BFCRS has not been validated as a tool to detect catatonia, retrospectively [27].

The ECT has been shown to be effective in management of prolonged catatonia and cases that have shown partial response to pharmacological treatments [10,25,26,28]. Therefore, it is of utmost importance to find out such clinical predictors for the sake of determining the responsiveness to benzodiazepines in the early phase of treatment so that the probable non responders can be identified and referred to tertiary care centres for the consideration of ECT at the earliest. A recent systematic review had clearly stated that developing a treatment protocol was difficult in catatonia management and that there was need for stringent treatment studies on catatonia to develop a treatment protocol [24].

With these lacunae in mind, a cross-sectional study was undertaken of inpatients presenting with catatonia with the aim of studying the socio-demographic profile, clinical signs and symptoms (phenomenology), clinical profile and predictors of treatment response. This would help in understanding which patient group should receive lorazepam and which should receive Modified Electroconvulsive Therapy (MECT), thus, helping in development of a consensus on treatment protocol of patients presenting with catatonia.

## MATERIALS AND METHODS

This cross-sectional analytical study was conducted at the Department of Psychiatry, North Bengal Medical College, Siliguri, West Bengal, India from January 2020 to December 2020. Statistical analysis and preparation of manuscript was done in January 2021 and February 2021. Ethical approval for the study was received from the Institution Ethics Committee (vide letter No IEC/NBMC/2019-20/119 dated 24/12/2019).

**Inclusion criteria:** The study included those patients who were admitted in the Inpatient Department and fulfilled the DSM-5 diagnosis of catatonia.

**Exclusion criteria:** The study excluded those with intellectual disability, cognitive impairment owing to organic problems or those who did not give consent.

Consecutive patients from the Outpatient Department who fulfilled the inclusion and exclusion criteria were admitted and studied. The cases were diagnosed by two faculty psychiatrists using DSM-5 criteria for catatonia [6]. Informed consent was taken from the patients and their primary caregivers. Assent was also taken from adolescent patients apart from consent from their parents.

**Sample size calculation:** Based on the prevalence data available on catatonia after the literature review, a four-year period prevalence of 4.8% [3] and 5.3% [14] was found using International Classification of Diseases (ICD-10) and DSM-5 criteria respectively. Using the formula for deciding the sample size (n) of a cross-sectional study $N=(Z_{\alpha/2})^2xpq/d^2$ the minimum sample size was calculated as 70. The Confidence Interval (CI) was taken as 95%, prevalence (p) of 4.8% and a precision (d) of 5%. Where $Z_{\alpha/2}$=standard normal deviation for 95% CI, the value was taken as 1.96. As per the calculation done using the above formula, 70 patients were recruited for the study during the study period of which incomplete data were available in four cases as two were discharged against medical advice and two were transferred to medicine ward as they had tested positive for SARS-CoV-2. These four patients were excluded from the final analysis. Efforts to recruit more patients were hampered due to lockdown during COVID-19 pandemic.

The patients were evaluated as per the semi-structured data sheet for socio-demographic details which was developed in the department and consisted of variables like age, gender, educational status, marital status, socio-economic status, religion, ethnicity and residential background. Clinical profile sheet consisted of duration of stay in hospital, family history of psychiatric illness and primary diagnosis. Each patient underwent thorough bed-side clinical neurological assessment by a neurologist of this Medical College whenever needed. The cases were diagnosed by two faculty psychiatrists using DSM-5 criteria for catatonia [6]. They were also evaluated on clinical profile parameters like duration of stay in hospital and family history of psychiatric illness.

### Bush Francis Catatonia Rating Scale (BFCRS)

All 66 patients were evaluated by the 23-item BFCRS [29] at admission and daily thereafter. In those patients who did not respond to lorazepam and received MECT, BFCRS scorings were not done on the day of receiving ECT. The BFCRS was developed in 1996 to be used globally with excellent validity, reliability and ease to administer. The inter-rated reliability was 0.93 in a study using 23-item scale [29]. A systematic review of all available catatonia rating scales found BFCRS to be preferred for routine use, because of its validity and reliability, and its ease of administration [30]. Validity, reliability and inter-rater reliability were assessed to be high while translating to Portuguese language in the Brazilian version of the scale [31], although concurrent validity was often found to fluctuate due to the course of catatonia and owing to criteria terminologies [30]. The scale comes with two variants- one longer version with 23 items aiming for assessing severity, and one shorter screening version (Bush Francis Catatonia Screening Instrument) with 14 items [29]. In the current study, the longer version was used. For severity, items 1-23 were rated using a scale of 0-3. The total BFCRS score was the sum of responses of all 23 items. The minimum and the maximum scores are 0 and 69 with higher scores indicating a worse outcome [29].

