

Research report

FACTORS INFLUENCING RELAPSE IN PATIENTS WITH SCHIZOPHRENIA

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ABSTRACT

Introduction: Relapse is a major factor for disability and poor quality of life in patients with schizophrenia. Several factors contribute to the relapse of symptoms in schizophrenia. Studying the modifiable factors helps in planning relapse prevention strategies. **Aims:** The study aimed to assess the factors influencing relapse among patients with schizophrenia. The study focused on selected modifiable factors such as stressful life events, perceived stress, expressed emotion, drug compliance and perceived stigma. **Methods:** A comparative design was used for this study. Tools used for data collection included a semi-structured interview schedule, Life Change Index Scale, Perceived Stress Scale, Medication Adherence Rating Scale, Family Emotional Involvement and Criticism Scale and STIG-9 questionnaire. Purposive sampling technique was used. The sample consisted of two groups of patients with schizophrenia, 50 patients in relapse and another group of 50 patients in remission. **Results:** The two groups were comparable in terms of socio-demographic and clinical variables, except for history of substance use. The mean (Standard deviation) scores of stressful life events were higher for the relapse group [159.82 (53.87)] compared to controls [114.42 (30.98), $p < 0.001$]; so also, for perceived stress [12.40 (3.54) and 7.26 (2.93), $p < 0.0001$]; expressed emotion [27.36 (6.19) and 17.24 (5.64), $p < 0.001$]; poor drug compliance [3.78 (1.94) and 7.60 (1.67), $p < 0.001$], perceived stigma [14.46 (3.53) and 12.38 (3.28), $p = 0.003$]. **Conclusion:** Knowledge of factors that contribute to relapse in schizophrenia will help mental health service providers to improve the standards of care. Interventions in schizophrenia should specifically target relapse prevention and improved quality of life.

Key words: Relapse, schizophrenia, risk factors

INTRODUCTION

Mental health problems are common in Kerala and an estimated 12.43% of the adult population is affected by mental health conditions.¹ The prevalence of mental health disorders in the state has been increasing over the years. Schizophrenia is a psychotic condition characterized by disturbance in

thinking, emotions and perception in presence of clear consciousness.² Prevalence of schizophrenia in Kerala is estimated to be 1.3%, affecting men and women alike, irrespective of social status.³ In the early course of schizophrenia, relapse prevention is of paramount importance. Schizophrenia patients can achieve both symptom remission and

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recovery in the early course of illness.⁴ Potential predictors of relapse in schizophrenia include demographic and clinical variables.⁵ A study on socio-demographic and clinical factors associated with relapse in schizophrenia suggests that the severity of illness, psychological stress and treatment-related issues like side-effects of medicines are related to relapse in schizophrenia.⁶ Influence of expressed emotion (EE) has been found to be one of the important predictors of relapse in schizophrenia.⁷ Similarly, a study on factors affecting relapse in schizophrenia revealed that irregularity in follow-up, presence of affective symptoms, self-neglect and lack of social contacts are risk factors for relapse in schizophrenia and it is important to recognize these factors in order to prevent relapses in schizophrenia.⁸ Another study about understanding family functioning and social support in unremitting schizophrenia has explained that patients with schizophrenia perceived more social support from friends than from their families. Providing better social support and understanding the family functioning will result in strengthening the family as a unit, so as to provide better care to the patient.⁹

Relapse in schizophrenia is associated with a longer time to response, development of negative symptoms, resistance to treatment and structural brain changes.¹⁰ Preventing relapse after recovering from an episode is critical as relapse is associated with an increased risk of clinical and functional deterioration.¹¹ Identifying the symptoms of relapse at an early stage can prevent the worsening of psychotic symptoms and can reduce morbidity. Knowledge regarding the modifiable factors will help to prevent relapse among patients with schizophrenia. There is a felt need to identify the factors influencing relapse among patients with schizophrenia. The purpose of this study was to find out the major factors that influence relapse among patients with schizophrenia after being treated and

discharged from psychiatric hospitals. This study examined the modifiable risk factors such as stressful life events, perceived stress, EE, medication adherence, perceived stigma and substance use. The objective of the study was to compare two groups of patients with schizophrenia, in relapse and in remission, to examine selected risk factors for relapse.

