# Influence of sociodemographic factors, diagnostic variations, and phenomenology toward the treatment response in adolescent catatonia in a tertiary care centre in Eastern India



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Submission: 08-12-2022 Revision: 30-01-2023 Publication: 01-03-2023

# ABSTRACT

Background: Catatonia remains an area of lesser research especially in the adolescent age group. It has subtle differences in the presentation and background diagnoses as compared to adult catatonia. There is paucity of literatures regarding the role of different sociodemographic and clinical factors attributing to different treatment response. Aims and Objectives: The aim of the study was to assess the association of socio-demographic features, background psychiatric diagnoses, and different catatonic symptoms with treatment outcome of adolescent catatonia. Materials and Methods: The study considered 10-19 years old patients admitted in the in-patient department as per diagnostic and statistical manual diagnosis. They were assessed by Pediatric Catatonia Rating Scale (PCRS) and treated with lorazepam initially with varying dosage and duration. Modified electroconvulsive therapy was administered in resistance. Factors of these two groups were statistically analyzed to assess predictability towards outcome. Results: There were 47 participants with mean age of  $16.66 \pm 1.21$  years of whom 29.8% showed positive family history of different psychiatric illnesses. Most of them came with schizophrenia and related disorders (53.2%), though mood disorders, conversion and organic brain diseases were also there. Among them 30 (63.8%) patients responded to lorazepam treatment. Positive family history, urban background, and catatonic severity in terms of higher PCRS score showed predictability to lorazepam non-response. Clinical features such as stupor, staring, negativism, withdrawal, mutism, urinary incontinence and refusal to eat or drink were associated with non-response, whereas waxy flexibility, stereotypy, verbigeration, and mannerism were seen in the response group. Conclusion: There is need to identify warning signs such as family history, greater symptom load and certain clinical features that can lead to resistance to the treatment with benzodiazepines based on this study. It can necessitate further large-scale study to alleviate disease burden to this young and productive population.

#### Access this article online

#### Website:

http://nepjol.info/index.php/AJMS **DOI:** 10.3126/ajms.v14i3.50024

E-ISSN: 2091-0576 P-ISSN: 2467-9100

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Key words: Adolescence; Catatonia; Predictors; Phenomenology; Treatment response

## INTRODUCTION

Over more than one and half centuries since its inception with the publication of the monograph "*DieKatatonie*" by Kahlbaum<sup>1</sup> in 1874, catatonia remains an enigma in terms

of phenomenology, etiopathogenesis, and treatment. Initially thought as a manifestation of organic diseases,<sup>2</sup> it was later considered as a subset of schizophrenia<sup>3</sup> or atypical psychosis.<sup>4</sup> At present, it was allotted a separate diagnostic altar as per the diagnostic and Statistical Manual (DSM-5)

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with syndromic presentation on the motor (posturing, rigidity etc.), affective (withdrawal), behavioral (mutism, negativism etc.), and regressive (enuresis) domains.<sup>5</sup>

Despite meager studies, catatonia among the children and adolescents remains in the clinical knowledge since the very beginning. Even the first clinical description from Kahlbaum showed many of the patients having onset in childhood.<sup>1</sup> Later childhood catatonia was distinguished from other disorders, mainly Propfschizophrenie as coined by Kraepelin<sup>3</sup> and autistic spectrum disorders, following the works of Leonhard who famously coined the term "infant catatonia."

Catatonia is conceptualized as a dominance of excitatory glutamate system over the inhibitory GAB Aergic one in the orbitofrontal and dorsolateral prefrontal cortex in the "Top-down hypothesis" along with dysfunction of motor sequence arbitration in the subcortical nuclei, namely, the basal ganglia.<sup>7,8</sup> Besides, hyperactive prefrontal<sup>9</sup> and malfunctioning right posterior parietal cortex<sup>8</sup> have also seen to diversify its manifestations. With such vast area involvement and considering the developmental landmark attained by the individual and catatonic features become more diverse in the child and adolescent age group.