After the provisional diagnosis, admission and detailed inpatient evaluation, the patients with catatonia were given oral or parenteral lorazepam at a dose of 4-16 mg/day for 1-2 weeks keeping with the treatment protocol as mentioned in prior studies [3-5,11,17,24,28]. As there is no consensus regarding the duration of benzodiazepine treatment in catatonia, so, patients who responded slowly were treated till complete resolution of catatonia (BFCRS scores zero) as per prior studies [32-36]. Benzodiazepine was continued for relatively longer duration in the patients who showed initial partial response or those who did not give consent for the MECT due to apprehension or lack of awareness [34]. The response assessment was done by daily administration of BFCRS. Decrease in the score (>50%) was considered as response along with the ability to move, accept feeds,

speak and communicate without any difficulty [9,22,23]. Adequate trial of lorazepam was defined in this study as having received 4-16 mg per day for at least 3-7 days [36,37]. Patients who showed poor response (<25% change in BFCRS scores)/partial response (>25 but <50% decrease in BFCRS scores) [9,37] to an adequate trial of lorazepam crossed-over and received MECT [2,38-40] thrice a week (on alternate days) unless there was a contradiction for the same like evidences of raised intracranial pressure, recent myocardial infarction or stroke etc., as per standard protocol [3,11] and were considered as Group II (Lorazepam non responder group or MECT Group). These groups were made after an adequate lorazepam trial to all 66 patients.

Group I (N=54)- Patients who responded to lorazepam and partial responders who did not consent for MECT.

Group II (N=12)- Included patients with poor response to lorazepam and partial responders who consented for MECT.

No concomitant psychotropic medications were given while patients were on lorazepam or MECT. When the BFCRS score came down to zero, lorazepam/MECT was stopped and the patients were evaluated for lifetime psychiatric illnesses as per DSM-5 [6]. After diagnosis, they were treated with antipsychotics, antidepressants and/or mood stabilisers as per the existing guidelines for different psychiatric disorders [41-43]. The duration of stay in hospital (in days) was calculated from the day of admission to day of discharge.

## STATISTICAL ANALYSIS

Univariate analyses were done by using mean and standard deviation for continuous variables and frequency and percentages for the discrete variables. Comparisons for discrete variables were carried out using the Chi-square tests and Fischer's-Exact test (wherever a cell had less than five subjects) and Student's t-test was used for continuous variables. Pearson's correlation and Spearman's rho were applied to find the bivariate correlation coefficients between two continuous variables and between two discrete variables respectively. Logistic and linear regression were then conducted using the variables that were significant at p-value <0.05 in the Univariate comparisons to find the predictive factors of treatment responsiveness. A p-value <0.05 was considered as significant. The data evaluation was done applying the Statistical Package for the Social Sciences (SPSS version 16.0 Chicago, IL).

## RESULTS

As mentioned in methodology out of the total 66 patients, 54 (81.82%) were in Group I (lorazepam responder Group) and 12 (18.18%) were in the Group II (lorazepam Non responder group or MECT Group).

[Table/Fig-1] showed that Group I had 54 of the 66 patients (81.82%) who showed good response to lorazepam. Only the remaining 12 of 66 patients (18.18%) were poor responders to lorazepam. When MECT was given they responded and showed significant improvement. The study subjects (n=66) had an age range of 15-48 years at the time of intake for the study which was comparable between the two groups. There were no differences in the socio-demographic profile like gender, marital status, educational status, occupational status, ethnicity, locality, family type and Socio-Economic Status (SES) except in religion where the lorazepam responders (Group I) had more muslims/non hindu patients (3.94, p-value=0.042). No one of the slow responders in this subgroup gave consent for ECT.