MATERIALS AND METHODS

A descriptive, comparative design was employed to answer the research question. The study was approved by the Institutional Ethics Committee, and administrative permission was obtained from the concerned authorities. Written informed consent was obtained from individual patients and their caregivers. Patients were recruited after consultation with the treating psychiatrist. The study was conducted at Government Mental Health Centre, Kozhikode, and Government Medical College Hospital, Kozhikode, Kerala. The total bed strength of these two tertiary care psychiatric care facilities is around 550. Individuals who were diagnosed as having schizophrenia, according to the ICD-10 Classification of Mental and Behavioural Disorders, Diagnostic Criteria for Research (ICD-10 DCR)¹² by the treating psychiatrist, were included. The study included two groups with 50 patients each, in the relapse and remission stages of schizophrenia. Empirically, the sample size was fixed at 50 for each group. The relapse group included patients with schizophrenia who were currently symptomatic, attending the outpatient clinic or were admitted. The remission group included a group of 50 patients who were in remission. Remission refers to the state of absence or reduction in disease symptoms for a minimum period of two months in patients who had an episode of schizophrenia diagnosed by the treating psychiatrist as per ICD-10 DCR criteria.¹² Patients having a grade 3 insight on standard mental status examination and those who can give response to questionnaires were included in the study. Exclusion criteria

included first-episode schizophrenia, significant disorganization, co-morbid intellectual disability, substance use disorders and cognitive impairment. Information was obtained from the patient and caregivers, as well as by reviewing patient records. Factors that change the course of schizophrenia and contribute to relapse were measured.

Stressful life events were measured with Life Change Index Scale, which is a 51-item scale with specific scores for each item to measure the stressful life events experienced by the individual in the last year.¹³ Perceived Stress Scale (PSS-4), a four-item self-report questionnaire was used for measuring psychological distress.¹⁴ The tool is available in the public domain. Expressed emotion was measured by the modified form of Family Emotional Involvement and Criticism Scale (FEICS),¹⁵ which is a 14-item, self-report 5-point scale (0-4). FEICS have two subscales, Perceived Criticism (PC) and Emotional Overinvolvement (EOI).¹⁵ The responses to items were graded on a 0 to 4 scale. Drug compliance was measured using Medication Adherence Rating Scale (MARS), a 10-item scale.¹⁶ Total scores on the MARS range between 0 and 10, with a higher score indicating better medication adherence.¹⁷ Permission was obtained from the authors for using and modifying this tool for this study.

Perceived stigma was measured using STIG-9 questionnaire. STIG-9 is a free, open-source, self-reported questionnaire used to measure perceived mental illness stigma.¹⁸ It is measured on a 4-point Likert scale with a total score ranging from 0 to 27. The tool is in the public domain for academic use. Socio-personal variables in this study included gender, religion, occupation, educational status, economic status and place of residence.

Clinical variables such as the age of onset of illness, duration of illness, number of hospitalizations and history of recent substance use were measured using an interview schedule prepared for this study. The conceptual

framework used for this study was based on a modified version of the vulnerability/stress model of schizophrenic relapse by Neuchterlein and Dawson et al.¹⁹

Content validity of the interview schedule for collecting socio-personal and clinical variables was established by experts from the field. The reliability and validity of the tools, Life Change Index Scale, PSS-4, FEICS, MARS, and STIG-9 have been established and represented in various studies.¹³⁻¹⁸ PC subscale and EOI subscale of FEICS showed stable item structure and reliability. Cronbach's alpha for PC was 0.82 and for EOI was 0.76. The Cronbach's alpha was 0.70 for PSS-4 and 0.65 for MARS. STIG-9 questionnaire was found to have excellent item and scale characteristics, high internal consistency and validity.¹³⁻¹⁸ The tools were translated into Malayalam and language validity was established.