More symptoms were added to the existing diagnostic criteria of catatonia as per the then DSM-IV by Wing and Shah, namely, reversal of day and night activities, Parkinsonian features and increase in repetitive and ritualistic behavior. <sup>10</sup> Initially, adult scales such as the Bush Francis Catatonia Rating Scale <sup>11</sup> or the Modified Rogers Scale for Catatonia <sup>12</sup> were used to describe the cases. Later Cohen in 2006 modified the Bush Francis Catatonia Rating Scale to form the Pediatric Catatonia Rating Scale (PCRS) which, along with 17 BFCRS items, include six more symptoms, namely, refusal to eat and drink, social withdrawal, incontinence, automatic compulsive movements, schizophasia or word salad, and acrocyanosis. <sup>13</sup>

Children and adolescents show certain changes in the presentation of catatonia as well. Although the actual prevalence cannot be measured due to paucity of the literature, 14 it is seen to affect pubertal age more than prepubertal age 10,15 and boys tend to be more affected with 2:1 gender ratio involvement. 16 Having to some extent more acute onset, adolescent catatonia offers almost same range of complications as that of the adults including risks of pneumonia, decubitus ulcer, thrombosis, malignant catatonia, and chance of mortality. 14

The current convention encourages the search of background diagnoses once the catatonic symptoms remit. As a contrast to the adult population, schizophrenia spectrum disorders dominate the psychiatric etiologies of

child and adolescent catatonia as seen in multiple studies with mood disorder being the second contributor. 13,14,16,17 Neurodevelopmental disorders such as autistic spectrum disorder and intellectual disability are also seen to be associated having many overlapping symptoms complicating the situation. Substance use, toxic drugs, anxiety disorders like dissociative, and conversion disorders also contribute to its causation with varying proportion. 14,16 It is also common to associate different organic diseases such as metabolic and genetic ones, infection, autoimmune diseases, and epilepsy with the catatonic presentation. 14

Treatment approach of childhood and adolescent catatonia is almost in the similar lines of that of the adults. GABAergic drugs like lorazepam<sup>19</sup> in varying dosage and duration, Zolpidem,<sup>20</sup> or glutamate antagonist like memantine<sup>21</sup> are useful pharmaceutical option. Electroconvulsive therapy (ECT) remains the choice in benzodiazepine resistance or in need of urgent response in severe life-threatening situations.<sup>22</sup>

As catatonia in childhood and adolescence is often detrimental to the immediate health of the affected with possible long-term adversities, little existing literature especially from India is considered a roadblock in identifying early manifestations and different treatment response depending on the diagnostic variation and phenomenology. Most of the Indian studies in this context are either case reports<sup>19,23</sup> or retrospective chart reviews.<sup>24,25</sup> One cross-sectional study assessed childhood and adolescent catatonia based on their background etiologies and clinical features, but it had its limitation in having only nine cases of adolescent catatonia.<sup>26</sup> One retrospective chart review, albeit being insightful about the phenomenology and background diagnoses, was less informative about the factors that could be associated with different treatment outcomes.<sup>24</sup> Based on that we have studied the catatonia cases of child and adolescent age group to assess difference in treatment response.

## Aims and objectives

The objectives of the study are as follows:

- 1. To assess the importance of different socio-demographic factors and background diagnostic variation over the treatment outcome of adolescent catatonia
- 2. To assess whether different catatonic symptoms are associated with better response to different treatment modalities in such cases.

## **MATERIALS AND METHODS**

Established in 1968 in the northern part of West Bengal, the North Bengal Medical College, situated in the gateway of North-East India, is an eminent tertiary care center with multidisciplinary postgraduate education consisting of inpatient and outpatient facilities. The Psychiatry department caters services to around 300 outdoor patients daily and approximately 40 indoor patients.

The concerned study was descriptive in design with purposive sampling. After getting the Institution Ethical Clearance, informed consents from the eligible admitted patients or their family members were taken. We included patients who had developed onset of the illness before completion of 18 years. <sup>14</sup> Patients with catatonia as diagnosed by two faculty psychiatrists using DSM-5 were included in the study. The patients were evaluated as per the semi-structured data sheet for sociodemographic details. The eligible patients were evaluated by the PCRS<sup>13</sup> consecutively by the psychiatrists for the stipulated 2 years (January 2020 to December 2021). Each patient was evaluated by the rating scale on every alternate day to assess the response.

