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A study of Sociodemographic factors, Clinical variables and Insight in patients with Treatment Resistant Schizophrenia.

Dr Shubhangi Singh[1], Dr Vikas Gaur[2]

1) Senior Resident , Department of psychiatry ,Patna Medical college and Hospital
2) HOD, Department of Psychiatry ,Mahatma Gandhi university of Medical sciences.

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I. Introduction

Schizophrenia is a very severe and disabling mental illness with an average prevalence of about 0.5 to 1.0 percent of the population in the world, and it contributes considerably to the burden of this disease.[1,2] There is a 2 to 3 fold increase in mortality risk as compared to the general population in patients with schizophrenia[3]. The annual incidence rate in India is 3.8-4.4 per ten thousand people.[4]

Schizophrenia is a disorder with multiple and complex etiology, and includes patients with varied clinical presentation, response to treatment and course of illness. Signs and symptoms can include changes in thought process, perception, cognition, behavior and affect.

According to Lindenmayer, up to one third of patients of schizophrenia continue to experience distressing disturbances in perception like delusions and hallucinations, thought disturbances and functional impairment, despite significant scientific and therapeutic progress.[5]

Treatment resistant schizophrenia (TRS) is an inadequate response to a succession of treatment in a patient of schizophrenia. The prevalence of TRS is has been found to be 30-50% in patients with the diagnosis of schizophrenia but even higher rates have been mentioned by some authors.[6]

TRS is present if the patient fulfills the following 3 criteria which are modified from those of Kane et al (1988) to be useful in everyday clinical practice:[7]

1) No period of good functioning in previous 5 years;
2) Previous non-response to at least 2 antipsychotic drugs of two different 400 mg equivalents of chemical classes for at least 4-6 weeks each at doses of chlorpromazine or 5 mg/day of risperidone;
3) Moderate to severe psychopathology, especially positive symptoms like conceptual disorganization, suspiciousness, delusions or hallucinatory behavior.

The large number and variety of risk factors associated with poor prognosis or poor response to treatment, reported in the literature, suggest that several pathophysiological mechanisms may contribute to the emergence of resistance. Epidemiological data reveal that the following have been associated with increased risk of treatment refractoriness.[8]

1. Male gender
2. Early age of onset
3. Positive family history
4. Absence of affective symptoms
5. Severe and lengthy premorbid manifestations
6. Longer duration of untreated psychosis
7. Low level of social functioning.

Most of the patients with psychotic disorders have poor insight. These patients appear to deny or fail to acknowledge that their symptoms are due to mental disorder.[9]

Broadly, Insight includes, awareness of mental illness (clinical insight), self-certainty about beliefs (Cognitive insight), and awareness of neuropsychological impairment (Neurocognitive Insight).
In this paper, we aim to study the sociodemographic factors, various risk factors associated and study the cognitive and clinical insight in with patients of Treatment resistant schizophrenia .

II. Materials And Methods

This study was an observational cross-sectional study conducted at Mahatma Gandhi Medical College and Hospital, a tertiary care hospital in Jaipur from January 2016 to March 2018.

The study protocol was approved by Ethics committee of Mahatma Gandhi Hospital.

SAMPLE POPULATION AND CHARACTERISTICS

65 consecutive patients of treatment resistant schizophrenia meeting the diagnostic criteria for Treatment Resistant Schizophrenia (TRS), who were attending Psychiatric Outpatient Department of Mahatma Gandhi Hospital (OPD), and fulfilling the inclusion and exclusion criteria were recruited for the study, by convenience sampling method.

INCLUSION CRITERIA

1. In age group: 18 to 65 years.
2. Sex: Males and Females.
3. Diagnosed as a case of Treatment Resistant Schizophrenia (TRS) by two senior consultant psychiatrists of Psychiatry Department at Mahatma Gandhi Hospital.