RESULTS

Analysis of socio-personal and clinical variables showed that the two groups were comparable on variables such as age, religion, marital status, type of family, residence, age of onset of illness and duration of illness. (Tables 1 & 2). In the relapse group, 62.0% (n=31) and in the control group, 54.0% (n=27) had three or more hospitalizations; whereas 38.0% (n=19) in the relapse group and 46% (n=23) in the control group had two or fewer hospitalizations ($\chi^2 = 0.54$, $p = 0.27$). There was an equal number of male and female participants in both groups. The two groups were significantly different in the history of substance use ($\chi^2 = 5.26$; $p = 0.02$). Among the 19 participants who reported substance use in the recent past, 14 (73.7%) belonged to the relapse group in comparison to the 5 (26.3%) in the remission group.

Risk factors for relapse investigated in this study were stressful life events, perceived stress, EE, medication adherence, and perceived stigma (Table 3). Results showed a significantly high score on Life Change Index Scale in the relapse group [159.82, Standard deviation (SD)

Table 1: Sample characteristics of patients with schizophrenia

Characteristics	Category	Relapse group (n ₁ =50) F (%)	Remission group (n ₂ =50) F (%)	Chi-square value (df)/ FE test	p-value
Age	21-30	12 (24.0)	12 (24.0)	0.47 (3)	0.93
	31-40	17 (34.0)	17 (34.0)		
	41-50	16 (32.0)	14 (28.0)		
	51-60	5 (10.0)	7 (14.0)		
†Religion	Hindu	28 (56.0)	33 (66.0)	4.24 (2)	0.31
	Muslim	22 (44.0)	16 (32.0)		
	Christian	0 (0.0)	1 (2.0)		
Marital status	Unmarried	7 (14.0)	15 (30.0)	1.26 (1)	0.53
	Married	28 (56.0)	20 (40.0)		
	Widow/Divorced/ Separated	15 (30.0)	15 (30.0)		
Type of family	Nuclear	24 (48.0)	26 (52.0)	3.51 (1)	0.06
	Joint	26 (52.0)	24 (48.0)		
Residence	Rural	42 (84.0)	34 (68.0)	8 (16.0)	16 (32.0)
	Urban	8 (16.0)	16 (32.0)		

* - Significant at 0.05 level, † - FE test applied, df - degrees of freedom, FE test - Fisher's exact test

= 53.87)] in comparison to the remission group (114.42, SD = 30.98) ($p < 0.001$). Similarly, FEICS total score was significantly high in the relapse group (27.36, SD = 6.19) than in the remission group (17.24, SD = 5.64) ($p < 0.001$).

FEICS-subscale scores, PC (relapse group - 15.12, SD = 4; remission group - 6.76 SD = 4.65; $p < 0.001$) and EOI (relapse group - 11.84, SD = 2.58; remission group - 10.48, SD = 1.97; $p = 0.004$) were also significantly high in the relapse group. Comparison of MARS scores showed a significantly low score in the relapse group (3.78, SD = 1.67) in comparison to the remission group (7.6, SD = 1.94), which was statistically significant ($p < 0.001$).

Psychological distress measured on PSS shows significantly high scores in the relapse group (12.40, SD = 3.54) compared to the remission group - 7.26 (SD = 2.93) ($p < 0.001$). Results also show that perceived stigma scores were significantly high ($p = 0.003$) in the relapse group (14.46, SD = 3.54) than in the remission group (12.38, SD = 3.28). The effect size (Cohen's d) for these variables was calculated and found to be moderate to large (Table 3).