After the provisional diagnosis, admission, and detailed inpatient evaluation, the patients with catatonia were given a trial of 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.3-5,21,27 Patients who responded slowly were treated for longer duration. Due to the scarcity of consensus regarding duration of lorazepam use in catatonia, difficulty in conducting modified ECT (MECT) maintaining the COVID protocol, and non-consent from the guardians of the patients for the MECT, lorazepam was administered for a longer duration in certain cases. 28-31 Patients who did not respond to lorazepam trial crossed-over and received MECT as per the standard treatment protocoland were considered as Lorazepam non-responder group.<sup>3,27</sup> After completion of taking prior consent from the Institution Ethics Committee and the guardians of the patients and evaluating for MECT, they were undergone MECT in compliance with the Standard Operating Procedure of COVID-19 pandemic thrice a week (on alternate days) unless there was a contradiction for the same. PCRS was applied on the day after MECT as per the protocol and further treatment was decided accordingly. Response was considered as complete resolution of catatonic symptoms with PCRS score becoming zero and improved functionality in terms of movement, taking food, speech, and communication.<sup>32</sup> Once they recovered from catatonia, they were evaluated for lifetime psychiatric illnesses as per DSM-5 and treated with antipsychotics and/or mood stabilizers as per the existing guidelines maintained in the in-patient department.<sup>3-6</sup>

## Statistical analysis

The data obtained were collected in Microsoft Office Excel Worksheet. Descriptive analysis was carried out using mean and standard deviation with range for continuous variables. Frequency and percentages were calculated for discontinuous variables. Comparisons were carried out using the Student's t test for parametric data and Chisquare test for the non-parametric data to assess statistical significance. Binomial logistic regression analysis was done to confer the predictability of different sociodemographic and clinical variables toward treatment response. Data analysis was done using the Statistical Package for the Social Sciences (SPSS version 22.0 Chicago, IL).

# **RESULTS**

During the time period of the study, 47 patients were selected having admitted with catatonia consecutively. Among them, 31 (66%) were male and 16 (34%) female. The mean age of the population was 16.66±1.21 years. Majority were from Hindu (72.3%), rural (72.3%), lower middle or lower socioeconomic status (51.1%), and student (44.7%). Fourteen patients (29.8%) had history of psychiatric illnesses in their family. The patients were treated as per the protocol initially with varying dosage of benzodiazepine (Lorazepam in this case). It was seen that 30 patients (63.8%) responded to lorazepam and the rest 17 patients (36.2%) were considered for MECT. With treatment, when the patients started to communicate, the background diagnoses were assessed. It was found that majority of them had history of psychosis (53.2%), although mood disorder (12.8%), conversion (12.8%), substance use (12.8%), and organic causes (8.5%) were also found.

We compared the sociodemographic data among the groups who did and did not respond to lorazepam. It is worth mentioning that, barring the family history (10% vs. 64.7%, P<0.001) and urban background (16.67% vs. 47.06%, P=0.025), none of the other sociodemographic factors showed any significant difference among the groups. We used independent sample t-test for the continuous normal data and Chi-square test for the non-parametric data (Table 1). It was seen that the mean of total duration of stay in hospital (19.45 vs. 26.35, P=0.001) and total PCRS score (20.67 vs. 28.35, P<0.001) was significantly different among the two groups. Regarding diagnostic variation, psychotic disorders were the majority in the non-response group (χ² value 19.972, P=0.001).

We assessed the predictability of these factors toward treatment outcome using binomial logistic regression. On logistic regression, the model explained 75.6% (Nagelkerke R<sup>2</sup>) of the variance in non-response to lorazepam and correctly classified 63.8% of cases. Using the Wald test to assess the significance of individual