EXCLUSION CRITERIA

1) Age :>65 and <18.
2) History of significant head injury.
3) Patients who were unwilling to perform test and those who were unable to perform test other than disability.
4) Intellectual disability
5) Patient meeting criteria for drug dependence and addiction.

Consent form formatted in Hindi language and was given to all participants of the study. Semi structured questionnaire for interview was designed to obtain details such as socio-demographic status, illness variables like age of onset, family history, number of hospitalizations and medical comorbidity.

Positive and negative syndrome scale was used to assess the severity of the psychopathology, to subgroup the patients in predominantly positive and negative subtype and the item G12 on general psychopathology scale was taken in consideration in this study for assessment of clinical insight in the patients and was compared with the various indices of Beck's Cognitive Insight Scale(BCIS) for co-relation between clinical and cognitive insight.

Cognitive insight was measured with the **Beck Cognitive Insight Scale (Beck et al., 2004)**, a 15-item self-report questionnaire that assesses both self-reflectiveness and self-certainty. Items that comprise the self-reflectiveness (SR) subscale measure objectivity, reflectiveness, and openness to feedback (e.g., "At times I have misunderstood other people's attitudes towards me," "Some of my experiences that have seemed very real may have been due to my imagination". The self-certainty (SC) subscale assesses decision-making and dogmatic certainty about beliefs and conclusions (e.g., "I know better than anyone else what my problems are," "I cannot trust other people's opinion about my experiences")

A composite index score (SR-SC index) is calculated by subtracting the self-certainty total from the self-reflectiveness total and is used as the principal indicator of cognitive insight. The possible score range of the BCIS SR-SC index is -18 through 27; higher scores indicate better cognitive insight.

III. Results

The mean age of the sample was 36.40. There were 45 (72.31 %) males and 18 females (27.69%)in our study. The maximum number of treatment resistant patient was in the age group of 31-45 years (28 patients, 43%). (Table 1). About 84% were married and Maximum number of patients in our study had received secondary education.(40.00%). The number of patients who were admitted less than 5 times owing to their illness were 54 and those admitted greater than 5 times were 11. The percentages were 83.08% and 16.92 respectively. The total number of cases with positive family history were 31 and with no family history of schizophrenia were 34 with 47.69% and 52.31% respectively. The number of cases with comorbid medical conditions were 29 with a total percentage of 44.62% and the number of cases without any medical comorbidity were 36 and their percentage was 55.38%.

The mean score of PANSS positive subscale was 19.60 while the standard deviation was 7.44. The mean score of negative subscale score was 19.66 while the standard deviation was 8.60. The mean and standard deviation of G12 PANSS item was 3.17 and 1.17 respectively. The mean and standard deviation of BCIS-SR subscale was 12.71 and 4.73 while the mean and standard deviation of BCIS-SC subscale was 7.32 and 3.17.

The correlation coefficient between G12 PANSS Insight item and BCIS-SR was –0.4408. The p value was 0.0002 and was statistically significant. The correlation coefficient between G12 PANSS Insight item and BCIS-SC was 0.3691. The p value was 0.0024 and was statistically significant. The correlation coefficient between the BCIS-SR and the BCIS-SC was 0.7606. The p value was statistically significant (p= 0.0001)

IV. Discussion

In our study, the mean age of the sample was 36.40. The maximum number of treatment resistant patient was in the age group of 31-45 years (28 patients, 43%). (Table 1)

Males participants clearly outnumbered females in the study group. (Table 2) According to various studies, male gender is associated with poor prognosis because of poor response to neuroleptics agents in comparison to females and this could be the reason behind less number of female participants in our study. Our study results are consistent with previous studies. [10,11,12]

Early age of onset has been found to be associated with greater dysfunction, with poor response to neuroleptics, increased risk of re-hospitalization and specifically to the treatment resistance. Majority of patients in our study had onset of illness in the range of 21 to 30 years. (Table 3) and our finding are similar to few other studies.[13,14]