[Table/Fig-2] showed that the two groups had comparable duration of stay in hospital. There were a total of 37 patients in the test groups having a diagnosis of Schizophrenia or Schizophrenia spectrum disorders {Group I: 28 (51.85%) and Group II had 9 (75%)} and thus, contributed to the major group presenting with catatonia. The most striking finding was a significant difference between the two groups on the criteria of positive family history of psychiatric illness where the non responders group (MECT Group) had about 58.33% patients with positive family history as compared to only 14.81% positive family history in the lorazepam responder group (p-value=0.001).

[Table/Fig-3] showed that total BFCRS scores as obtained on the day of admission were higher (27.08±5.82) in the group II (ECT Group) as

| Variables | Group I n (%) | Group II n (%) | Statistical test of significance | |
|---|---|---|---|---|
| | | | $\chi^2$/Student's t-test, df=1 | p-value |
| Age (years, Mean±SD) Range (15-48 years) | 25.25±7.03 | 23.25±4.30 | 0.943 (df=64) | 0.347 |
| **Sex** | | | | |
| Male | 35 (64.81) | 8 (66.67) | 0.015 | 0.903 |
| Female | 19 (35.19) | 4 (33.33) | | |
| **Marital status** | | | | |
| Currently single | 9 (16.67) | 3 (25) | 0.458 | 0.679 |
| Married | 45 (83.33) | 9 (75) | | |
| **Education** | | | | |
| Less than metric | 7 (12.97) | 2 (16.67) | 0.114 | 0.663 |
| More than metric | 47 (87.03) | 10 (83.33) | | |
| **Occupation of patient** | | | | |
| Housewife/Student/ Unemployed | 21 (38.88) | 4 (33.33) | 3.221 (df=2) | 0.200 |
| Skilled worker | 29 (53.70) | 6 (50) | | |
| Professional | 04 (7.42) | 2 (16.67) | | |
| **Socioeconomic class** | | | | |
| Upper/Middle | 37 (68.52) | 10 (83.3) | 1.051 | 0.305 |
| Middle lower/Lower | 17 (31.48) | 2(16.67) | | |
| **Religion** | | | | |
| Hindu | 40 (74.07) | 12 (100) | 3.94 (df=1) (Fischer's-Exact Test) | 0.042* |
| Islam/Others | 14 (25.93) | 0 | | |
| **Family** | | | | |
| Nuclear | 37 (68.51) | 7 (58.33) | 0.458 | 0.515 |
| Non nuclear | 17 (31.49) | 5 (41.67) | | |
| **Locality** | | | | |
| Urban | 17 (31.48) | 3 (25) | 0.195 | 0.659 |
| Rural | 37 (68.52) | 9 (75) | | |
| **Ethnicity** | | | | |
| Bengali | 44 (81.48) | 10 (83.34) | 0.023 | 0.880 |
| Nepali/Others | 10 (18.52) | 2 (16.66) | | |

**[Table/Fig-1]:** Comparison of socio-demographic profile of Group I (N=54) and Group II (N=12).
* p-value <0.05 was considered as statistically significant

| Variables | Group I n (%) | Group II n (%) | Statistical test of significance | |
|---|---|---|---|---|
| | | | $\chi^2$/Student's t-test value (df) | p-value |
| Duration of stay at hospital (days, Mean±SD) | 17.44±7.41 | 17.41±8.91 | 2.496 (df=64) | 0.991 |
| **Family history of psychiatric illness** | | | | |
| Positive | 8 (14.81) | 7 (58.33) | 10.588 (df=1) | 0.001** |
| Negative | 46 (85.19) | 5 (41.67) | | |
| **Primary diagnosis** | | | | |
| Bipolar disorder | 15 (27.78) | 1 (8.33) | 3.159 (df=3) | 0.368 |
| Unipolar depression | 3 (5.55) | 0 | | |
| Schizophrenia spectrum | 28 (51.85) | 9 (75) | | |
| Dissociative/Others | 8 (14.82) | 2 (16.67) | | |

**[Table/Fig-2]:** Comparison of clinical profile of Group I (n=54) and Group II (n=12).
**p-value <0.001 was considered as statistically highly significant

compared to the lorazepam responders group (19.09±5.26) (Group I). Higher scores on subscales of immobility, mutism, staring, grimacing, rigidity, negativism, mitgahen and autonomic abnormality were seen in the non responder group (Group II) as compared to Group I.