DISCUSSION

Several factors have been studied as possible reasons for relapse in schizophrenia, affecting the outcome seriously. Most patients with schizophrenia experience multiple relapses.²⁰ We compared factors such as stressful life events, perceived stress, EE, medication adherence and perceived stigma between two groups of schizophrenia patients, with relapse and remission. The groups were statistically comparable on socio-personal and clinical variables, except on history of substance use. We found that a significantly high proportion of participants in the relapse group had a history of substance use in the recent past. Several studies have reported that substance use is a strong predictor of relapse in schizophrenia, particularly in male patients.²¹⁻²²

This study found that stressful life events were significantly high among the relapse group. It is a recognized fact that stress plays a key role in the pathophysiology of schizophrenia and there is a considerable increase in stress among patients compared to healthy volunteers.²³ Previous studies have reported the significance of stressful life events, along with other factors,

Table 2: Comparison of groups based on clinical variables

Variable	Relapse group Mean (SD) n ₁ =50	Remission group Mean (SD) n ₂ =50	t-value (df = 98)	p-value
Age of onset of illness in years	23.98 (5.84)	24.48 (7.14)	0.38	0.70
Duration of illness in years	13.52 (8.46)	14.9 (8.81)	0.80	0.42

* - Significant at 0.05 level, *df* – degrees of freedom, SD – standard deviation

Table 3: Comparison of groups based on the study variables

Variable	Relapse group Mean (SD) n ₁ =50	Remission group Mean (SD) n ₂ =50	t-value (df = 98)	p-value	Cohen's <i>d</i>
*Life Change Index Scale	159.82 (53.87)	114.42 (30.98)	5.17	<0.001	1.03
*Family Emotional Involvement and Criticism Scale (FEICS)	27.36 (6.19)	17.24 (5.64)	8.55	<0.001	1.71
*Perceived Criticism (FEICS –Subscale)	15.12 (4.00)	6.76 (4.65)	9.64	<0.001	1.93
*Emotional Over-involvement (FEICS- Subscale)	11.84 (2.58)	10.48 (1.97)	2.96	0.004	0.59
*Medication Adherence Rating Scale (MARS)	3.78 (1.94)	7.60 (1.67)	10.56	<0.001	2.1
*Perceived Stress Scale	12.40 (3.54)	7.26 (2.93)	7.91	<0.001	1.58
*Perceived Stigma Questionnaire (STIG-9)	14.46 (3.53)	12.38 (3.28)	3.05	0.003	0.61

* - Significant at 0.01 level, *df* – degrees of freedom, SD – standard deviation

as predictors of relapse in patients with schizophrenia.²⁴ Stressful events are often beyond the patient's or caregivers' control to prevent their occurrence. Stress-management interventions, with psychoeducation and relaxation techniques integrated into treatment plans of patients with mental disorders, have been found to be effective in reducing objective and subjective stress and improving psychological health.²⁵

EE, an adverse family environment, is one of the robust predictors of relapse in schizophrenia.²⁶ Our study found that EE, as well as its components, perceived criticism and emotional over-involvement, were also significantly high among the relapse group in comparison to the remission group. EE is one of the major psychosocial stressors and it has a direct association with the recurrence of the illness.²⁶ Perceived Criticism, refers to the

increased tone, tempo, and volume of communication of caregivers that occurs when the patient frustrates them. It was found that 70% of critical comments were found to focus on the negative symptoms of schizophrenia rather than on the florid symptoms of delusions and hallucinations.²⁶

Adherence to medication is one of the essential factors in deciding the outcome of schizophrenia. Generally, medication adherence in schizophrenia is poor.²⁷ Medication non-adherence in schizophrenia may be due to factors such as lack of insight, psychopathology, stigma, substance use disorder and cultural and socioeconomic status.²⁸ Impaired insight has been strongly linked to antipsychotic medication non-adherence, and interventions to enhance insight early during treatment are important.²⁹ Our study has found a significantly low

medication adherence score in the relapse group in comparison to the remission group. If medication adherence is addressed appropriately, relapse in schizophrenia can be reduced. Reasons for poor medication adherence in schizophrenia include patients' negative attitude toward their medication.³⁰ Psychoeducation of the patients and relatives based on the principles outlined in the Clinical Practice Guidelines by the Indian Psychiatric Society may provide insight into the illness and need for medication which in turn promotes recovery.³¹