Sociodemographic features	Lorazepam response (n=30) (%)	Lorazepam non-response (n=17) (%)	t-value/χ² value	P-value
Mean age	16.60±1.07	16.76±1.44	0.447	0.657
Gender				
Male	19 (63.33)	12 (70.59)	0.254	0.614
Female	11 (36.67)	5 (29.41)		
Religion				
Hindu	21 (70)	13 (76.47)	0.227	0.634
Muslim	9 (30)	4 (23.53)		
Background				
Urban	5 (16.67)	8 (47.06)	5.009	0.025*
Rural	25 (83.33)	9 (52.94)		
Socioeconomic				
Middle	14 (46.67)	9 (52.94)	0.171	0.679
Lower	16 (53.33)	8 (47.06)		
Education				
Below matric	14 (46.67)	8 (47.06)	0.001	0.979
Above matric	16 (53.33)	9 (52.94)		
Occupation				
Student	12 (40)	9 (52.94)	7.202	0.126
Housewife	0	1 (5.88)		
Unskilled	8 (26.67)	0		
Semiskilled	3 (10)	3 (17.65)		
Unemployed	7 (23.33)	4 (23.53)		
Family history	,	,		
Present	3 (10)	11 (64.7)	15.527	P<0.001
Absent	27 (90)	6 (35.29)		
PCRS score	20.67±4.89	28.35±6.89	4.105	P<0.001
Duration of stay	19.43±4.65	26.35±6.89	5.375	0.001*
Diagnosis				
Psychosis	12 (40)	13 (76.47)	19.972	0.001*
Mood disorders	6 (20)	0		
Conversion	6 (20)	0		
Substance	6 (20)	0		
Organic	0	4 (23.53)		

\*Correlation is significant at the 0.05 level (2-tailed)

independent variables, it was found that urban background (P=0.031) and increased severity of the disease as depicted from the high PCRS score (P=0.032) was significantly associated with increased likelihood of Lorazepam resistance whereas the association in case of duration of hospital stay (P=0.219) or positive family history (P=0.067) was not statistically significant predictor.

We assessed the presence of different catatonic symptoms as per the PCRS checklist among the groups of response and resistance to lorazepam treatment, compared the means using Chi-square test (Table 2). It was seen that features such as stupor, staring, negativism, withdrawal, mutism, urinary incontinence, and refusal to eat or drink had higher mean scores in the non-response group, whereas symptoms such as waxy flexibility, stereotypy, mannerism, and verbigeration had higher score in the response group. Although, due to the inter-correlation among the symptoms, the predictability toward the treatment response could not be calculated using regression analysis.

## DISCUSSION

In this study it was seen that the adolescent population that presented with catatonia to the hospital were mostly from pubertal and post-pubertal age group. That mean age was found to be around 17 years corroborated with studies done abroad as well in India. 10,15,24 The gender difference was noted with a male female ratio around 2:1. Such gender difference was found in prior studies, 16 though it can be said that it is a small sample size and male children used to get more treatment-seeking attention from the family in certain social structure of our country.<sup>24</sup> Furthermore, it was seen that around 30% of patients have 1st or 2nd family members with history of psychiatric disorders chiefly psychotic and bipolar disorders. It is seen that catatonia has a strong genetic loading with multiple psychiatric illnesses and catatonic schizophrenia showed much more genetic susceptibility than other subtypes of schizophrenia.<sup>33,34</sup> Other sociodemographic parameters such as more samples from Hindu, rural, lower middle,

Table 2: Significant catatonic symptoms associated with treatment outcome Lorazepam response (n=30) Lorazepam non-response (n=17) χ²-value **Symptoms** P-value Stupor 29.94 < 0.001 Waxy flexibility 30 13 17.01 < 0.001 23 17 12.62 0.006 Staring Negativism 7 17 32.71 < 0.001 Stereotypy 18 2 15.24 < 0.001 Withdrawal 22 17 23.54 <0.001 13 <0.001 Mutism 16 23.44 Mannerism 18 2 10.62 0.005 16.79 Incontinence 10 11 < 0.001 Verbigeration 14 2 6.25 0.044 Refusal to eat or drink 23 16 0.009 11 52

\*Correlation is significant at the 0.05 level (2-tailed)

or lower socioeconomic background were at par with the population in the catchment area concerned.<sup>35</sup>

This study revealed higher proportion of schizophrenia and other psychotic spectrum disorders as background diagnoses in the catatonia cases. This was corroborative to prior studies done on child and adolescent catatonia where, unlike that of adult cases, psychotic spectrum disorders were associated with larger distribution. 13,14,16,17,24 Although it is often argued that over long-term observation, sometimes, the diagnosis of brief psychosis and unspecified psychosis can be changed into affective disorders.<sup>36</sup> Apart from the psychotic spectrum, affective, conversion, and substance use, and organic etiologies were also found albeit at the lower proportions. Studies based on similar age range found almost similar distribution. 13,14 One interesting finding in this study was that there was no diagnosed case of neurodevelopmental disorders associated with catatonia unlike prior studies. 13-17,24 Possible explanations can be the small sample size as well as the relative low prevalence of autistic spectrum disorders in Eastern India,<sup>37</sup> absence of all-encompassing population representation during the COVID-19 pandemic or the general lack of awareness from the family members to seek for treatment in cases with intellectual disability.<sup>38</sup> Further studies in this locality will likely elaborate this matter.