| Variables | Group I Mean±SD | Group II Mean±SD | Statistical test of significance: Student t-test (F-value, df=64, p-value) |
|---|---|---|---|
| Total BFCRS score (at admission) | 19.09±5.26 | 27.08±5.82 | 0.194, Group II>Group I, p-value <0.001*** |
| **Individual 23-item BFCRS subscale scores** | | | |
| Immobility | 0.31±0.69 | 2.50±0.90 | 0.982, Group II>Group I, p-value <0.001*** |
| Mutism | 0.88±1.04 | 2.83±0.57 | 24.847, Group II>Group I, p-value <0.001*** |
| Staring | 1.24±0.93 | 2.66±0.49 | 10.965, Group II>Group I) p-value <0.001*** |
| Posturing | 1.38±0.94 | 1.91±1.08 | 0.029, 0.092 |
| Grimacing | 0.42±0.74 | 1.25±0.75 | 0.006, Group II>Group I, p-value=0.001** |
| Echopraxia | 0.38±0.73 | 0.08±0.28 | 11.319, 0.165 |
| Stereotypy | 0.79±0.91 | 0.16±0.38 | 34.935, Group I>Group II, p-value=0.024* |
| Mannerism | 0.44±0.71 | 0.16±0.38 | 8.574, 0.201 |
| Verbigeration | 0.62±0.89 | 0.50±0.90 | 0.310, 0.653 |
| Rigidity | 2.48±0.50 | 3.00±0.00 | 8.471, Group II>Group I, p-value=0.001** |
| Negativism | 0.48±0.90 | 1.66±1.07 | 0.346, Group II>Group I, p-value <0.001*** |
| Waxy flexibility | 2.83±0.69 | 0.75±1.35 | 16.360, Group I>Group II, p-value <0.001*** |
| Withdrawal | 0.68±0.96 | 2.08±0.99 | 0.460, Group II>Group I, p-value <0.001*** |
| Excitement | 0.50±0.84 | 0 | 35.117, Group I>Group II, p-value=0.045 |
| Impulsivity | 0.22±0.53 | 0 | 10.875, 0.160 |
| Automatic obedience | 0.64±0.85 | 0.83±1.02 | 3.755, 0.514 |
| Mitgahen | 0.31±0.84 | 2.08±1.31 | 6.540, Group II>Group I, p-value <0.001*** |
| Gegenhalten | 1.96±1.16 | 1.83±1.19 | 0.170, 0.730 |
| Ambitendency | 1.05±1.15 | 0.50±0.90 | 3.158, 0.124 |
| Grasp reflex | 0.53±1.00 | 1.00±1.47 | 8.292, 0.192 |
| Perseveration | 0.44±0.88 | 0.50±0.90 | 0.187, 0.845 |
| Combativeness | 0.12±0.33 | 0 | 9.571, 0.193 |
| Autonomic abnormality | 0.31±0.66 | 0.91±0.90 | 3.88, Group II>Group I, p-value=0.010* |

**[Table/Fig-3]:** Comparison of BFCRS Scores of Group I (Lorazepam Responder Group, N=54) and Group II (Lorazepam Non responders/MECT Group, N=12).
*p-value <0.05 was statistically significant; **p-value <0.01 was statistically highly significant; ***p<0.001 was statistically extremely significant

[Table/Fig-4] showed that the severity of catatonia as measured by Total BFCRS score had significant correlation in people of Nepalese and non Bengali ethnicity (Spearman's rho=0.255; p-value=0.039). Hindus had higher severity of catatonia as compared to Non Hindus (Spearman's rho value=0.307; p-value=0.012). Positive family history of psychiatric illness had highly significant correlation with catatonic severity (Spearman's rho=0.512; p-value <0.001). Good response to lorazepam correlated with those who did not have a family history of psychiatric illness (Spearman's rho=0.401; p-value=0.001).