Perceived stigma in schizophrenia is considered a modifiable environmental risk factor that influences the course of illness. Our study has found significantly high perceived stigma scores in patients with relapse of schizophrenia. Stigma is a clinical risk factor and barrier to outcome in schizophrenia and the response to stigma needs to be individually tailored for clinical practices.³² Dealing with the perceived stigma associated with mental illness helps in improved medication adherence and ultimately affects the course of illness.³³

Conclusions

Relapse is a critical negative event in schizophrenia as it is associated with significant clinical and functional deterioration. Understanding the factors associated with relapse prepares mental health professionals to deal with modifiable factors. In this study, two groups of patients, 50 patients in relapse and 50 patients in remission state of schizophrenia were compared to understand the factors contributing to the relapse. It is concluded that factors such as adverse life events, perceived stress, high family levels of EE, poor medication compliance and perceived stigma as well as substance use contribute to relapse in schizophrenia. A broader approach in management targeting these factors may improve the quality of life of patients with schizophrenia, and the relationship may be investigated in the future.

Strengths and limitations

This study did not look into the multivariate nature of the factors that contribute to relapse and their interaction effects. Despite the limitations, this study contributes to the understanding of the important issue of relapse in schizophrenia.

Conflict of interests

Nil

REFERENCES

1. Shaji KS, Raju D, Sathesh V, Krishnakumar P, Punnoose VP, Kiran PS, et al. Psychiatric morbidity in the community: A population based-study from Kerala. *Indian J Psychiatry* 2017;59:149-56.
2. Patel KR, Cherian J, Gohil K, Atkinson D. Schizophrenia: overview and treatment options. *P T* 2014;39:638-45.
3. India State-Level Disease Burden Initiative Mental Disorders Collaborators. The burden of mental disorders across the states of India: the Global Burden of Disease Study 1990-2017. *Lancet Psychiatry* 2020;7:148-61.
4. Ventura J, Subotnik KL, Guzik LH, Helleman GS, Gitlin MJ, Wood RC, et al. Remission and recovery during the first outpatient year of the early course of schizophrenia. *Schizophr Res* 2011;132:18-23.
5. Brown E, O'Donoghue B. T238. Rates and predictors of relapse in an Australian first episode psychosis cohort. *Schizophr Bull* 2020;46(Suppl 1):S323.
6. Chabungbam G, Avasthi A, Sharan P. Socio-demographic and clinical factors associated with relapse in schizophrenia. *Psychiatry Clin Neurosci* 2007; 61:587-93.
7. Amaresha AC, Venketasubramanian G. Expressed emotions in schizophrenia: An overview. *Indian J Psychol Med* 2012;34:12-20.
8. Rajkumar S, Thara R. Factors affecting relapse in schizophrenia. *Schizophr Res* 1989;2:403-09.