As the treatment outcome was concerned, 63.8% of the patients responded to lorazepam treatment of varying dosage and duration. Prior studies conducted among children and adolescents as well as among persons of mixed age range found a varying proportion of lorazepam response from 50% to 85%. <sup>13-17,24,25,36</sup> The varying rate of response in different studies can be attributed to delay in presentation to treatment facilities as well as the duration of untreated illness. <sup>32</sup> In this case, prolonged lorazepam treatment due to difficulty to pursue ECT protocol during pandemic could be one contributory reason as well. We have found that among different sociodemographic variables, history of psychiatric illness in the family

was significantly associated with the non-response group (P<0.001) as shown in Table 1. As shown in the previous studies, periodic catatonia has a strong genetic predisposition with identification of multiple allelic area responsible, the chance of being resistant to conventional treatment is also higher. 33,34 In this study, patients with urban background were found to be associated with lorazepam resistance (P=0.025) and also with a significant predictive value toward non-response (P=0.031). Whether this finding has some impact on the population basis that is to be tested with larger sample size in an elaborative approach. Most of the patients with lorazepam non-response showed psychotic spectrum as background diagnosis, which was in contrast to the prior Indian study where affective and psychotic background shared such outcome equally.<sup>24</sup> Further follow-up study regarding the long-term outcome of the diagnoses would likely enlighten this.

As shown in Table 1, non-response to lorazepam was also seen in association with longer hospital stay and higher catatonic severity which had significant predictive value toward non-response as well. Both these features were seen in most of the studies done in adolescent catatonia or catatonia in all age groups. <sup>13-17,24,34</sup> The finding further consolidates the notion of using benzodiazepines at the early stages of symptom onset which can decrease the disease burden which will otherwise need longer treatment.

It was found that features such as stupor, staring, negativism, withdrawal, mutism, urinary incontinence, and refusal to eat or drink were significantly correlated with Lorazepam non-response, whereas symptoms such as waxy flexibility, stereotypy, verbigeration, and mannerism were correlated to Lorazepam response (Table 2). In a prior Indian study involving catatonia of all age groups, mutism was significantly associated with non-response and waxy flexibility and grasp reflex were seen in the response group. <sup>32</sup> However, this finding is not unanimous as a study previously found just opposite findings with mutism, immobility, and withdrawal in the response group

and posturing, grimacing, and waxy flexibility in the nonresponse group.<sup>27</sup> Clearly, many factors including genetic diversity, mode of presentation, delay in treatment seeking, age distribution, and sample size in the study design may attribute to the variation rendering the need for further large scale research in this domain.

## Limitations of the study

This study had its limitation in small size of the sample population as well as to maintain a cohort over long-term to observe difference in the longitudinal course over time. During the pandemic, due to the initial logistic problems, the accessible population might not mirror the target population in proper sense. Furthermore, treatment like ECT was often delayed due to COVID-19 protocol. It shows the need of further research over long time with a large population so that the void in this treatment modality can be addressed properly.

## CONCLUSION

This study attempted to identify different factors associated with adolescent catatonia especially factors that can install warning signs of possible resistance to conventional treatment with benzodiazepines. It is seen if there is family history of psychiatric illness or the symptoms render higher severity of the disease, there is every chance of resistance. Different individual symptoms and their correlation with treatment response were also assessed in need for early identification of possible predictors so that early initiation of proper treatment can diminish the disease severity and longer duration of treatment required.

## **ACKNOWLEDGMENT**

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UM- Concept and design of the study and revision of the manuscript; PB- Statistical analysis and data interpretation and review of literature; JB- First draft of the manuscript, coordination, and result interpretation; and AKL- Data collection, clinical examination, revision of the manuscript, coordination, and result interpretation

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Source of Support: Nil, Conflicts of Interest: None declared.