When duration of stay in hospital was correlated with BFCRS scores there was significant positive correlation found (Spearman's correlational coefficient=0.344; p-value=0.005). It was also found that younger age of presentation had significant correlation with higher BFCRS scores (Spearman's correlational coefficient=0.471; p-value <0.001). [Table/Fig-5a] showed the bivariate correlations between subscale variables of BFCRS that were found to be significant in [Table/Fig-3] with lorazepam non response/ECT Group. The higher total BFCRS scores correlated significantly with lorazepam Non response (ECT group) (rho=0.469; p-value <0.001). The subscale correlational analysis showed that patients who scored high on immobility ((rho=0.705; p<0.001), mutism (rho=0.624; p-value <0.001), staring (rho=0.563; p<0.001), grimacing (rho=0.424; p-value <0.001), rigidity (rho=0.405; p-value=0.001), negativism (rho=0.437; p<0.001), withdrawal (rho=0.482; p-value <0.001) and autonomic abnormality (rho=0.322; p-value=0.008) correlated significantly with non response to lorazepam and good response to ECT.

[Table/Fig-5b] showed the bivariate correlations between subscale variables of BFCRS that were found to be significant in [Table/Fig-3] with lorazepam responder group. It showed that scores on subscales of stereotypy, waxy flexibility and autonomic abnormality had significant negative correlation with group as a variable. This meant that higher the scores on these three subscales, better was the response to lorazepam.

[Table/Fig-6] showed the coefficients of linear regression between the significant (p-value <0.05) subscales of BFCRS (independent variables) found in the univariate analyses and lorazepam responders/non responders (dependent variable). Immobility (OR=3.598; 95% CI=0.069 to 0.244, p=0.001) and grimacing (OR=3.462; 95% CI=0.066 to 0.249, p=0.001) predicted non response to lorazepam and good response to ECT. Presence of waxy flexibility predicted good response to lorazepam (OR=4.824 CI=0.234 to -0.097, p-value <0.001).

The model summary in [Table/Fig-7a] showed the strength of the relationship between the model and the dependent variable (lorazepam responder group/lorazepam non responder group). R, the multiple correlation coefficients, is the linear correlation between the observed and model-predicted values of the dependent variable. R square ($R^2$) statistic indicated the percentage of the variance in the dependent variable that the independent variables predict collectively. Its large value indicated a strong relationship. As 12 predictors were added to the model, each predictor would explain some of the variance in

| Variable | | Gender | Religion | Ethnicity | Locality | SES | Occupation | Education | Family history | Primary diagnosis |
|---|---|---|---|---|---|---|---|---|---|---|
| BFCRS | Rho | -0.214 | -0.307 | 0.255 | 0.235 | -0.189 | 0.120 | 0.073 | -0.512 | 0.154 |
| | p-value | 0.085 | 0.012* | 0.039* | 0.058 | 0.129 | 0.336 | 0.558 | <0.001*** | 0.217 |
| Lorazepam response | Rho | -0.015 | -0.245 | 0.019 | 0.054 | -0.126 | -0.118 | 0.042 | -0.401 | 0.164 |
| | p-value | 0.905 | 0.048* | 0.883 | 0.664 | 0.313 | 0.345 | 0.740 | 0.001** | 0.188 |

**[Table/Fig-4]:** Bivariate correlation of total BFCRS scores with socio-demographic and clinical profile variables (Spearman's rho/p-value)
*p-value <0.05 was statistically significant; **p-value <0.01 was statistically highly significant; ***p<0.001 was statistically extremely significant

| Variable | | Total BFCRS score | Immobility | Mutism | Staring | Grimacing | Rigidity | Negativism | Withdrawal | Mitgahen | Autonomic abnormality |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Group II | Rho | 0.469 | 0.705 | 0.624 | 0.563 | 0.424 | 0.405 | 0.437 | 0.482 | 0.560 | 0.322 |
| | p-value | <0.001*** | <0.001*** | <0.001*** | <0.001*** | <0.001*** | 0.001** | <0.001*** | <0.001*** | <0.001*** | 0.008** |

**[Table/Fig-5a]:** Bivariate correlation coefficients of lorazepam non response (Group II) with total and various subscale scores of BFCRS (Spearman's rho/p-value)
*p-value<0.05 was statistically significant; ** p-value<0.01 was statistically highly significant; ***p<0.001 was statistically extremely significant

| Variable | | Stereotypy | Waxy flexibility | Excitement |
|---|---|---|---|---|
| Group I | Rho | -0.268 | -0.694 | -0.254 |
| | p-value | 0.030* | <0.001*** | 0.039* |