9. Sawant NS, Jethwani KS. Understanding family functioning and social support in unremitting schizophrenia: A study in India. *Indian J Psychiatry* 2010;52:145-9.
10. Emsley R, Chiliza B, Asmal L. The evidence for illness progression after relapse in schizophrenia. *Schizophr Res* 2013;148:117-21.
11. Pelayo-Terán JM, Gajardo VGG, de la Ortiz-García de la Foz V, Martínez-García O, Tabarés-Seisdedos R, Crespo-Facorro B, et al. Rates and predictors of relapse in first-episode non-affective psychosis: a 3-year longitudinal study in a specialized intervention program (PAFIP). *Eur Arch Psychiatry Clin Neurosci* 2017;267:315-23.
12. World Health Organization. The ICD-10 classification of mental and behavioural disorders: diagnostic criteria for research.. Geneva: WHO; 1993.
13. Holmes TH, Rahe RH. The Social Readjustment Rating Scale. *J Psychosom Res* 1967;11:213-21.
14. Cohen S, Williamson G. Perceived stress in a probability sample of the United States. In: Spacapan S, Oskamp S (Eds). *The social psychology of health. The Claremont symposium on applied social psychology.* 1988. CA: Sage publications. Pp. 31-67.
15. Shields CG, Frank P, Harp JJ, McDaniel SH, Campbell TJ . Development of the Family Emotional Involvement and Criticism Scale (FEICS): A self-report scale to measure expressed emotion. *J Marital Fam Ther* 1992;18:395-407.
16. Thompson K, Kulkarni J, Sergejew AA. Reliability and validity of a new Medication Adherence Rating Scale (MARS) for the psychoses. *Schizophr Res* 2000;42:241-7.
17. Owie GO, Olotu SO, James BO. Reliability and validity of the Medication Adherence Rating Scale in a cohort of patients with schizophrenia from Nigeria. *Trends Psychiatry Psychother* 2018;40:85-92.
18. Gierk B, Löwe B, Murray AM, Kohlmann S. Assessment of perceived mental health-related stigma: The Stigma-9 Questionnaire (STIG-9). *Psychiatry Res* 2018;270:822-30.
19. Nuechterlein KH, Dawson ME, Ventura J, Gitlin M, Subotnik KL, Snyder KS, et al. The vulnerability-stress model of schizophrenic relapse: A longitudinal study. *Acta Psychiatr Scand* 1994;89(S382): 58-64.
20. Lauriello J. Prevalence and impact of relapse in patients with schizophrenia. *J Clin Psychiatry* 2020;81(1): MS19053BR1C.
21. Ayuso-Gutiérrez JL, del Río Vega JM. Factors influencing relapse in the long-term course of schizophrenia. *Schizophr Res* 1997 19;28:199-206.
22. Olivares JM, Sermon J, Hemels M, Schreiner A. Definitions and drivers of relapse in patients with schizophrenia: a systematic literature review. *Ann Gen Psychiatry* 2013;12:32.
23. Betensky JD, Robinson DG, Gunduz-Bruce H, Sevy S, Lencz T, Kane JM, et al. Patterns of stress in schizophrenia. *Psychiatry Res* 2008;160:38-46.
24. Lauriello J. Prevalence and impact of relapse in patients with schizophrenia. *J Clin Psychiatry* 2020;81(2): MS19053BR1C.
25. Klainin-Yobas P, Ignacio J, He HG, Lau Y, Ngooi BX, Koh SQD. Effects of a stress-management program for inpatients with mental disorders: a feasibility study. *Biol Res Nurs* 2016;18:213-20.
26. Amaresha AC, Venkatasubramanian G. Expressed emotion in schizophrenia: an overview. *Indian J Psychol Med* 2012;34:12-20.
27. Razali SM, Yusoff MZAM. Medication adherence in schizophrenia: a comparison between outpatients and relapse cases. *East Asian Arch Psychiatry* 2014;24:68-74.
28. Phan SV. Medication adherence in patients with schizophrenia. *Int J Psychiatry Med* 2016;51:211-9.
29. Kim J, Ozzoude M, Nakajima S, Shah P, Caravaggio F, Iwata Y, et al. Insight and medication adherence in schizophrenia: An analysis of the CATIE trial. *Neuropharmacology* 2020;168:107634.
30. Bäuml J, Froböse T, Kraemer S, Rentrop M,

- Pitschel-Walz G. Psychoeducation: a basic psychotherapeutic intervention for patients with schizophrenia and their families. *Schizophr Bull* 2006;32 (Suppl 1):S1-S9.
31. Sarkhel S, Singh OP, Arora M. Clinical practice guidelines for psychoeducation in psychiatric disorders general principles of psychoeducation. *Indian J Psychiatry* 2020;62(Suppl 2):S319-S323.
32. Shrivastava A, Bureau Y, Rewari N, Johnston M. Clinical risk of stigma and discrimination of mental illnesses: Need for objective assessment and quantification. *Indian J Psychiatry* 2013;55:178-82.
33. Sirey JA, Bruce ML, Alexopoulos GS, Perlick DA, Friedman SJ, Meyers BS. Stigma as a barrier to recovery: Perceived stigma and patient-rated severity of illness as predictors of antidepressant drug adherence. *Psychiatr Serv* 2001;52:1615-20.