Most of the subjects in our study were married. (Table 4), (56.92%) belonged to urban background. (Table 5) and around 40% had received Secondary level education.(Table 6) The result of our study were similar to Kamble K. et al.[15]

It is a common assumption that a Treatment Resistant Schizophrenic may have a history of multiple hospitalizations due to his or her illness, and previous studies have also tried to find out a relationship between total number of rehospitalisation and Treatment resistant Schizophrenia but were inconclusive. Factors such as poor treatment compliance, poor social support or a history of violence can be a reason for multiple hospitalizations in a Schizophrenic patient irrespective of whether he is a treatment responder or treatment resistant.[15] One interesting finding in our study was that around 83% (Table 7) cases were hospitalized less than 5 times in their life time owing to their illness while the remaining patients had been hospitalized multiple times and it is likely that in addition to the reasons mentioned above, majority of these patients illness was not severe enough thus requiring hospitalization.

The presence of family history of schizophrenia has been postulated to be a poor prognostic factor.In this study, 47% of patients had family history of schizophrenia (Table 8). Similar results were also reported in one similar study done by Kamble K. et al.[15]

It has been reported that patients with severe mental illness like schizophrenia are more prone to physical illness as reported by few authors Maj,M. et. al.[16] ,De Hert M et .al.[17] Caroline P. Carney et.al.[18]The number of cases with medical comorbidities in our sample were 29(44.62%). (Table 9). Our results were consistent with the findings of the above mentioned studies.

In our study, majority of cases had the Total duration of Illness of more than 15 years (38.46%) followed by 29.23% patients with TDI between 6 -10 years.(Table 10)

The clinical insight was calculated by the G12 PANSS item and the mean score was 3.17 with a standard deviation of 1.17. (Table 21). Our study result was similar to that of M.A. Cooke et al.[19]

The BCIS-SR mean score (12.71) in our study sample correlated to the results of various other studies. (Table 21). Similar findings were reported in the study by Pedrelli et. al.[20](BCIS-SR =12.5), and Beck et. al.[21](BCIS-SR = 13.0). The results of our study were less than that observed in the study by Bora et.al [22](BCIS-SR = 15.3). The mean BCIS-SC score in our study was 7.32. (Table 21) It was similar to the studies by Pedrelli et. al.[20](BCIS-SC =7.2), and Beck et.al. [21] (BCIS-SC = 7.9).

According to literature, individuals with active psychopathology would have high score on the Self-Certainty subscale and lower score on the self-reflectiveness subscale.[23]

V. Conclusion

TRS has highly variable presentation and course, and patients with TRS are very heterogeneous group. According to current knowledge and clinical practice, TRS is difficult to treat. With respect to sociodemo graphic factors we found the following:

a) Males clearly outnumbered females in our study.
b) Early age of onset was seen in patients of TRS in our study.
c) Most of the subjects were married in our study.
d) A positive family history of schizophrenia is a risk factor for TRS.

e) Patients with severe mental illness like schizophrenia are more prone to physical illness as well.

Poor clinical insight (i.e. insight of illness) is considered a characteristic feature of schizophrenia, and it is important factor for determining prognosis, as well as for prescribing appropriate treatment and management. The PANSS G12 insight item was modestly correlated with both BCIS dimensions: positively for self-certainty and negatively for self-reflectiveness. Both correlations were in the expected direction, with higher PANSS G12 item scores (poorer clinical insight) associated with scores indicating poorer cognitive insight (higher self-certainty and lower self-reflectiveness).

To conclude in spite of 60 years of psychopharmacology, Treatment Resistant Schizophrenia remains an enormous challenge. The etiology of TRS appears to be heterogeneous, complex and poorly investigated. Cognitive insight can help the patient in better understanding of his own psychotic experiences and erroneous beliefs. Assessing Cognitive insight is of potential importance, as a mediator of response to cognitive behavior therapy and increase in cognitive insight could be associated with reduction in positive, negative and general symptomatology in patients with Treatment resistant schizophrenia.

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