**[Table/Fig-5b]:** Correlation of lorazepam Response (Group I) with various subscale scores of BFCRS (Spearman's rho/p-value).
*p-value <0.05 was statistically significant; ** p-value <0.01 was statistically highly significant; ***p<0.001 was statistically extremely significant

$R^2$=0.173; Nagelkerke $R^2$=0.283. Catatonia severity (BFCRS scores) also predicted non response to lorazepam (OR=8.183, CI=0.013 to 0.443, p-value <0.01), Cox and Snell $R^2$=0.282; Nagelkerke $R^2$=0.461. Family history of psychiatric illness was the only factor which predicted the severity of catatonia when BFCRS scores was taken as a dependent variable (OR=16.257, CI=4.467 to 75.797), Cox and Snell $R^2$=0.249; Nagelkerke $R^2$=0.379.

| Model | Unstandardised coefficients | | Standardised coefficients | t-value | Significance | 95% Confidence interval | |
|---|---|---|---|---|---|---|---|
| | Beta | Standard error | Beta | | | Lower bound | Upper bound |
| 1 (Constant) | 1.217 | 0.282 | - | 4.321 | p<0.001*** | 0.652 | 1.782 |
| Immobility | 0.156 | 0.043 | 0.451 | 3.598 | 0.001** | 0.069 | 0.244 |
| Staring | -0.011 | 0.042 | -0.029 | -0.263 | 0.794 | -0.095 | 0.073 |
| Mutism | -0.025 | 0.048 | -0.078 | -0.510 | 0.612 | -0.122 | 0.072 |
| Grimacing | 0.158 | 0.046 | 0.326 | 3.462 | 0.001** | 0.066 | 0.249 |
| Stereotypy | 0.004 | 0.044 | 0.009 | 0.095 | 0.925 | -0.084 | 0.092 |
| Rigidity | 0.091 | 0.087 | 0.116 | 1.046 | 0.300 | -0.083 | 0.262 |
| Negativism | 0.013 | 0.047 | 0.035 | 0.282 | 0.779 | -0.081 | 0.107 |
| Waxy flexibility | -0.166 | 0.034 | -0.497 | -4.824 | p<0.001*** | -0.234 | -0.097 |
| Withdrawal | -0.007 | 0.037 | -0.021 | -0.193 | 0.848 | -0.082 | 0.068 |
| Mitgahen | -0.036 | 0.043 | -0.107 | -0.831 | 0.410 | -0.122 | 0.051 |
| Autonomic abnormality | 0.045 | 0.041 | 0.087 | 1.111 | 0.272 | -0.037 | 0.127 |
| Excitement | -0.048 | 0.041 | -0.097 | -1.169 | 0.248 | -0.130 | 0.034 |

**[Table/Fig-6]:** Coefficients of linear regression analysis between significant subscales of BFCRS as independent variable and lorazepam Responders/lorazepam non responders as dependent variable.
*p-value <0.05 was statistically significant; **p-value <0.01 was statistically highly significant; ***p<0.001 was statistically extremely significant

the dependent variable and that the variance was not simply due to chance. The adjusted $R^2$ attempted to yield a more honest value to estimate the $R^2$ for the study subject. The higher $R^2$ (0.791) and adjusted $R^2$ (0.743) suggested that 79% of the data fits the regression model and that the independent variables adequately explains the variance in the dependent variable.

| Model | R | $R^2$ | Adjusted $R^2$ | Standard error of the estimation |
|---|---|---|---|---|
| 1 (Constant) | 0.889[a] | 0.791 | 0.743 | 0.19693 |

**[Table/Fig-7a]:** Model summary[b] showing strength of relation between model and the dependent variables.
[a]Predictors: (Constant), autonomic abnormality, excitement, grimacing, waxy flexibility, rigidity, stereotypy, negativism, staring, withdrawal, immobility, mitgahen, mutism; [b]Dependent variable: Lorazepam Response/Non Response (ECT) group

The Analysis of Variance (ANOVA) [Table/Fig-7b] showed that the F-value (12, 53) was equal to 16.680 with a p-value of <0.001 which states that probability that the results obtained were due to random chance are very minimal. Therefore, the group of 12 independent variables showed statistically significant relationship with the dependent variable and that the group of independent variables reliably predicted the dependent variable.

| Model | Sum of squares | Degrees of freedom (df) | Mean square | F-value | Sig. |
|---|---|---|---|---|---|
| Regression | 7.763 | 12 | 0.647 | 16.680 | 0.000[a] p-value <0.001 |
| Residual | 2.0055 | 53 | 0.039 | | |
| Total | 9.818 | 65 | | | |

**[Table/Fig-7b]:** Analysis of Variance (ANOVA)[b] table for linear regression analysis.
[a]Predictors: (Constant), autonomic abnormality, excitement, grimacing, waxy flexibility, rigidity, stereotypy, negativism, staring, withdrawal, immobility, mitgahen, mutism
[b]Dependent variable: Lorazepam Response/Non Response (ECT) Group
p<0.001 was statistically extremely significant

Coefficients of logistic regression analysis between significant socio-demographic and clinical variables as independent variables and lorazepam responders/lorazepam non responders as dependent variable showed that family history of psychiatric illness predicted non response to lorazepam and good response to MECT (OR=5.496, CI=1.402 to 22.364, p-value <0.01), Cox and Snell

## DISCUSSION

This cross-sectional analytical study is one of the few studies in India to find the socio-demographic and clinical correlates determining the treatment response in patients with catatonia. Previous Indian studies on this topic had inconclusive evidence, having less data on co-medications [3], inadequate sample size [5], selection bias owing to exclusion of less severe outpatient catatonia cases and absence of follow-up data [3,4,21,22]. This study tried to overcome these shortcomings to some extent.

A high response rate (81.8%) to lorazepam was seen in this study. The retrospective studies from India found response rates ranging from 17.6% to 50% [3,4,21,28]. One prospective study from India showed high remission rates of 75% and partial remission rates of 18% [9] which was similar to this study. Prospective cohort studies from other Asian countries [18-20] and Western countries [15,35,40,44] showed remission rates ranging from 66% to 100%. The poor response rates to lorazepam in previous retrospective studies [3,4,21,22] could be due to the fact that selection bias led to inclusion of cases with higher severity whereas this study design included all consecutive patients presenting to the OPD with a DSM-5 diagnosis of catatonia irrespective of their severity leading to lesser chance of selection bias. A cross-sectional [5] and three prospective studies [9,45,46] available from India and those from the west [15,17,35,47-49] suggest that lorazepam is useful in management of catatonia. In a systematic review of seven retrospective chart reviews it was found that 53-93% of lorazepam non responders patients responded to ECT [35]. A systematic review of 20 years of research in catatonia suggests that catatonia due to general medical conditions and catatonia due to psychiatric illness can be treated similarly [49] and another one showed that the response rates in ECT ranged from 59-100% [24]. Moreover, due to lack of definite treatment protocols different researchers have used different dosing protocol of lorazepam for management of catatonia [3,46,50,51]. Another reason of greater lorazepam response in this study could be that some patients where ECT consent could not be obtained were treated with lorazepam for a longer time and response was achieved later. Diverse genetic makeup due to variation in the ethnicity of the patient population pattern in this region might have

led to different response in the present study as well, although it requires a bigger study to conclude.

The average age of 25 years (range 15-48) in the study subjects suggested that catatonia was most prevalent in young adults who are in their mid-twenties that was reflected in earlier studies [5,52]. Both lorazepam and MECT group showed almost similar socio-demographic and clinical profile. However, the most striking finding was that the MECT group had almost 60% patients with positive family history of psychiatric illness as compared to 15% in the lorazepam group. This finding conformed to the existing notion of 11-19% of genetic loading in catatonia as per existing Indian [4,5] and Western studies [36,49]. That the genetic loading can be a factor in non response to lorazepam was not cited much barring a study showing high degree of heritability (59%) in periodic catatonia [38]. This finding needs to be replicated in larger prospective studies.

As per background diagnoses were concerned, it was found that most of the major psychiatric disorders conforming to existing literature illustrating catatonia as a disorder of diverse causation. However, any specific psychiatric diagnosis did not show poorer response to lorazepam which suggests that lorazepam was effective irrespective of the underlying psychiatric diagnosis. This finding supports the previous Indian studies [3-5,28,46,48]. The days of hospital stay was more or less the same across both the groups with mean duration being 17 days. Lorazepam was administered for extended duration to those patients who did not give consent for MECT and did not show signs of deterioration on prolonged lorazepam either. This strategy of using lorazepam for longer periods or till remission as was found in earlier studies as well [33,34] was followed successfully here.

Total BFCRS scores were significantly higher in the Group II (MECT Group) as compared to the lorazepam responders group (Group I). This was seen in bivariate correlational analysis as well. This suggested that those patients who score high on BFCRS responded less to lorazepam rendering MECT as treatment of choice in such patients. That MECT could be used in more severe catatonia at earliest was found in previous study as well where life threatening catatonia was treated with MECT upfront [25].

The significant correlation of BFCRS with ethnicity on bivariate analysis suggested that people of Nepalese and other tribal ethnicities had higher scores on BFCRS viz., higher catatonic severity. Ethnicity might have a role in catatonic severity as shown in a catatonia prevalence study where South Asian ethnicity had predominance [53]. However, accessibility to healthcare facilities and lack of awareness of the disorders among those living in hilly and inaccessible areas also might have some contribution [54]. On bivariate analysis, the family history of psychiatric illness had very significant correlation to catatonic severity suggesting that people with higher genetic loading tended to have higher severity of catatonia and therefore also tended to respond less to lorazepam and more to MECT. This resulted in longer duration of stay in hospital for those with genetic loading [55]. The subscale correlational analysis showed that patients who scored high on immobility, autism, staring, grimacing, rigidity, negativism, withdrawal and autonomic abnormality correlated significantly with good response to MECT and non response to lorazepam. On the other hand high scores on stereotypy, waxy flexibility and excitement correlated significantly with good response to lorazepam. Immobility and grimacing had predictability towards lorazepam non response and waxy flexibility had predictability towards lorazepam response in the linear regression analysis as well. There were differences in finding regarding the correlation of these signs and symptoms among prior studies as waxy flexibility and grasp reflex predicted lorazepam response in one study [21] whereas mutism, immobility and withdrawal predicted the same in another [35]. In another study, predicting clinical responsiveness to MECT in management of catatonic patients it was found that quicker response was associated with gegenhalten and waxy flexibility, whereas patients having echo phenomena predicted slow response [45]. Given such differences, it could be asserted that the response to catatonia appeared to be associated with severity of catatonia and the presence of certain variable catatonic signs [56]. On regression analysis using the variables that showed significance with p-value <0.05 during the univariate analysis, it was found that ethnicity did not predict the response or non response to lorazepam. However, presence of family history of psychiatric illness and BFCRS total score were the factors which determined which patient would respond to lorazepam and who would be non responders. A previous study also found that duration of catatonic symptoms as well as the severity also affected the response rate to catatonia [46]. Moreover, when BFCRS scores were kept as dependent variable then also the presence of family history of psychiatric illness predicted which patients would score high on BFCRS.

### Limitation(s)

It was a cross-sectional study having a shorter duration of study and therefore, had a smaller sample size. A prospective study would have been better. The final diagnosis was made at the time of discharge after resolution of catatonic symptoms, therefore, it could not be ascertained whether their presentation changed over time and whether, there was recurrence of catatonic symptoms.

## CONCLUSION(S)

The observations in the present study concluded favorably towards the lorazepam administration in catatonia. It suggested first line application of modified electroconvulsive therapy in more severe catatonic manifestations with immobility and grimacing as predicting factors. Apart from that lorazepam produced most significant result irrespective of background psychiatric diagnoses. The study identified that higher score of BFCRS, higher genetic loading, presence of catatonic signs of mutism, rigidity, immobility, withdrawal and negativism correlated with poor response to lorazepam and good response to MECT. Simultaneously higher scores of waxy flexibility, stereotypy and excitement correlated with good response to lorazepam. These could help us to predict treatment response and urgent referral to higher centers from rural healthcare centres. This could provide insight into the prediction and planning of the appropriate treatment protocols in this psychiatric emergency.

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